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SHARING KNOWLEDGE EMPOWERING CARE

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EDITORIAL TEAM

FROM THE EDITOR-IN-CHIEF'S DESK

Our first issue of Manipal Medical Journal was launched on 18 August, 2020 and we had planned to make our next issue a "COVID Special". At that time many of our colleagues were skeptical about the relevance of COVID by December. As it happens, it is the burning topic as numbers have increased with the ongoing festive season, more mobility of people, the North India's winter chill and a general casualness in people with respect to wearing masks & maintaining social distancing.

Thus, our COVID special issue has great impact since most of the articles reflect the experience of different specialties in handling this pandemic. A good number of consultants from Manipal Hospital Jaipur have joined our Department of Academics & Research and we are extremely happy to have two of them on our Editorial Team. More power to us!

This issue also contains human interest stories "My Tryst with COVID" wherein some of us have recollected our experience with COVID infection & our journey to recovery. I also joined their ranks recently and have realized that it is one of the most unpredictable & dangerous viruses for which even now we have no set protocol worldwide. Since March the pandemic has been evolving and the numbers are worrisome and the changes in drug treatment & testing strategies have seen a sea change as the months have gone by.

As Health Care Workers we have never had the luxury of working from home & have been at the forefront tackling suspected, Non-COVID & COVID patients. This issue of Manipal Medical Journal is special and in a way symbolizes the year 2020. On a positive note two of our Physician Assistants cleared their final exams from MAHE (Manipal Academy of Heigher Education). This was the first batch of PA'S from Manipal Hospital Delhi so this was special.

I thank Mr. Pramod Alagharu, Regional COO, Manipal Hospitals for enthusiastically supporting this special issue and Mr. Raman Bhaskar, Hospital Director who has always patiently solved our problems.

Thanking our Patron & Chief of Clinical Services, Dr. Yugal K Mishra for his active support and encouragement. Dr (Lt Gen) C S Narayanan VSM , HOD Neurology & patron for active involvement in the journal.

My special thanks to the Editorial Team for their noteworthy contributions that have built up this issue. My Editor Dr. Vikas Taneja who is ever active, supportive, enthusiastic & super-efficient! Great to have you in my team.

My associate Editors Dr. Kunal Das & Dr. Peush Bajpai who have come out with novel ideas to enrich the journal and have always given constructive suggestions.

Thanks to Dr. Prashant Vashishth & Dr. Ashu Singal for being supportive as always.

Our creative team of Mr. Abhishek Mishra & Ms. Rituparna Roy who are as excited as us about the COVID special issue!

Last but not the least Dr. Sakshi Bhardwaj, our Academic Coordinator who has coordinated all activities superbly & kept us all well connected.

Stay safe & happy reading!!

Dr (Lt Col) Leena N Sreedhar
Editor-in-Chief Manipal Medical Journal

MESSAGE FROM THE CEO

Dear friend,

I take this opportunity to wish you a very happy and healthy New Year – 2021. Your contribution to making our hospital a world-class health institution is enormous and I appreciate your commitment.

Indeed, we all were grossly engaged in our routine services with our expertise and experience to maintain excellence in our Centres of Excellence till the initial two months of the year. But when the global health crisis-COVID-19 hit us and an unprecedented lockdown was imposed to contain the virus, testing and tiring period began for all our doctors, paramedics, and teams from various departments of the Hospital. It was a time to collectively put our best to deal with the pandemic. It was immensely inspiring to witness the extraordinary efforts put by you as frontline warriors amidst such adversity.

As the pandemic unfolded, our Hospital responded with agility, resilience and compassion to adapt to the new normal and in the process, you went through all hardships. Some of our colleagues got infected as well. I respect and honour your commitment and sacrifice for selfless service rendered to the Hospital. With patients' care and safety being our top priority, it was vital for us to provide best-in-class services. It is very promising to note that with your support we have been delivering clinical outcomes that are on par with the global best centres. I am sure we will continue to maintain our excellence in each area of healthcare management and delivery.

Stay Safe and Healthy. Wish you a very Happy New Year.

Mr Pramod Alagharu,
CEO HCMCT Manipal Hospitals, Dwarka, New Delhi

MESSAGE FROM HOSPITAL DIRECTOR

First of all, I wish you a safe, healthy, and prosperous 2021 and appreciate your dedication & commitment to deal with the unprecedented challenges we all faced in 2020. With COVID-19, we witnessed enormous changes in our response and management and I am very proud to observe that each staff of the Hospital contributed significantly in this extraordinary circumstances.

The untamed spread of the COVID-19 virus, over the past 10 months, has caused unimaginable crisis across the globe. Never before, in recent history, have we encountered a challenge of this dimension that has so profoundly impacted almost every human on this planet. Hence, I would like to first express my deepest respect for our doctors, health care and other workers who have endured immense hardship to fight such a formidable battle. We had taken a resolution to provide extensive support to the distressed patients and we successfully took all urgent measures to provide them the best treatment and care. With your support we were also able to introduce several innovative measures to deal with the situation.

I am happy to note that you are committed to building a path to a healthier tomorrow for the patients who come to our hospital for treatment for any disease. And I hope to instill a disruptive approach we would enhance our adaptive capacity to deal with such challenges in the future as well.

There is no doubt that the task ahead will be daunting. The healthcare sector is at the cusp of transformation in terms of care and delivery. As we know people, process, and technology are the backbones of our hospitals, your hard work, expertise, experience, commitment and dedication would surely help us to attain a higher stage of advancement in providing our services to people.

Mr Raman Bhaskar,
Hospital Director
HCMCT Manipal Hospitals Dwarka, New Delhi

MESSAGE FROM THE EDITOR

We have been facing the COVID-19 pandemic for the last 9 months and the war seems unending. All of us as medical professionals are facing various challenges in handling this pandemic, whether it is our patients, ourselves or our families and loved ones. We have been fighting, day and night and will need to continue this till the end of this pandemic.

At this point it is important for us as healthcare professionals to keep ourselves updated of all the recent knowledge about the pandemic, be it different presentations across different specialties, management protocols, drugs being used or vaccines undergoing various phases of clinical trials. At this point, I am happy to announce our second issue of Manipal Medical Journal (MMJ), which is "COVID SPECIAL".

I feel proud to say that we have received some very informative and thought provoking articles related to COVID-19. This issue presents the amount and variety of work done across specialties during this pandemic, be it related to COVID-19 or not. I thank all the departments who have really worked hard and sent in their articles for this "COVID Special" issue. The enthusiasm has been great and this issue has 50% more articles as compared to the previous issue and also articles from our center at Jaipur.

My request to all the specialties to make a little effort to showcase the amount of good work they are doing, by sending their articles for the journal. Infact, I wish that this Journal in due course of time becomes the face of our institution. As the Editor, I feel honoured to say that the Department of Academics & Research, under the able leadership of Dr. Leena N Sreedhar is really putting in all the efforts to highlight the best clinical & academic work being carried out across various departments.

Our motto – "Sharing Knowledge, Empowering Care."

Dr. Vikas Taneja
Editor, Manipal Medical Journal

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Impact of COVID-19 Pandemic on Radiological Services – (Our Experience)

M.L. Bera
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ABSTRACT:

COVID-19 pandemic has created a horror within a short span of time and spread worldwide with approximately 39 million confirmed cases and more than one million deaths globally as on mid October 2020. India is also a major victim of this pandemic, but fortunate enough to face it a bit late compared to front runner countries like China, Italy and USA. This gave us an added advantage of getting time to study and understand the disease process and plan for effective preventive measures. Though COVID-19 outbreak started in December 2019 with worldwide spread, India experienced it with an increasing frequency in the month of March 2020, and accordingly first lockdown was imposed on 23rd March 2020 to prevent further spread of the disease.

As a result of the COVID-19 pandemic, radiology departments have experienced a rapid decline in imaging volumes & reduced revenue collection. This has important implications on the short-term & long-term economic stability of Radiology departments across all practice settings, particularly the private & start-up institutions. Frontline healthcare workers (HCWs) including radiology staff are more susceptible to COVID-19 infection due to their close proximity to patients & prolonged working hours. This review is aimed at summarizing the impact of COVID-19 pandemic on the departmental work flow, imaging volumes as well as physical, mental and behavioral health of health-care workers (HCWs) working in the Radiology department.

Keywords: Coronavirus Disease, COVID-19 Pandemic, Health-care workers (HCWs).

INTRODUCTION:

The Coronavirus disease (COVID-19) pandemic has made a profound impact worldwide. It is one of the serious public health crisis of this century and the most serious significant geopolitical event of our generation with significant impact on socio-demographic composition. The necessary state owned policy measures to overcome its spread and containment has resulted undesired downstream effects with detrimental effects on the economy and increase in unemployment. This has led to decrease in the health care spending nationwide with substantial loss of revenues to healthcare industry. The imaging services are also badly affected, more so the screening division (mammography, BMD, USG etc.) and more value added specialized investigations with higher reimbursement values like MRI, CT scan and interventional procedures. At the same time, a phenomenal increase in low reimbursement value services like X-rays has been noted, which are resource intensive investigations with lower revenue collection. These challenges have been more pronounced in private hospital-based facilities and Diagnostic Centers. In addition, this industry is experiencing substantial increase in expenditure from facility modifications and increased staffing to overcome the COVID-19 threat. For radiology set-ups, caring for patients with COVID-19 has increased the complexity of departmental operations with extra financial burden in the form of increased operational costs to support prevention & containment of the disease process. This includes cost for PPEs, masks, gloves, sanitizers, room sanitization process etc.

The reduction in demand for imaging services with net revenue loss has had substantial impact on private radiology practices, which are heavily dependent on examination volumes. Volumes in radiology have reduced by 60%-70%, varying from center to center and has gone beyond financial viability. Our hospital also experienced similar situation, but the hospital management has been able to ease out the financial brunt effectively. Though the volumes have started showing upward trend, indicating a short lasting phase, it is too early to predict how hospital business would shape up in future.

OUR EXPERIENCE:

This article analyzes factors and their impact on radiological services in light of the COVID-19 pandemic at the individual capacity in the context of non-binding self-restriction requests.

The impact of COVID-19 pandemic has been extensive with far reaching consequences. This has slowed down the economy worldwide, disrupted the socio-economical & geo-political structures and paralyzed the healthcare sector. Though the entire healthcare industry is badly affected, radiological services are one of the worst affected group. Imaging centers are also found to be vulnerable place for disease transmission, being a transit place for **COVID-19 positive patients,** non-COVID patients & healthy individuals and need special deliberation. In particular, this study focuses on the impact of COVID-19 pandemic on **(a) Work Flow, (b) Work Load** (work volume) and **(c) Work Force** (Frontline Workers in Radiology Dept.) based on the observed distribution of various factors (as applicable to the cause) on day-to-day performance basis as part of self-assessment of their impact on service quality.

a) Impact on Work Flow:

During lockdown starting 23rd March 2020 till first unlock on 01 Jun 2020, the movements were halted and the entire community was confined to indoor as part of state sponsored policy to contain the spread of

COVID-19. During this period, healthcare providers were instructed to avoid elective surgical procedures and conserve healthcare resources for care of COVID-19 patients. Furthermore, various guidelines were provided by ICMR and Centers for Disease Control (CDC) to reschedule non-urgent outpatient visits. The other factors included fear among general population to visit hospitals for minor ailments. This led to a sharp drop in radiological investigations during the lockdown period compared to non-COVID period.

b) Impact on Work Load:

Subsequent to various state sponsored and institutional public health policies to curb COVID-19 pandemic coupled with unemployment, socio-economical & geo-political factors, the radiological services across the country have experienced a sharp decline in imaging volumes. This has important implications on the short-term and long-term economic stability of radiology departments across all practice settings.

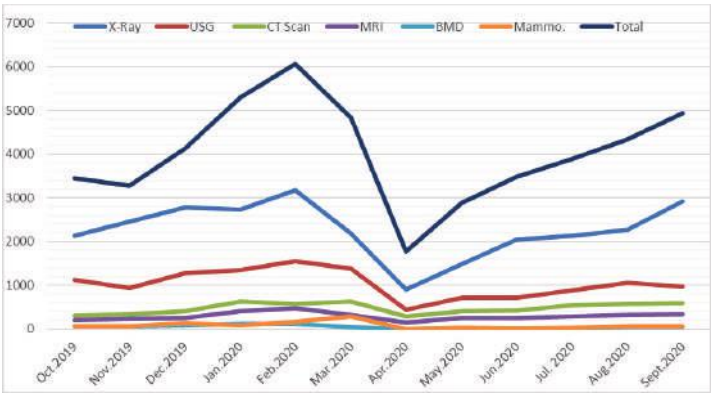
Data set for study (Study Group):

The imaging volumes (Total and modality wise) performed at our center during the period starting October 2019 till September 2020 on monthly basis have been considered for study. This data set has been further divided into pre-COVID-19 period (Oct.2019 to Feb.2020) and post-COVID-19 period (Mar.2020 to Sept.2020) and subjected to statistical analysis to assess the magnitude of its impact on imaging services **(Table 1 & Image A).**

Table 1
Imaging volumes (Total & modality wise) for the period Oct 2019 – Sept 2020

Month	X-Ray	USG	CT Scan	MRI	BMD	Mam-mo.	Total
Oct.2019	2129	1121	308	199	063	58	3446
Nov.2019	2451	938	343	228	069	59	3272
Dec.2019	2781	1281	406	261	080	125	4137
Jan.2020	2728	1338	635	403	112	078	5294
Feb.2020	3179	1554	578	470	111	172	6064
Mar.2020	2179	1376	622	314	054	280	4825
Apr.2020	894	436	292	143	002	004	1771
May.2020	1481	711	398	259	007	025	2881
Jun.2020	2053	711	430	249	017	018	3478
Jul. 2020	2125	877	540	292	022	029	3885
Aug.2020	2272	1060	573	318	046	063	4332
Sept.2020	2924	963	592	343	052	062	4936
Total :	27196	12366	5717	3479	635	973	48321

Image-A
Line diagram based on monthly data set (Imaging case volumes - Total as well as modality wise) depicting their trends during pre-COVID & post-COVID periods



RESULTS & STATISTICAL ANALYSIS:

The results from this study revealed an overall decline in the imaging volumes (Total as well as modality wise) during the COVID-19 pandemic, compared to peak pre-COVID period recorded during Feb.2020. The trend has shown a transition period with a steep decline of imaging volumes across the board over a 4 week period during April 2020 (71% fall) with "**V-shaped**" recession curve to suggest short-term in nature. The worst affected modalities were mammography, BMD & USG. Furthermore, this study has demonstrated a surge in X-ray examinations during recovery phase compared to other imaging modalities (being the mainstay imaging tool for initial imaging of COVID-19 or suspected cases). Deterioration of imaging volumes also varied by location with the largest decline observed in the outpatient settings followed by the emergency department and inpatient settings. With time & after first unlock, the situation gradually improved with reversal of downtrend and by the end of September 2020 almost 81% work flow had been restored compared to the figures recorded in April 2020.

Since the duration of the pandemic remains uncertain, this study may assist in guiding short-term and long-term practice decisions based on the magnitude of imaging volume decline across imaging modalities during the pandemic. Importantly, this data may play a vital role in demonstrating the impact on Radiology practices in near future.

c) Impact on Work Force (Physical, psychological & behavioral impacts):

HCWs are at higher risk for developing physical, mental and behavioral health consequences due to their close proximity with COVID-19 patients during working hours. Inadequate and suboptimal hand hygiene before and after contact with patients, improper PPE, close contact with patients (12 times/day), long daily contact hours (≥ 15 h), and unprotected exposure are the commonest causes for higher incidence of COVID-19 amongst HCWs. COVID-19 pandemic also had significant psychological & behavioral impact on HCWs, which included overwhelming situations, social disruption of daily life, feeling vulnerable for getting infected and fear

of transmitting the disease to families and loved ones.

Implementation of various strategies may help to reduce the burden of health consequences on HCWs and include adequate provision and training on the use of PPE, strict infection control practices, shorter shift length, and provision of mental & behavioral health support services (including Yoga). Protecting the HCWs, through appropriate measures is a crucial tool in national emergency public health response to fight the outbreaks. If timely measures are not taken, a new surge of patients suffering from psychological morbidity will emerge.

Data Set for Study (Study Group):

A total of 28 workers consisting of Radiologists, Radiology technicians, Staff Nurses, Front Desk assistants, Medical transcriptionists and General Duty Assistants working in the Radiology Department have been considered for study **(Table 2)**.

Table 2
Number of staff working in the department with COVID-19 related manifestations

S. No	Type of working staff	Total no	Nature of duty	No. contracted COVID-19	Mental and behavioural manifestations	Remarks
1.	Radiologist	7	Direct patient contact	Nil		Nil
2.	Radiology technicians	11	Direct patient contact	01(a)	02(b)	Legend- (a) & (b)
3.	Staff nurse	1	Direct patient contact	Nil	Nil	Nil
4.	Front desk assistant	3	Direct patient contact	Nil	Nil	Nil
5	Medical transcriptionists	4	No patient contact	01(aa)	Nil	Legend- (aa)
6	General duty Assistant (GDA)	2	Direct patient contact	Nil	Nil	Nil
	Total staff	28		02	02	

Legend :– (a) & (aa) Found to have familial spread (b) one had severe anxiety that he had caught COVID-19 (got tested multiple times) and the other had fear that he was putting his family at risk of contracting the disease.

Note: (1) There are effective preventive measures and use of protective gears against COVID-19 in the Department.

RESULTS:

In our study, out of 28 workers, one radiography technician and one medical transcriptionist contracted COVID-19 infection during the study period. Contact tracing revealed family source of disease spread, since both had multiple family members suffering from COVID-19 prior to their infection. Two of our radiology technicians developed minor psychological & behavioral changes, of which one had severe anxiety with self-perception of being caught by COVID-19 (got tested multiple times with negative results) and the other had fear that he was putting his family at risk of contracting the disease.

CONCLUSION:

The COVID-19 pandemic represents a massive global crisis in the recent times affecting the global economy, increased unemployment and disruption of socio-demographic composition. This has led to substantial reduction in healthcare spending causing a substantial fall in radiological examinations. The volume reduction in imaging services coupled with increased operational cost during this pandemic has caused financial non-viability of private imaging centers. COVID-19 pandemic has also had an impact on physical, mental or behavioral health of frontline HCWs in imaging division. This pandemic has created a flutter across the community and there is a pressing need to analyze its impact on the institutional structures, socio-demographic composition and other dimensions of societal differentiation.

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My Tryst with COVID-19

The COVID-19 pandemic, has affected the whole world in various ways in a short span of time. The first case was identified in December 2019 in Wuhan, China. The outbreak was declared a Public Health Emergency of International Concern in January 2020 and a Pandemic in March 2020. As of 9 November 2020, more than 50.5 million cases have been confirmed, with more than 1.25 million deaths reported worldwide.

People across the world are sharing their experiences of dealing with COVID-19 and there are hundreds and thousands of unique stories about the effect of this pandemic. Healthcare personnel (Doctors & nurses), being the frontline warriors are also getting affected (either themselves or their family members) and have their own experiences to share. In this article, we present the experiences of some of our colleagues who had a tryst with COVID-19 and how they handled it.

Dr. Kapil Gupta

Consultant, Department of Emergency Medicine, Manipal Hospital, Dwarka

It all started on evening of 27 March 2020, I distinctly remember receiving our first COVID patient in emergency room. Patient was actually sick and required ventilatory support. Anxiety began to shoot up so as to who is going to be first person to come in close contact with that patient. We were aware that we knew nothing about COVID-19 infection by then and being brave may have its consequences. However, being an emergency room physician, that's what we were trained for. At this point I and my senior Dr. Sushant decided to tackle this emergency without any fear in our minds. Following that day, we started to receive COVID patients every day and with experience of managing these patients, we became more and more confident with time.

Few months passed, treating COVID patients became our daily routine and then came this day 30th June 2019. I was playing with my baby girl in drawing room at home and received call from my junior that he started to develop symptoms like fever, cough and body aches & was concerned about testing for COVID-19. Following that conversation I came to know about another colleague who was also having similar symptoms. I thought I might also have been infected as all three of us had interacted closely during our last shift. There were lots of concerns in my mind, even though I was asymptomatic, but I stopped thinking and went to sleep.

At around 2 am the same night I also started feeling cold with lot of shivering. I went to another room, turned off the fan and tried to get some sleep but felt very weak from inside. When I checked the body temperature, it recorded 100ºF and I was sure I had caught COVID. I didn't sleep the whole night making plans as to how to proceed from now on. All I was focused about was my daughter (Talisha) and wife with whom I was in close contact and could have infected them also. The mere thought of it was making me nervous. I thought of shifting both of them right in the morning as they were not having any symptoms, get the test done and get myself into isolation. I was sure my daughter would not stay away from me in same household, despite having adequate arrangements for isolation. So I shifted them to my in-law's home, gathered some groceries on the way and came back home after giving samples for COVID at hospital.

There was no doubt in my mind and the news of being COVID positive was told to me by my colleague. Just to keep the moment light, my colleagues asked not to overthink and let the time pass, involve myself into activities, suggesting to watch pending web series on Netflix, read novels etc., in short to keep myself mentally engaged. All of my colleagues and seniors within department and the management team assured me that they stood by me in these difficult times in every way possible. One my colleague who stayed in my society was of great help during these tough times by buying me daily groceries and checking on me every now and then.

I had all the equipment for monitoring at home and I remained asymptomatic for most of the times but palpitations and severe weakness started on 7th day of my illness. I felt so weak that my routine activities were hampered. I stayed in bed for most of times and used to stand in my balcony and watch outside thinking of when is this going to get over. On the 9th day, fever started to come again and palpitations started to become more apparent. I was wondering whether things would get worse from here. I used to check my pulse and oxygen saturation very often. My pulse rate was around 120 bpm for next 2-3 day but oxygen saturation never dipped which was a relief but there was some discomfort while lying supine in bed.

Various thoughts come to my mind, when I was alone in single room for so many days. It was the worst time I could have ever experienced. Sometimes I used to go into trance and remember best moments spent with my friends & family. I missed my niece and daughter badly throughout that time and I used to video call them every single day. Seeing me on phone my daughter used to cry a lot as she's just 2 yr old. It was very difficult to console her and I had to make false promises every day that I shall be meeting her very soon and hug her. Finally, the day came when I got myself retested. I was so excited all dressed up just waiting to hear the report to be negative so that I could just move out of the house and meet my family, wife and my darling little baby girl.

I guess these difficult times give us an opportunity to think and rethink about the moments that we lived and cherished with our loved ones and then we realize how busy we were during those times and should have

spent more time with them. Then again this is what we have signed up for and our loved ones also understand that we have equal responsibility towards our patients. I rejoined the department on 16th July, which I missed a lot during that time. I am really grateful to my colleagues for such a grand welcome with the entire department standing in a row and applauding for me as I entered, one such precious moment which will go down the memory lane and will be cherished forever.

What Would You Do If Your Child Had Coronavirus? For Us, It Was 'Room Service' Food!!

Dr. Lona Mohapatra

Consultant & Head, Department of Pathology, Manipal Hospital, Dwarka

Three weeks before he was to travel to Madrid for his Masters, my son Biplab, came in brief contact with a friend who was COVID positive.

Fingers crossed, prayers sent up, but Biplab tested positive as well. Immediate isolation; necessary medications given, a strict regime of steam and gargling with amla, lemon and haldi concoctions was started. The silver lining, as my husband instantly recognized, was that Biplab would be equipped with antibodies for his new adventure.

Diet was high proteins, fluids plenty, I kept a table outside his room and made his favorite meals. Sunny-side up eggs with buttered toast, sausages and fresh watermelon juice, all nicely arranged on a tray -- Biplab being an Instagram kid was delighted by a beautiful display. I'd stand outside his room and announce: "Room Service." He would giggle.

He remained absolutely asymptomatic throughout, but we were still worried. Our family had many advantages which held us in good stead to nurse him. But the quarantined are lonely and my son was no exception. None of us could comfort him in person when he had to go into solitary confinement in his room. Our short chats through his bedroom door became important, and his phone was his lifeline to the outside world. We had innumerable WhatsApp chats and video calls, and planned his packing for college like this. After two weeks it was time to re-test. Fingers crossed again, he tested negative…phew!! I entered Biplab's room after 17 days. He hugged me so tight and probably shed a little tear. What a relief!

It's ironic to say we feel lucky, when my son tested positive for COVID-19. And, compared to many others who have lost loved ones, I know that we are truly fortunate. Our brush with the coronavirus puts a lot into perspective. The value of family ties, the sustenance and comfort that food can bring, good humor that can provide salve during a lonely quarantine.

Four days after his quarantine ended, he flew the nest. Now he is in Madrid, confident and empowered with a negative COVID RTPCR report and positive COVID antibodies.

Dr. Vikas Taneja

HOD, Pediatrics & PICU, Manipal Hospital, Dwarka

COVID-19 pandemic has affected the whole world and people are gradually adapting and reorganizing their lives to the new normal. Being in the healthcare sector, we have been fighting with COVID head on but when my spouse got affected with COVID, it felt like facing a big challenge for which I was never prepared. I knew that being a doctor I have a high chance of catching the infection and transmitting it to my family, so I took utmost care protecting my family. But this time I was asymptomatic and COVID had come to me through community transmission. I was seeing people getting quarantined but actually going through it was really challenging. There were mixed feelings to start with – excited to show that I can manage my home also, fear if anyone else catches the infection or needs to be hospitalized, confused about how to manage my kids all by myself. The only thing that stuck to me was to keep a positive attitude and take the challenge head on.

The challenge started off with adapting to the new routine of managing home – starting from morning tea, exercise, waking up the kids for online classes, cleaning of the whole house, washing of clothes, managing breakfast, lunch, evening tea and dinner, and ending with cleaning up the kitchen and falling to bed for a nice deep sleep. It was exciting to start with but with each passing day, it felt like a huge task. The next big emotional challenge was my wife being isolated and literally managed like a prisoner. A table was kept outside her room and food, water, clothes etc. were placed on it. She would open the door partially with mask and face shield, pick things up and similarly keep the used things back. I also followed the same way handling all her used things with mask, face shield and gloves and taking utmost precautions to clean everything thoroughly. With severe malaise in the initial days she rested most of the time and I felt helpless that I could not even ease her with a light massage. The day the quarantine period got over, she literally burst into tears and her facial expressions said everything. The third challenge was to keep the kids busy and motivated during these times. We spent lot of time together, talking, playing, watching movies, old family photographs and even doing late night adventures like making tea and Maggie, coke & dance party etc. This was the only time I felt grateful that COVID brought me close to my kids.

There were a lot of learnings and self-realizations –

- It's a big effort ladies make to take care of their house and family which men can never realize.
- Always show your love for your family. It's not worth fighting over petty issues.
- A doctor is important for a patient only till he is sick, but for the family, a doctor is the most important person. A doctor's time is equally important for his family also.
- Doctor-patient relationship is important but should be within professional limits.
- Keeping a positive attitude helps you tide over the most difficult times also.

Dr. Lalit Sehgal

HOD, General & Liver Transplant Anesthesia, Liver Critical Care, Manipal Hospital, Dwarka

The alarm bells…

It was the month of January when we started getting news about a mysterious disease in the east. By February end / March beginning, the picture gets further scary. We start getting unconfirmed videos of inhumane ways of treatment to contain infection on WhatsApp. And, then the news of infection landing in India. It is still a few asymptomatic cases. Early March, frightening news from Europe about healthcare workers dying, starts pouring in. It's not been even a month that I had taken the charge and suddenly this..., the fear of unknown is looming. Seems, the invisible threat can be close and can come from anywhere, anytime and to anyone.

The preparations begin…

The precautions begin. The inter-disciplinary discussions begin. The knowledge sharing with friends and colleagues in India and abroad begins through various chat groups on social media. And here comes the first draft Standard Operating Protocols (SOP) through a collaborative effort. And then the COVID core group meetings. Soon we were having more meetings and less work.

The big issue of protecting self while ensuring safety for self and all. On personal front, in the wake of if lightning strikes, the backup plan(s) all are discussed. The fear is visible. But conveyed just like a soldier can't stay home in middle of a war and so were we. Soon, the threat comes closer and the hospital has first few patients.

Then the testing for COVID-19 begins from an outsourced facility. Hence, all preoperative results are relayed to me daily. And the 'NEGATIVE' becomes the word with highest positive impact in life every day.

The first case and on…

May end, the positive cases start getting reported in preoperative period. And, 30th May, first COVID-19 positive case came for LSCS. The day I remembered all my teachings and the teachers who would keep us out of OT and take full command where the risk was to the healthcare workers. And with support of our senior technicians and nurses I got a feeling of graduation through the SOPs. In June, the threat of infection got further close socially as few known got infected. The precaution levels are further escalated.

It Eventually Strikes…

Come mid-July, when it seemed to be sailing safe and smooth, all precautions in place, I developed change in taste (exaggerated salt in everything). Myalgias, malaise, dry cough and feeling of feverishness followed. Soon I realized that it was a flu different from the one which I have had annually around this season and I isolate myself and go for the test. While waiting for the report, I called my colleague that it seems finally it has gripped me, and treatment was started. And as I feared, I got the report tested positive. Soon the cough aggravated (I never had this kind acute exacerbation of asthma), saturation going down and tension at home on the rise. I started getting calls from Delhi health department for checking my well-being, enquiring my vitals. Majority was the time when I would have gone to sleep few minutes back! Despite the best attempts, the saturation kept going southwards and I decided in consultation with my colleague to get admitted.

While the ambulance arrived, oxygen was initiated, and the thoughts of uncertainty were wandering, I reached the hospital and to the ward. Alone and coughing, oxygen was continued, and other medications were started. My wife was rightly worried. She was fixing alarms in the night to check upon my vitals. However, I was confident that our hospital has a good ICU team, and I was in safe hands. But here I realized that majority of them too had tested positive and were quarantined!!! The blood sugar started shooting up. I was thinking about what if I develop hyperglycemic coma during sleep. This fear didn't let me sleep properly for two nights. Thankfully, the symptoms did not aggravate and around Day 4, started settling and I was off oxygen. One of the nurses involved in my care acknowledged that I looked much worse at admission. But it was not over yet. The labs were still deranged, which started improving by Day 6. Now I was restless to go home. Day 7, I got discharged. It was so good to see all physically, including Festus (our golden retriever). Though it was a week, but it seemed like months and years!

Mostly, I spent time alone except the video calls with family & friends. Along with the disease, the loneliness brought lowliness. But I realized that I was blessed with a beautiful family and a group of friends and colleagues who always tried to keep my morale boosted up and supported the family in difficult times. In fact, dispelling his fears and risks, BCP came to shift me to hospital. That's what we call true friends.

Post Recovery and on…

After another fortnight, I finally joined back with a thought that it will be balm for my pains of isolation. But I

realized the energy levels were no longer the same. I felt fatigued on climbing a single floor. By evening I would get cramps and felt totally drained. Though unwillingly, I used to sleep off in the middle of the meetings. Driving to work kept me afloat and slowly but surely, I got back to my 'new normal' wherein I learnt energy conservation techniques and to channelize it well. Within fifteen days of my joining, again I got a reference for five month old child, COVID-19 positive, for emergency surgery. **And the show must go on….**

Dr. Peush Bajpai

Head, Medical Oncology, Manipal Hospital, Dwarka

It all started with a Negative RT-PCR which I undertook because of fever and upper respiratory symptoms. My symptoms subsided for the most part. Then a week later I developed shortness of breath. I waited the night out, but I think it will be a night I will always remember. The feeling of inability to get enough air into the body scared me more than I would like to admit. I reached the hospital at five in the morning and got admitted after being stabilized in the emergency room. My wife had accompanied me till here, but she could go no further, as COVID ward was off-limits to attendants. This was the time I could not be with my family – my wife, my kids and my parents and could only hope for their good health.

Meanwhile, my wife also tested positive with mild symptoms and self-isolated herself at home. Now came the dilemma before us – what about the kids? Should we let them stay with our parents? But what if they are carriers? Should we let them in with my wife? But then they would get the disease.

Finally, with advice from pediatrician, we decided to let the children in with my wife, hoping they both would get a milder form of the disease, which they did. I was discharged after a stay of 5 days from the hospital, and we began our long journey of home isolation.

We divided the house in 2 portions with a big table as barrier. The cared-fors became the care-givers, our parents took care of us, and themselves. Fortunately, they had tested negative. The mood inside the isolation camp was like a vacation for the first few days, then crept up boredom and fatigue. Somehow the days passed and we were deemed fit to join society and work. We were fortunate enough to have escaped the dreaded complications of COVID-19 and thankful to God for sparing our elders.

As I write this small memoir, it seems like an old dream, but we all live with this disease every day. This is the New Normal.

Dr. Yashica Gudesar

HOD, Department of Obstetrics & Gynecology, Manipal Hospital, Dwarka

"You don't need to have it to feel it."

We were eagerly waiting for the vacation, as board exam was a long penance for the whole family. Just then, like an unexpected winter rain, came the news "COVID is here, LOCKDOWN starts". As a doctor I never stopped. First day to the hospital was too scary. All roads empty, markets closed, not a single soul around. Driving alone thinking about the new peaceful chaos. As a warrior going for war without a gun. Sanitizer and masks were my friends, door handles, lifts, papers, files all were my biggest enemies. Napkins, gloves, clothes, non-touch technique, foot technique, elbow technique, I kept practicing in my mind. Not even a single day till September I was at home; Romans & Countrymen I am an obstetrician. Not even lockdown could stop babies from being born.

March to September seemed so long. For one-month world was at halt, no work besides emergency, house hold work was the next entertainment. Cooking methi chicken for the contest was cool and it brought back pre-practice era memories. Cooking is not for which I was born and the fun ended soon. Hospital got busy. Obstetrics is unending and full-time work. No break as a gynecologist but the positive side was, we were not jobless or penniless. OPD's opened, patients with problems or who were at the verge of delivery kept the work going on. Online consults lying in hibernation came to life during COVID.

The care of my family was a task initially but at home we won over by practicing daily. I feel I was doing most of the hygiene practices beforehand but just improvised on them. Removing shoes at the gate, removing hospital clothes separately, not touching the lift buttons and trying to sanitize every now and then. Handling paper and mobiles has been a tough task in the OPD. Using mail, WhatsApp, non-touch technique, gloves, were not successful in long run. Using sanitizer every time, avoiding face and eyes with fingers, washing as much as possible and wearing gowns and PPE where ever possible were the best ways which helped me out of this turmoil. Elderly parents at home is a little scary for the doctors. I discussed isolation protocol at home, society rules and testing protocols. I even discussed about bank details and passwords in case someone is very sick.

The scare of being the next took a toll for all, rich, poor, young and old. How precious life is, was self-explanatory. Partying and travelling stopped, people learnt new ways to stay busy at home; had wonderful time with their families, eating together, playing games, making meals together, exercising, and giving time to each other. We all slowed down a little to enjoy our life. COVID in families has really created a havoc just like a storm who uprooted all trees but it has also been a boon, especially quality family time. But for a doctor it is like going out every day when the rest are keeping safe

at home away from the worries of the daily dangers.

Which family was going to be next was always in mind? All those awaiting their COVID tests had sleepless nights. The wait for the vaccine seems endless with no final date. Online classes, media exposure for young and old has increased. Schools and teachers are going crazy. The break time is over, parents and children are equally bored. My first day out in the restaurant seemed like another day in 2019 but we kept pointing each other not to forget COVID. Not wearing a mask is like not wearing clothes. Markets and shopping malls all have started and going for a movie or marriage party will also happen one day. But COVID has changed the perspective of life in me. It has made me realize that one can always slow down, but can't blame people and circumstances around for one's condition. Take the reins of your life in your hands. You can change a lot around you, it's just that you don't know when and how to take a turn. But I know now that it's really me who knows when to change.

Shalini

Physician Assistant, Department of Obstetrics & Gynecology, Manipal Hospital, Dwarka

Life was going on smoothly with a new start of 2020 but suddenly came to a halt. And there was a complete lock down due to COVID-19. I, being in medical profession did not run away from my duty. With the support of my seniors and colleagues, I continued to work and on one fine day I also developed mild symptoms. There were mixed feelings of anxiety, fear, panic and alas my test came positive on 4 July 2020. It was like the whole world had changed around me. But with the support of my guide and family I could keep my morale high. Then, I developed high grade fever, diarrhea and breathlessness and was advised admission. With God's grace, my symptoms improved and I was discharged on 10th day.

It was difficult for me to stay at home as I was not happy with the quarantine leave as I am a much active person. Being a Physician Assistant in Obs & Gynae, I missed assisting in deliveries and in certain cases. Apart from this I was assisting myself in taking hot steam, betadine gargles and mixed home remedies so that I can rejoin my duties again after testing negative. It was fun to complete number of web series and shows after a long time as they were on my favorite list for long but I was unable to watch them in any manner. Taking long hour naps and enjoying my own company was good fun but on the other hand I was missing my scolding and my consultants. They were calling me every other day just to make sure that I was fine and always told me to enjoy this COVID period.

I was advised a repeat test after 17 days. I was ready to get a negative report and join my duty with full motivation, but another thunderstorm came in my life, the report was again positive. My fever had improved but I had severe body aches, joint pains and anosmia. I patiently waited for another 10 days, kept my family and myself motivated and finally got a negative report on 31 July 2020. After skipping a month from my work, I was back on my duties with full enthusiasm, cheerfulness and a zeal to work and help patients irrespective of their COVID status. This was my journey during COVID and it goes on……. **LIFE IS BEAUTIFUL AND IT GOES ON…..**

Dr. Monika Gupta

Consultant GI, HPB and Minimal Invasive Surgeon, Manipal Hospital, Jaipur

COVID-19 hasn't left any stone unturned to make our lives miserable in all aspects. We can find each and every human being alive on earth, cribbing about it and discussing so many negative aspects. The illness took away some of our clinicians, which have been major setback events for the medical community. **My tribute to all medical doctors who have become the proud corona warriors – they the real heroes of the world.** In a sense every one of us has suffered a lot in the tryst with this fierce enemy called COVID-19.

The first case in India was detected in January in Chennai. First case in Rajasthan was detected in February end. On February 24th, I had to leave for Italy to present a lecture in a gastroenterology conference (let me remind you it was non-COVID era for all of us in India). I left, on my way to Delhi from Jaipur I realized that some reports of strange infection are coming from Lombardy, Italy and the president had imposed lockdown in that district. I didn't believe it, till I checked it again and again, tried asking the hotel hosting the conference – "Is it a reality?" and "Is the conference being held or not?" Well, they informed us timely that there was nothing in Rome and conference was being held as planned. We bought masks and sanitizer, reached happily at Rome and checked in the hotel. First time in life, although unwillingly, I carried and started using alcohol handrub spray outside the OR - the 'Amrit' of 2020 – the sanitizer. Never knew that formality of carrying it & using it is going to save me from so many queries and doubts back home.

Although there was nothing at Rome, but travelers in flight were from all areas, so on my trip back home I was advised to quarantine for 15 days. "Fifteen long days without work!!" are too long. I cannot even stay comfortable for 15 hrs without work, that too in own city, that too when patients were waiting to be operated. One of the patients waiting was a foreigner, who consulted me around 15 Feb and was to be operated for cancer stomach as soon as I land in India, 28th Feb!! Since the encounter was with the monster - COVID-19, it was testing me also with all teeth sharpened.

One, that I was returning from Rome (anyone would ask – 'Oh my God', you went to Italy?? so quarantine was

essential), second, my patient who had cancer stomach (needing early surgery) was coming from Spain (High COVID Incidence Area), although came to India in early February (before spread), third, that he was China born and his wife was Italian, fourth, that I could not see/ meet patients and operate during quarantine. Only thing was that the patient wished to get operated in India and was a dedicated patient with faith. So his surgery got delayed, and was operated in March but his discharge was on 22 March (the lockdown started!!) The issues were – The patient had cancer, needed early surgery but had to waste 15 days.

The patient was difficult to manage as origin of birth, country of living and wife's country of origin and added to it – my Rome travel complicated it all (it was a serious issue in initial lockdown). It was difficult to counsel – as wife was 81 yr old, who was there on day of surgery and wasn't willing to stay with patient in hospital (due to fear of catching COVID in hospital premises), my team had to detail the condition on phone. Even if she was willing, lockdown was so strictly imposed in initial phase that police won't allow an Italian person to roam around. So practically the caretaker nurses, patient and I were on toes to take care, explain the major surgery and recovery, discharge, communication, sending patient to hotel, arranging dressings & stitches removal. Anyone from anywhere could raise the objections due to anti-COVID, and also anti-Italy atmosphere generated out of fear of COVID.

Finally we did it and he received chemotherapy while waiting for Visa. The patient reached back home in Spain happily on July 15. That's the beauty of our Manipal Family that we could manage such precious and difficult case despite so much hurdles.

I must make a note of many positive things brought in with the COVID times & lockdown, that penning all of them down here may be cumbersome. I, in fact all of us introspected and I realized what intuition (Gut Feel) means. In February, when I was not getting the visa very smoothly in spite of my clean travel history abroad and it was delayed till the penultimate day of travel, I was not getting positive vibes to travel till the day of travel. When I went to Italy, I realized that the vibes weren't positive there also. People were much fearful and probably stressed.

During lockdown once I sat alone (being quarantined healthy), I realized what my goals are in 2020. I happily adjusted, slept for a day or two, managed my father's illness with full efforts, initiated academic tasks, rejuvenated myself, and gathered knowledge on masks, PAPR, respirators to prepare for upcoming pandemic time. Most important is – I made a 'Things to do' list!! I realized that person inside me can really adjust to holidays and slow down my life in order to naturally enjoy the real speed of oneself. Slow, interested and nourishing the mind with mythology, spirituality, cooking recipes and lots of reading. Lockdown reduced expenses. The basic needs reduced, fear for spending anything was so big that all of us nearly managed life with minimum possible expenses. In fact 'What to buy?' 'Where to get it?' was the major issue plus 'Why to spend?'!! It made us real fitness seekers. Last but not least it made me realize importance of my own life as a corona warrior, as a doctor and as a precious family member.

Shini Kurian

MICU Nurse

It was a beautiful day like every other day, I got ready and left with my husband for my work. On the way I was feeling something wrong. I even informed my husband and he asked me to take leave and stay home, but I ignored and continue working. Later my in-charge noticed that I am looking sick and she asked me to take rest for the day. I called my husband back to pick me up.

Later in the evening I got sicker. I had symptoms like fever and started shivering as well. I consulted a doctor. At night when I reached the hospital I was scared. They asked me to get admitted as my chest x ray was not normal. Same night my colleague also got admitted. Next morning we both woke up with no symptoms except no taste and smell. Next day the COVID report came positive.

I had good support from my family. It is hard to stay isolated but I was home quarantined after 1 week. Home remedies like hot water gargles and steam also helped. With my experience I would love to tell everyone, we need to have strong will power. I repeated my test after 14 days and it came negative. I cannot say those 14 days were fun, but after recovery I was happy. I have started working again and I am going to be mother soon. My advice to all: Always stay strong and positive.

Dr (Lt. Col) Leena N Sreedhar

Consultant Obstetrics & Gynaecology,
HOD Academics & Research, Manipal Hospital, Dwarka

My Tryst is in two parts

Before – "What I had written before getting the COVID infection".

Ever since the pandemic started and lockdown happened, our clinical and administrative committees were meeting regularly to check on preparedness to handle COVID patients. Obstetrics was one such speciality where COVID preparedness was a must. While all who came in labour eventually turned out to be COVID negative, the advantage was that I could perfect the technique of donning and doffing of PPE much before I got the first COVID positive patient. It was on the evening of 27th May when I was informed that the high risk pregnant patient whom I had admitted in the morning in the isolation ward was COVID positive.

She was prepared for Caesarean section on 28th May 2020. The young woman had a Bad Obstetric History and the baby at 38 weeks had started showing signs of placental insufficiency which meant that I could not wait. I remember that day when I put into practice all that I had read and learnt. For the anaesthesia team it was also their first case so we discussed everyone's role before we donned the PPE. The case went off well and the lady was blessed with a healthy baby girl. At that time the guidelines warranted hospital isolation so that was done.

There was no looking back since then. Our labour Room was well divided into red and green zones depending on patients being suspected, known COVID positive and COVID negative. Having good administrative support, adequate supplies of PPE and a supportive team of nurses ensured that there was no confusion in handling obstetric cases whether in the day or at night.

As I write this I have delivered more than a dozen COVID positive mothers and I accept the fact that we will all have to work and live with this virus. It has been a big stress watching your colleagues and their family members getting infected and wondering if you are next.

My family was my biggest support factor especially my parents, both octogenarians, who understood why I refrained from visiting them. My father, a retired Officer of the Indian Army kept my spirits high despite their being isolated in a containment zone themselves. My husband, being a doctor himself and heading a COVID hospital of the Armed Forces, fully understood my commitment to my patients.

So the show must go on and we must work as well as protect ourselves.

My daughter has joined as first year PG resident in a leading COVID hospital in Delhi and has already done two stints in COVID ward duties and my son is studying in a part of USA still reeling under the pandemic.

The pandemic has touched all of us in some way or the other and we healthcare workers on the frontline have been and still are the most vulnerable. We have to take care of ourselves so that we can take care of our patients!!

After – "My experience after getting the infection"

We were 8 months into the pandemic. Being an Obstetrician and Gynaecologist I had delivered a number of known COVID positive mothers and emergency cases which later were found to be positive. Observing COVID protocols in labour room, donning & doffing PPE, handling OPD patients with all precautions was becoming the new normal way of managing my practice of obstetrics and gynecology. I was happy to shift into my new home during navratras and my husband & I were looking forward to having the extended family over for a pre- Diwali celebration.

It was on 7th November that I suddenly felt very tired and giddy while performing a hysterectomy and had to take a break. However I completed my surgeries for the day & went home.

Being an obstetrician I have been used to exertion & working at odd hours, but this was an unusual symptom. I woke up the next morning (Sunday) with a fever (100-101ºF) and intense body ache. I started taking Tab Doxycycline, Tab Ivermectin and Dolo-650, Vit C, Vit D and Tab Zinconia. I noticed a loss of taste and smell. I got my COVID test and as expected it was positive on 9th November. So I immediately went into home isolation.

All Diwali plans were cancelled. My husband who is heading a COVID hospital in Pune & was on leave extended his leave so as to look after me, ensuring I took my meals on time. We talked across the corridor. He also cooked some delicious meals for me. Tender coconut water helped me to get over the myalgia, soups and rasam helped the throat especially the latter which was really soothing.

The fever waxed and waned and by Diwali afternoon 14th Nov, I was afebrile. The myalgia was intense and I kept a watch on my Sp02 especially after taking a 3 minute walk around the house in my place of isolation.

Routine biochemical tests showed a rise on the 7th day, which I was told was not alarming, so I was reassured. I was in constant touch with our physician and adhered to all the medications. I read books (fiction or nonfiction) and saw some great movies on Netflix & Amazon Prime. The only person I couldn't prevent coming into my room was my 10 yr old dog Muffin who insisted on being by my side which was very reassuring!!

On 19 November I retested and was COVID negative. I was overjoyed that my husband continued to be COVID negative. I was back to work in the hospital on 23 November. Although the aches and pains continued I was glad to be back and at the helm of affairs. COVID 19 taught me a few things which I would like to share with my colleagues

- Trust your physician implicitly.
- This is a strange virus & can have an unpredictable course.
- Believe in statistics, 90% of us will recover completely
- Don't panic! Avoid multiple inputs from multiple doctors even if they are your batchmates!
- Be strict & disciplined with yourself in home isolation
- Eat nutritious meals & remain well hydrated even if it means going to the washroom a number of times!
- Deep breathing exercises, steam inhalation and warm saline gargles are very helpful.
- Positive thinking helps in recovery.
- Talking to your family helps you keep yourself motivated to recover fast.

I am grateful to my family, friends and to God Almighty for seeing me through these testing times. Life has its strange moments! After joining back on 23rd November, I safely delivered a COVID positive mother on 26 November!

Back to the world of obstetrics and its work as usual at Manipal Hospital Dwarka.

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INFORMATION CORNER

Results of the Physician Assistant Course across specialties being conducted by Manipal College of Health Professions, a unit of Manipal Academy of Higher Education, Manipal

S. No.	Name	Specialty	Qualification	Exam/ Result
1	Jitesh	Neurosurgery	BSc-Nursing	Finals, completed PA course
2	Nitish	ENT	BSc-Nursing	Finals, completed PA course

COVID-19 and Non-Communicable Diseases – Opinion of the Key Stakeholders from Manipal Hospital, Delhi.

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Keywords: COVID-19, Non-Communicable diseases (NCDs)

INTRODUCTION:

In the last 20 years, this is the third time that a novel Corona virus (SARS-CoV-2) has struck us and this time the outbreak has been a global one. The earlier outbreaks of corona virus were in China in 2002 (SARS: Severe Acute Respiratory Syndrome) and Gulf countries (MERS: Middle East Respiratory Syndrome). In terms of fatality, the case fatality rate of SARS-CoV-2 is 3.44% which is low as compared to previous outbreaks of the virus[1]. On the other hand, Non-communicable diseases (NCDs) kill nearly 40 million people each year with more than 80% deaths from the developing world. Cardiovascular diseases account for most NCD deaths, (17.9 million people annually), followed by Cancers (9.0 million), Respiratory diseases (3.9 million), and Diabetes (1.6 million)[2]. Any of these comorbidities coupled with COVID-19 can have a detrimental impact. Carrying forward the essence of Madame Curie's words "Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less". This article covers some pertinent issues opined by various specialists at our hospital with respect to the management of some major NCDs during this pandemic. The opinions were taken over a telephonic conversation with the concerned specialists by the author.

DIABETES MANAGEMENT DURING THIS PANDEMIC:

Diabetes and hyperglycemia bring about certain degree of immunosuppression due to poor neutrophil action and poor chemotaxis of mononuclear cells in response to the virus apart from a slow and poor humoral response. In view of ongoing stress because of COVID-19 there have been episodes of hyperglycemia in non-diabetics as well. **Dr Charu Goel** (Internal Medicine) opines that COVID-19 can give a push to "on the fence" pre-diabetics and unmask diabetes due to stress. Moreover, use of drugs like steroids can worsen the glycemic control and on the other hand HCQS can lead to hypoglycaemia in diabetics. **Dr Vineet Surana** (Endocrinologist) is quite emphatic when he says that insulin should not be stopped in diabetics on insulin therapy. He quotes the guidelines of Association of Physicians of India[3], as he mentions about pancreato-pathy, which reflects of increased apoptosis of the insulin secretory cells in pancreas. He agrees with the word Sugar tension[2] (Diabetics and Hypertension) and explains that the two subgroups, which if present in a patient increases the susceptibility to a more severe form of infection.

HYPERTENSION – ACE INHIBITORS /ARB'S AND THEIR STATUS:

As the understanding of COVID-19 entry into the respiratory and gut epithelium was understood, it was realized that it is the ACE receptors which play an important part where the virus gets anchored initially. There were speculations that the usage of ACE inhibitors would upregulate the ACE receptors and its use could prove detrimental in case of COVID-19 entry into the body[4]. This hypothesis gained momentum early in this pandemic however several studies refuted this claim and so does **Dr Sarita Gulati** (Cardiologist). She quotes from recently published study from Oxford University, which looked at nearly 8.3 million patients and found that ACE /ARBs would rather be beneficial in patients on these medications ailing from COVID-19 infection, hence these medications shouldn't be stopped[5].

COVID-19 AND HEART:

Dr Bipin Dubey (Cardiologist) mentions increased risk of cardiovascular morbidity due to the pro-inflammatory state in a COVID-19 patient. Pre-existing cardiovascular disease seems to be linked with worse outcomes and increased risk of death in patients with COVID-19. Moreover COVID-19 itself can also induce myocardial injury, and endothelial injury says **Dr Yugal K. Mishra** (Chief of Medical Services and Cardiothoracic Surgeon) resulting in arrhythmia, acute coronary syndrome and venous thromboembolism. Also there has been increased concern of polypharmacy causing morbidity during this pandemic[6]. **Dr Rajnish Sardana** (Cardiologist) points out the increased risk of QTc prolongation in patients on Hydroxychloroquine (HCQS) and Azithromycin especially those who have renal dysfunction along with other comorbidities. Hence, he advises a baseline ECG and thereafter serial ECG monitoring during the treatment. **(Table 1)**

	Drug	Interactions and effects.	Action to be considered
1.	Antibiotics		
	Macrolides (Azithromycin etc)	QT prolongation and arrhythmias	Avoid co-prescription, if utmost essential assess basal QT by ECG and serially monitor
	Quinolones (Ciprofloxacin etc)	QT prolongation and arrhythmias	Avoid co-prescription, if utmost essential assess basal QT by ECG and serially monitor
2	Anti-arrhythmic drugs (Amiodarone, disopyramide procainamide quinidine amiodarone sotalol)	QT prolongation and arrhythmias	Avoid co-prescription, always weigh the risks and benefit and seek expert opinion if needed.
3	Anti-diabetic drugs including Insulin	HCQ lowers blood sugar levels.	May need to monitor blood sugar levels and may need to reduce dose of antidiabetic drugs
4	Betablockers (Metoprolol, Carvedilol, Bisoprolol etc)	HCQ increases drug levels of BB interfering with its metabolism at higher doses	Can be continued, but this monitoring may be needed
5	Digoxin	HCQ increases Digoxin levels at high doses.	Can be continued, but monitoring may be needed

Hydroxychloroquine when used as prophylaxis – precautions to be noted. [7]

LUNG AND COVID-19:

Respiratory failure has been the major cause of morbidity and mortality globally in this pandemic. The underlying pathophysiology has been pinned to ACE 2 receptors and pulmonary vascular angiogenesis which has now been studied in lung autopsies[8]. COPD & Asthma have not been linked as major comorbidities for patients acquiring this infection. Nonetheless, COPD has been a major risk factor for serious infections[9].

Dr Puneet Khanna (Pulmonologist) quotes the GOLD guidelines[10] (Global Initiative for Obstructive Lung Disease) that these patients should continue their doses of metered dose inhaler steroids which can be used with a spacer. He quotes that if a nebulizer is to be used, good nebulization practices should be followed as nebulizers generate aerosol particles in the size of 1–5 μm, which can carry the virus deep into the lung. He also mentions that asthmatics, in particular should be careful about using disinfectants as it can trigger an exacerbation. Also important is that these subsets of patients should take stringent precautions and get annual flu vaccination done.

KIDNEY AND COVID-19:

Lung and Kidney are the two major determinants of outcomes in COVID-19[11]. Patients with pre-existing chronic kidney disease (CKD) including End stage renal disease (ESRD) are at a higher risk of severe COVID-19 infection. These patients have a 14-16 times higher mortality with nearly 15-30% of the dialysis patients succumbing to the illness[11]. The various factors attributable are a lower immunity, previously existing comorbid conditions like diabetes, hypertension and frequent visits to the hospital for dialysis.

Dr Saurabh Pokhriyal (Nephrologist) explains that the real challenge in CKD patients on maintenance dialysis is continuing dialysis because missing dialysis sessions can cause high morbidity and lead to mortality from acute pulmonary oedema or cardiac arrhythmias secondary to hyperkalaemia. Patients presenting with fluid overload can mimic COVID due to symptoms like breathlessness and chest X-Ray showing lung infiltrates. The compulsion of COVID-19 testing in such patients leads to further delay in dialysis therapy.

CANCER AND COVID-19:

The patients with advanced cancer and haematological malignancies carry an intrinsic higher risk of adverse COVID-19 outcomes and seem to have a higher risk of mortality. The drivers of the outcome in cancer patients are older age and comorbidities. Also important is the fact that Oncologists have challenged the principle "primum no nocere" to deliver a larger therapeutic benefit to their patients. This benefit is at the risk of being jeopardized by the current pandemic. Certain principles have been adopted widely. **Dr Anusheel Munshi** (Radiation Oncologist) states that there is an increasing use of Hypo fractionated regimes (delivering bioequivalent doses) whenever possible. This reduces the number of patient visits and is also a resource sparing strategy for hospitals. Similarly, the use of single fraction radiotherapy regimen in palliative situations need to be encouraged[12]. **Dr Vedant Kabra** (Surgical Oncologist) quotes that cancer care has taken a backseat because of the chaotic situation but time has come to move forward as 'Cancer and COVID-19' is like facing the 'Devil and Deep Sea'. Surgeries which are essential and translate into a survival benefit shouldn't be delayed further. The **author (Medical Oncologist)** feels that conversion to oral medication after taking into account evidence-based medicine is an important step on cutting down patient visits. Moreover teleconsultation is another important way to cut down on hospital and follow up visits, and if feasible, should be used frequently.

CONCLUSION:

The pandemic is showing no signs of waning off. It is time now to address these NCDs promptly in this "New Normal" and not shy away from certain bold but evidence-based decisions.

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Cellular Phones and Wi-Fi in COVID times: Is there a cause for concern?

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Mobile phones first came to use in the early 1990s for professional work-related reasons, and henceforth have attained tremendous growth, becoming able symbols for consumer status and needs. At present, nearly 5 billion people worldwide own cellular phones. India had 500 million smartphone users as of December 2019, which means over 77 percent of Indians are now accessing wireless broadband through smartphones[1]. Further, moving forward after 2G, 3G and 4G, India is soon set to welcome 5G networks.

The pandemic of COVID has brought the world to a grinding halt. Till now it has affected 35 million people, causing 1 million deaths[2]. The world economy has been nearly stranded. Government agencies, private companies and individuals have devised innovative means to tide over the crisis. Measures like work from home using Laptops, internet based virtual platforms and cellphone systems are being extensively used to avoid people to people contact. All this has resulted in an internet and software boom, a fact well reflected in the steep climb of the shares of IT companies across the world. However, this has also meant an exponential increase in time an individual is exposed to electromagnetic radiation. The critical question is, does this increased exposure pose a health risk to individual or our society?[3]

Technically speaking, mobile phones and towers emit electromagnetic radiation (Radiofrequency, RF) that is essentially non-ionizing. (frequencies between 300 MHz and 300 GHZ). The specific absorption rate (SAR) measures the energy dose that subjects exposed to RF absorb and is provided by all cellphone manufacturers. The non-ionizing nature of these radiations means that unlike X rays and Gamma rays, these electromagnetic radiations do not have the ability to cause DNA breaks. Also reassuringly till now, all the major studies done across the world have failed to conclusively prove a connection between cellphones, cell towers and tumors. These studies include large studies from Nordic countries, US and Europe. Till date, these trials and studies have been reassuring that cellphone and towers do not pose a health risk[4]. Most of the studies however suffer from the lacunae of recall bias, selection bias and call data reliability issues. Another critical issue is that the effects of this electromagnetic dose deposition takes long to manifest. In some cases, this duration may be 10 years or more. It is for this reason that robust studies with long term outcomes are eagerly awaited.

All electromagnetic radiations are governed by an interesting law known as the inverse square law. This essentially means is that if we increase distance from the source by a factor of 2, the exposure gets reduced by 1/4th. It is for this reason, that distance from the device is a critical factor which decides the exposure received from a particular device. A person using a mobile phone kept at 30–40 cm away from their body – for example when text messaging, accessing the Internet or using hands free device– will therefore have a much lower exposure to radiofrequency fields than someone holding the handset against their head. It is for the same reason that, if indeed a true risk exists, children would be at particular risk because their skulls are thinner and underlying tissues of brain are more exposed. Also the cumulative lifetime exposure of children to cell phones is likely be greater than the exposure of current adults, since they are likely to have started using cellphones at a much early age. Several ongoing studies are investigating potential health effects in children and adolescents.

In 2011, an expert panel of the International Agency for Research in Cancer (IARC) – a WHO specialized agency, classified radiofrequency electromagnetic fields as possibly carcinogenic to humans (Group 2B), a category used when a causal association is considered credible, but when chance, bias or confounding cannot be ruled out with reasonable confidence[5]. This did raise some concerns but in view of lack of credible evidence, the scientific community could not come to a firm conclusion.

Many nations in the world have moved to 5G technology to improve the speed and capacity of wireless technology. A popular theory has linked 5G to the spread of COVID-19, leading to misinformation and the burning of 5G towers in some cities of the world[7]. 5G uses a higher frequency of radio waves compared to its older generations. The frequency of this new wireless technology still remains very low[8]. Many scientific bodies and organizations have assured that at present there is no evidence that links 5G network to the spread of COVID-19.

Till long term results related to the effects of electromagnetic radiation on humans are out, it may be reasonable for us to observe some simple precautions[6].

1) Use the cell phone whenever it is really needed. For most routine work and casual talks, use the regular landline connection or a wired ear phone.
2) Discourage children from excessive talking using cell phones
3) Avoid cell phone use when the signal is weak (since phones tend to emit more radiation when signals are weak).
4) Consider alternating between left and right ear while talking on cellphone.
5) Use texting (SMS) instead of calling when possible.
6) Keep the Wi-Fi switched off when not in use.

To summarize, it may be some time before we know if the friendly gizmos in our hands or the invisible Wi-Fi signals have the ability to cause serious health issues. For the time being, we can be rest assured, and go on with our webinars and con-calls!

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INFORMATION CORNER

Important Health Days & Events	
1st – 7th Sep	National Nutrition Week
12th Sep	World First Aid Day
21st Sep	World Alzheimer's Day
29th Sep	World Heart Day
10 Oct	National Mental Health Day
12th Oct	World Arthritis Day
15th – 19 Oc:	World Obesity Awareness Week
16th Oc:	World Anesthesia Day
17th Oct	World Trauma Day
29th Oct	World Stroke Day
1st Nov	Lung Cancer Awareness Month
10th Nov	World Immunization Day
12th Nov	World Pneumonia Day
14th Nov	World Diabetes Day
15th – 21st Nov	Newborn Care Week
19th Nov	World Pancreatic Cancer Day
20th Nov	World COPD Day

Momentous Moments of Medicine Hepatitis C – Nobel Prize Winners in Medicine In 2020

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"The Nobel Prize in Physiology or Medicine 2020 was awarded jointly to Harvey J. Alter, Michael Houghton and Charles M. Rice "for the discovery of Hepatitis C virus."[1]

Harvey J. Alter
The Nobel Prize in Physiology or Medicine 2020
Born: 1935, New York, NY, USA
Affiliation at the time of the award: National Institutes of Health, Bethesda, MD, USA
Prize motivation: "for the discovery of Hepatitis C virus."
Prize share: 1/3

Michael Houghton
The Nobel Prize in Physiology or Medicine 2020
Born: United Kingdom
Affiliation at the time of the award: University of Alberta, Edmonton, Canada
Prize motivation: "for the discovery of Hepatitis C virus."
Prize share: 1/3

Charles M. Rice
The Nobel Prize in Physiology or Medicine 2020
Born: 1952, Sacramento, CA, USA
Affiliation at the time of the award: Rockefeller University, New York, USA
Prize motivation: "for the discovery of Hepatitis C virus."
Prize share: 1/3

THE NOBEL PRIZE

On 27 November 1895, Alfred Nobel signed his last will and testament, giving the largest share of his fortune to a series of prizes in Physics, Chemistry, Physiology or Medicine, Literature and Peace – the Nobel Prizes. Between 1901 and 2020, the Nobel Prizes and the Prize in Economic Sciences were awarded 603 times. 934 Laureates and 28 organizations have been awarded the Nobel Prize between 1901 and 2020. Of them, 86 are Laureates in Economic Sciences. A small number of individuals and organizations have been honoured more than once, which means that 930 individuals and 25 unique organizations have received the Nobel Prize in total.

NOBEL PRIZE IN MEDICINE AND PHYSIOLOGY 2020

The Nobel Prize in Physiology or Medicine was awarded jointly to Dr. Harvey J. Alter, Michael Houghton and Charles M. Rice on Monday for the discovery of the hepatitis C virus, a breakthrough the Nobel committee said had "made possible blood tests and new medicines that have saved millions of lives."

POST-TRANSFUSION HEPATITIS

Every war throughout the centuries has been marked by massive outbreaks of jaundice which we know were probably cases of infectious hepatitis. However, in many cases were percutaneous inoculation of products contaminated with human blood, occurring in World War II that were traced to contaminated lots of yellow fever vaccine and later shown to be caused by Hepatitis B virus (HBV).[2] Extensive studies characterized two forms of hepatitis, one that was fecal-oral in its transmission mode and was called infectious hepatitis or Hepatitis A, and one that was predominantly transmitted by contaminated serum and hence termed serum hepatitis or Hepatitis B.

Post-transfusion hepatitis (PTH) was very common in the 1970's especially among heart surgery patients. Studies done in open-heart surgery patients, who were sampled every 1 to 2 weeks post-transfusion for 3 months and then monthly for an additional 3 months. Consecutive, weekly ALT elevations to greater than 2 times the upper limit of normal were considered evidence of PTH if other causes were reasonably excluded. It was observed that the incidence of PTH, when prospectively determined, was inordinately high at approximately 30%, and that the primary risk factor for PTH, in the absence of donor hepatitis testing, was the use of paid-donor blood. It was found that recipients of at least 1 unit of paid-donor blood had a 51% incidence of PTH compared to only 7% of those who received all-volunteer donor blood.[3]

In the 1970s, Dr. Alter led a team of scientists in discovering that most cases of post-transfusion hepatitis couldn't be linked to Type A or B viruses — a

hint to the existence of a pathogen that had not yet been described.

In the 1980s, Dr. Houghton, along with two colleagues Qui-Lim Choo and George Kuo, became the first to identify and formally name the Hepatitis C virus as the infectious culprit. During that period, Michael Houghton and his colleagues at the Chiron Corporation and Dan Bradley at CDC performed cloning experiments with serum/plasma derived from both humans and chimpanzees infected with Non-A Non-B Hepatitis (NANBH). They approached the issue by collecting pellets from plasma of highly pedigreed NANBH cases, to extract nucleic acid from the pellet, and then reverse transcribe extracted RNA. The derived cDNA was then cut with restriction enzymes and inserted into a phage GT-11 expression vector that was used to infect Escherichia coli in culture. The selection of this phage vector was critically important because any transfected viral gene product would be expressed by the bacteria into the surrounding medium. The work led to the development of a diagnostic test to identify the virus in blood, enabling doctors and researchers for the first time to screen patients and donors.[4] Dr. Houghton's work, which isolated the virus's genetic sequence, bolstered the case that it was a new pathogen and distinct from the viruses behind Hepatitis A and B.

Dr. Rice's genetic experiments added important details to scientists' understanding of the virus, showing that it could be isolated in the lab and cause disease in an animal host, the chimpanzee. These studies nailed the Hepatitis C virus as the sole infectious agent responsible for the mysterious "non-A, non-B" cases of hepatitis and set up a crucial animal model for future studies.

CONSEQUENCES OF THE WORK

Dramatic reductions in PTH were observed after adoption of an all-volunteer donor system and introduction of first-generation assays for HBsAg.[5] Rest of the PTH cases were ascribed to the agent of NANBH, later renamed the HCV. By the early 1980s, prospective NIH studies showed that PTH incidence hovered around 6%. In 1990, the first-generation assay for anti-HCV was introduced and we measured a decline in post-transfusion hepatitis incidence to 1.1%. A more sensitive anti-HCV assay was introduced in 1992 and by 1997 hepatitis incidence in the NIH study had decreased to virtual zero. It has been mathematically estimated that current PTH risk resides between one case in every 1.5 to 2.0 million transfusions, a remarkable decline from the 30% incidence observed in 1970.[7]

About 71 million people worldwide live with a chronic infection of the Hepatitis C virus, a blood-borne pathogen that can cause severe liver inflammation, or hepatitis, and is typically transmitted through shared or reused needles and syringes, infected blood transfusions and sexual practices that lead to blood exposure. There has been a dramatic progression in treatment efficacy for chronic HCV infection. Early treatments with interferon alone had only a 6% sustained efficacy if administered for 6 months and 16% if administered for a year. This was accompanied by major side effects and diminished quality of life. In 1998, ribavirin was added to interferon and sustained efficacy increased to 42%. In 2001, a pegylated formulation of interferon was developed that provided slower degradation and thus higher serum levels of interferon that allowed for weekly dosing and together with ribavirin increased efficacy to 55%. Based on sequencing and 3-dimensional structure determinations, oral directly acting agents (DAAs) were developed that targeted key replicative and enzymatic sites in the HCV virion. The first of these was directed at the viral NS3-NS4 protease and when this protease inhibitor was added to pegylated interferon and ribavirin, the sustained virologic response (SVR) rate increased to 70%. The major breakthrough came with the development of DAAs targeted to the viral polymerase (NS5B) and the replication complex (NS5A). These oral DAAs, combined into a single pill, negated the need for interferon and ribavirin and greatly simplified treatment, as well as minimizing side effects. Efficacy with oral DAAs increased to more than 90% SVR and recent iterations can achieve 98% to 100% efficacy across all HCV genotypes and greater than 90% efficacy even in patients with compensated cirrhosis.[6] Such high levels of SVRs, which is equivalent to cure, were unimaginable only a decade ago. It is a tribute to molecular biology, crystallography, advanced drug-screening technology, and investigator persistence. It is also a tribute to collaboration between industry, academia, and the government toward a common goal.[7]

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Laboratory Diagnosis of Novel Coronavirus SARS-CoV-2 – Challenges & Learning Experience

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INTRODUCTION:

The latest coronavirus disease pandemic (COVID-19) caused by novel Coronavirus virus (SARS-CoV-2) emerged in Wuhan-China on 31 Dec 2019 and has caused a new public health crisis threatening the world. As on date (5 Nov 2020), worldwide there are 48 million plus cases of COVID-19 with 1.2 million deaths. India reported its first case on 30 Jan 2020 and as on date (5 Nov 2020) has 8.3 million plus cases with 1.2 lakh deaths. India also has the dubious distinction of having the second highest number of COVID-19 cases in the world. In the last twenty years, there have been three different coronavirus outbreaks: SARS-CoV-1 in 2003, MERS-CoV in 2012, and SARS-CoV-2 pandemic in 2019. Rapid detection of cases by various laboratory tests is paramount to control the pandemics.

SARS- CoV-2 Structure

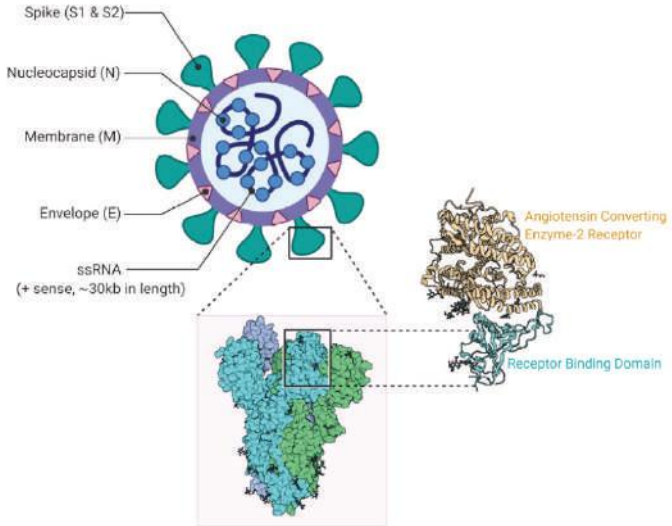


Figure 1

Image courtesy: Cascella M, Rajnik M, Cuomo A, et al. Features, Evaluation, and Treatment of Coronavirus (COVID-19) [Updated 2020 Aug 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. [Figure, SARS- CoV 2 Structure. Contributed by Rohan Bir Singh, MD; Made with Biorender.com]

Available: https://www.ncbi.nlm.nih.gov/books/NBK554776/figure/article-52171.image.f3/

STRUCTURE OF SARS-CoV-2 (FIG. 1)

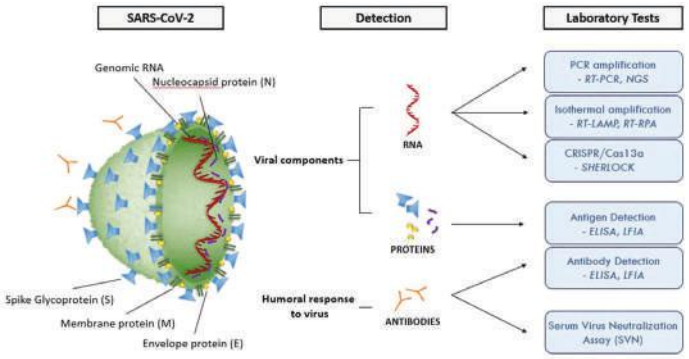
Coronaviruses are enveloped, single-stranded, positive-sense RNA viruses which belongs to the subfamily Coronavirinae. SARS-CoV-2 is surrounded by a lipid bilayer membrane, containing structural membrane (M) and envelope (E) proteins that interact to form the viral envelope. This layer also contains spike glycoproteins (S) that give the characteristic "corona" appearance of this family of viruses. The spike proteins bind specific host cell receptors to facilitate host cell attachment and entry. Spike glycoprotein has two functional domains: S1 and S2. S1 is responsible for the binding with its receptor angiotensin-converting enzyme 2 (ACE2) on host cells and defines the host range of the virus. S2 is the transmembrane subunit that facilitates viral and cellular membrane fusion. The nucleic acid-associated protein binds the RNA genome and forms the nucleocapsid (N)

THE ROLE OF DIAGNOSTIC TESTING IN THE SARS-CoV-2 PANDEMIC:

The cornerstone in controlling this pandemic is 'Test, Track and Treat'. The primary goal of the epidemic containment of COVID-19 is to reduce the infection transmission in the population by reducing the number of susceptible persons or by reducing the basic reproductive number (R0). Since there are no vaccines or specific treatment options for COVID-19, the only way to contain the infection is to diagnose and isolate the infected persons who are contagious and can transmit the infection.

The various diagnostic modalities for SARS-CoV-2 testing include[1]: **(Fig 2)**

a) Molecular testing by RT PCR or CBNAAT – done on respiratory specimens
b) Antigen testing - done on respiratory specimens
c) Antibody testing – done on blood specimens



From: Ref 1: D'Cruz RJ, Currier AW and Sampson VB (2020)

Laboratory Testing Methods for Novel Severe Acute Respiratory Syndrome-Coronavirus-2(SARS-CoV-2).

Front. Cell Dev. Biol. 8:468. doi: 10.3389/fcell.2020.00468

Fig. 2

Test modalities for SARS-CoV-2

Table 1
Specimens for SARS-CoV2 testing

Specimen Types	Collection devices	Transport conditions	Storage conditions
Upper respiratory tract specimens: Nasopharyngeal swab, Oropharyngeal swab	Dacron or flocked swabs in VTM	4°C	Within 5 days: 4°C Longer than 5 days: -70°C
Lower respiratory tract specimen: sputum	Sterile container	4°C	Within 48 hr: 4°C Longer than 48 hr: -70°C
Lower respiratory tract specimen: bronchial washing	Sterile container	4°C	Within 48 hr: 4°C Longer than 48 hr: -70°C
Lower respiratory tract specimens: tracheal aspirate and transtracheal aspirate	Sterile container	4°C	Within 48 hr: 4°C Longer than 48 hr: -70°C
Lower respiratory tract specimen: lung biopsy	Sterile container with saline	4°C	Within 48 hr: 4°C Longer than 48 hr: -70°C
Serum	Serum separation test tube : adults and children, 3–5 mL; infants, 1 mL	4°C	Within 5 days: 4°C Longer than 5 days: -70°C

MOLECULAR ASSAYS

Primers targeting different sections of the virus genetic sequence including the envelope E gene, the RNA-dependent RNA polymerase (RdRp) gene, and the N gene are used for RT PCR. Targeting the E gene is reported for highest sensitivity, followed by the RdRp gene for confirmation. The WHO recommends PCR amplification of the viral E gene as a screening test and amplification of the RdRp region of the orf1b gene as a confirmatory test.

REAL TIME REVERSE TRANSCRIPTASE-POLYMERASE CHAIN REACTION (RT-PCR)

RT-PCR method is considered to be gold standard for diagnosis of COVID-19 infection as well as asymptomatic carriers[2]. Several RT- PCR protocols for detection of SARS-CoV-2 RNA have been posted by world health organization on its website and commercial assays are designed based upon these protocols. The RT-PCR test includes extraction of RNA from the patient specimen, conversion to DNA and PCR amplification with SARS-CoV-2-specific primers. Most of them consist of 40-45 amplification cycles. In general these assays have estimated limit of detection ranging from 100 – 1000 viral RNA copies per millilitre of transport media[3]. The test is run in batches and the procedure takes around four hours to complete. Most of the commercial assays are qualitative and results are reported as detected, not detected and indeterminate. The sensitivity of RT-PCR from various systematic reviews is about 70% and specificity is 95%.

RT-PCR tests have limitations when used to guide decision making for individual patients. Positive test can be useful to diagnose COVID-19, a negative test cannot be considered definitive to exclude infection. This is because some patients with COVID-19 do not have high levels of virus detectable in the upper respiratory tract.

CYCLE THRESHOLD

The cycle threshold (Ct) indicates the number of cycles in RT PCR test needed to amplify viral RNA to reach a detectable level. The Ct value can vary due to many factors including site of respiratory sample, type of local immunity and how the sample is collected and transported. The Ct values are not standardized across various PCR platforms and diagnostic kits, so test results cannot be compared across different assays. Moreover, no clinical studies have validated use of Ct to guide management.

INDETERMINATE RESULT

The indeterminate or inconclusive RT PCR results could be due to virological causes, sample quality and technical issues in RNA extraction[4]. The most common reason for indeterminate result is problems related with RNA extraction. It may vary with different kits and systems (automated or manual) used for nucleic acid extraction. The automated robotic extraction system has greater precision in terms of purity and yield of extracted RNA in comparison to manual extraction process. The other causes are inappropriate sample collection technique (inadequate swabbing), poor quality of viral transport medium and deficient cold chain during sample transport. In some cases, an indeterminate result could be due to identification of only one of the two or more genes of the RT PCR assay. This can happen at very early or late stage of infection due to low viral load levels. Rarely, inconclusive result could also occur due to nonspecific binding of PCR primer or probes in late PCR cycles. The management of indeterminate RT PCR results includes repeat extraction, repeat PCR from fresh RNA extract in case of failure of internal control and occasionally repeat freshly collected sample is required if the cause is virological.

RAPID & POINT OF CARE NAAT: REVERSE TRANSCRIPTION-LOOP-MEDIATED ISOTHERMAL AMPLIFICATION

Loop-mediated isothermal amplification (LAMP) was developed as a rapid, accurate, reliable, and cheaper technique to amplify the target sequence at a single reaction temperature instead of sophisticated thermal cycling equipment needed in RT-PCR. It can be done as a point of care test and is simple and rapid.

In India, there are two such tests available:

- Cepheid Xpert SARS-CoV-2
- TruNat test.

All tests require a similar sample preparation procedure that involves placing the swab sample into the viral transport media and pipetting the sample into a single-use disposable cartridge—this sample preparation step

takes approximately 2–10 min. The test procedure takes 45- 60 minutes.

The Cepheid Xpert SARS-CoV targets the N2 and E genes and the limit of detection is 250 copies/ml. Trunat COVID-19 is a cartridge based assay by MolBio Diagnostics Pvt Ltd. This targets the E gene and RdRp gene with a detection limit of 407 copies/ml; the sensitivity and specificity being 100%. **(Fig 3)**

Yang et al[5] showed that RT-LAMP and RT-PCR have the same sensitivity and both can detect a 20-fold diluted sample. Additionally, according to Yang et al., the detection limit of LAMP is 1000 copies/mL, which is equal to the rRT-PCR kits. Most importantly, studies have shown that RT-LAMP analysis is extremely specific because it uses six to eight primers to identify eight different regions on the target DNA. A variety of clinical sample types may be used, including oral, throat, nasal, or nasopharyngeal swabs.

To sum up, cartridge based tests have a comparable sensitivity and specificity to RT PCR. They are rapid (takes one hour) and do not need specialized equipment or infrastructure. Upto 4 tests can be done at a time. The cost is approximately Rs. 1400 per test.

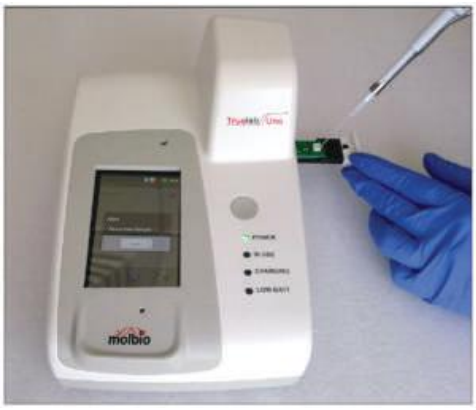


Fig. 3

TruNat (MolBio Diagnostics Pvt Ltd)

ANTIGEN DETECTION

In antigen detection tests, the antibody to SARS-CoV-2 is coated on a card. The patients sample is added to the card. The test can be interpreted as positive or negative after 15 minutes of putting the sample into the well by appearance of test and control lines, which can be read with a naked eye, requiring no specialized equipment. Maximum duration for interpreting a positive or negative test is 30 minutes. As per the ICMR advisory, those who test negative for COVID-19 by rapid antigen test should be definitely tested sequentially by RT-PCR to rule out infection, whereas a positive test should be considered as a true positive and does not need reconfirmation by RT-PCR test.

Serological antigen assays can target S1 and S2 domains of the S protein that binds angiotensin-converting enzyme-2 (ACE-2), an integral transmembrane protein in the lung alveolar epithelium that serves as the initial attachment site for SARS-CoV-2, or N proteins.

In India, 3 rapid antigen kits have been approved by ICMR. Standard Q COVID-19 Ag Test by SD Biosensor, Coris BioConcept COVID-19 respi strip, LabCare diagnostics ltd COVID-19 antigen lateral device. SD biosensor is an immunochromatography rapid test, using nasopharyngeal or throat swab for detection of COVID-19 specific antigen. A study in Malaysia done with this kit showed sensitivity of 80% and specificity of 100%.[6]

Castro[7] in a meta-analysis of diagnostic tests in Brazil found the sensitivity of two rapid antigen tests for SARS-CoV-2 to be 70-86% with a specificity of 95-97%.

In view of its high specificity while relatively low sensitivity, ICMR recommends the use of Standard Q COVID-19 Ag detection assay as a point of care diagnostic assay for testing in the following settings in combination with the gold standard RT-PCR test:

i) Containment zones or hotspots - All symptomatic ILI patients presenting in a healthcare setting and are suspected of having COVID-19 infection.

ii) Asymptomatic patients who are hospitalized or seeking hospitalization, in the following high-risk groups: Patients undergoing chemotherapy, Immunosuppressed patients including those who are HIV+; Patients diagnosed with malignant disease; Transplant patients; Elderly patients (>65 yrs of age) with co-morbidities (lung disease, heart disease, liver disease, kidney disease, diabetes, neurological disorders, blood disorders).

iii) Asymptomatic patients undergoing aerosol - generating surgical / non-surgical interventions: Elective/emergency surgical procedures like neurosurgery, ENT surgery, dental procedures; Non-surgical interventions like bronchoscopy, upper GI endoscopy and dialysis

In another study by **Sochy et al**[8] comparing the rapid antigen test and RT PCR, the specificity of rapid antigen test was 100%, but the overall sensitivity of the COVID-19 Ag Respi-Strip was 30.2%. They suggested that COVID-19 Ag Respi-Strip should not be used alone for COVID-19 diagnosis.

To sum up, rapid antigen tests are easy to use, cheap and can be done as a point of care test. However, the sensitivity of the test is 30-40%. Hence all negative tests of suspect SARI cases should be retested by PCR.

Immune Response in COVID-19

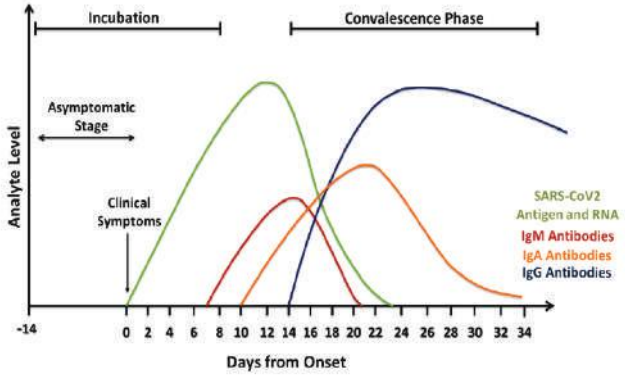


Figure courtesy Viruses 2020, 12, 582; doi:10.3390/v12060582

Fig. 4

Estimation of Biomarker levels in COVID 19 infection.

SEROLOGY

IgM antibody response occurs earlier than that of IgG, with positive IgM antibodies in 70% of symptomatic patients after 8–14 days and about 90% of total antibodies test positive within 11–24 days. On the other hand, IgG antibodies can be detected around 20 days after viral infection and they persist for a long time. Compared to PCR, the IgM detection rate was reported to be lower in the first 5 days post symptom onset (100% for PCR vs.71.4% for IgM), but was higher afterwards (44.3% for PCR vs 87.9% for IgM). Detection of specific antibodies (IgM, IgA and IgG to SARS-CoV-2 spike protein) is useful to confirm SARS-CoV-2 infection in patients with PCR-positive COVID-19, essential in infected but asymptomatic subjects and in COVID-19 patients first examined many weeks after the disease onset or in those with a low viral load. An IgA-Ab response to the S protein was detectable already in week 1 in 3/4 (75%) patients

The SARS-CoV-2 S glycoprotein that mediates attachment and entry into cells is surface exposed and is a key target for the production of host neutralizing antibodies. This feature has made the S protein the focal target of antibody and vaccine development. The N is also a key target for antibody design.

These serological assays are also essential to test the susceptibility or resistance to subsequent re-infection and to perform epidemiological and surveillance studies. These tests are also being used to screen donor blood (convalescent plasma) to be transfused to patients with severe COVID-19.

Rashid et al[3] analysed the diagnostic performance of COVID serology assays. The kits used detected combined IgG and IgM antibodies while some kits detected these antibodies separately. These tests were based on immunochromatography principle and easy to perform on whole blood or serum samples. The results were available within 15 minutes. The sensitivity for both IgM and IgG tests ranged between 72.7% and 100%, while specificity ranged between 98.7% and 100%. Other platforms for serological assays for SARS-CoV-2 include ELISA and lateral flow Immunoassays

FELUDA (CRISPR TECHNOLOGY)

The Tata Group and CSIR-IGIB (Institute of Genomics and Integrative Biology) developed Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) coronavirus test 'Feluda'. The test is named after a fictional detective from West Bengal created by renowned film-make Satyajit Ray. CRISPR is a genome-editing technology to diagnosing diseases. Feluda- the acronym for FNCAS9 Editor Linked Uniform Detection Assay- uses indigenously developed CRISPR gene-editing technology to identify and target the genetic material of SARS-CoV-2. The CRISPR technology can detect specific sequences of amino acids within a gene of DNA and uses enzymes (functioning as molecular scissors) to snip it. The CAS9 protein is impregnated on a strip to interact with the SARS-CoV-2 sequence in the patient's sample. The test results are available in 20-30 minutes. The test has 96% sensitivity and 98% specificity for detecting the novel coronavirus.

SUMMARY

Table 2

Summary of main testing methods for COVID-19

Method	Sample	Detected material	Best time for testing	Time taken for test	% sensitivity specificity	Cost in Rupees	Limitation
RT PCR & CBNAAT	Nasopharyngeal swab Oropharyngeal swab Bronchoalveolar lavage, Tracheal aspirates	Viral RNA	1-7 days	24 hours	70-96% Gold standard test	2500	High cost of reagents & equipments Cross reaction with corona viruses
Antigen test	Nasopharyngeal swab	Protein	1-7 days	30 minutes	30% sensitive, 100% specific	400	Low sensitivity
Antibody test- ELISA, Card test	Blood	Antibodies IgM, IgG, IgA	IgM- 8-14 days, IgG- 21 days onwards	1-2 hours	70%- 90%		

- No test gives 100% accurate results. There is no gold standard for COVID-19 testing[7].
- A positive RT-PCR test for COVID-19 test has more weight than a negative test because of the test's high specificity but moderate sensitivity
- A single negative COVID-19 test should not be used as a rule-out in patients with strongly suggestive symptoms

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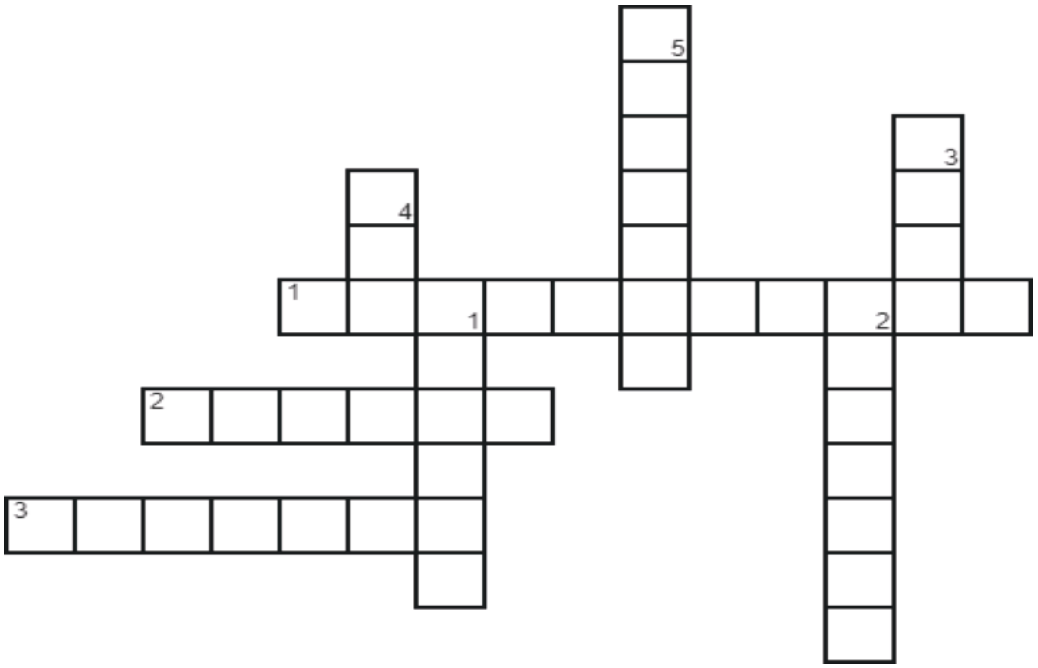
MMJ CROSSWORD

COVID-19 vaccines and drugs:check your knowledge quotient

— **Dr. Peush Bajpai** (Head of Medical Oncology, HCMCT Manipal Hospitals Dwarka, New Delhi)



Across

1. Drug for arthritis and COVID 19.
2. A viral vector vaccine
3. India's indigenous COVID-19 vaccine Bharat Biotech is developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV).

Down

1. Common name for COVID 19
2. Vaccine with 95% efficacy
3. genetic material in Pfizer vaccine.
4. number of doses of vaccine.
5. The Russian Vaccine

* Answers on the last page

Multisystem Inflammatory Syndrome in Children (MIS-C): A life-threatening mysterious complication of SARS-CoV-2

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ABSTRACT:

Multisystem Inflammatory Syndrome in children (MIS-C) is an emerging disease which is temporally associated with COVID-19. It is considered to be an aberrant immune response to SARS-CoV-2 and manifests as hyperinflammatory syndrome with multi-organ involvement. It has overlapping features with Kawasaki Disease/Kawasaki Disease Shock Syndrome/ Toxic Shock Syndrome. Most of the children respond well to IV Immunoglobulin and steroids. The cardiac complications-cardiogenic shock/acute cardiac decompensation/coronary artery aneurysms can be life threatening. So, with ongoing pandemic of COVID-19, pediatricians have to be vigilant and consider MIS-C as a differential diagnosis in any child/adolescent presenting with persisting fever and clinical/laboratory evidence of inflammation. Here we describe a review of MIS-C and 3 cases with three different presentations.

INTRODUCTION:

COVID 19 - a disease that possibly emerged in a small animal market of Wuhan, China, was declared a global pandemic by WHO on March 11, 2020. The initial reports suggested that the clinical manifestation of COVID-19 were milder in children compared to adults.[1] However, in mid-April, a number of case series from European countries and North America described clusters of children and adolescents presenting with clinical features of Kawasaki Disease/Toxic Shock Syndrome requiring ICU admission, who had temporal relation to SARS-CoV-2.[2,3,4]

REVIEW OF LITERATURE:

S. Riphagen et al, observed an unprecedented cluster of eight children with hyperinflammatory shock, showing features similar to atypical Kawasaki disease, Kawasaki disease shock syndrome, or toxic shock syndrome (typical number is one or two children per week) in UK during a period of 10 days in mid-April, 2020.[2] Lucio Verdoni et al, also found a 30-fold increased incidence of Kawasaki-like disease in Italy in the month of March and April 2020.[3] Later, similar cases were reported from other European countries and North America also.[4,6]

WHO and CDC described the disease entity as Multisystem Inflammatory Syndrome in Children (MIS-C) where as RCPCH described it as Paediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2 (PIMS-TS).[5-7] On May 14, 2020, CDC published an online Health Advisory that summarized the manifestations of reported multisystem inflammatory syndrome in children (MIS-C), outlined a case definition, and on May 15th 2020, WHO also developed a preliminary case definition and case report form for MIS-C.[5,6] The RCPCH definition of the illness differs from that of CDC and WHO as it does not require the proof of infection/exposure of SARS-CoV-2.[5-7] **(Table 1)**

In India, S Balasubramanian et al, reported the first case of Hyper-inflammatory Syndrome in a child with COVID-19 from Chennai in July 2020.[8] Later Jain et al, described the presentation, treatment and outcome of 23 children with MIS-C with COVID-19 from four tertiary hospitals in Mumbai, India which was one of the most severely affected cities in India.[9]

Multisystem Inflammatory Syndrome is considered to be an aberrant immune response to SARS-CoV-2 as it is observed to develop 3-4 weeks after infection with the virus. The definition of MIS-C is based on 6 principles- Age, persistence of fever, laboratory markers of inflammation, symptoms and signs of multi-organ involvement, lack of alternative diagnosis and temporal relation to COVID-19. However, it has overlapping clinical features of Kawasaki Disease/ Kawasaki Disease Shock syndrome/ Toxic Shock Syndrome. Kawasaki Disease is a vasculitis that typically presents with high fever and acute mucocutaneous inflammation in children <5 years of age. Although typically a self-limiting condition, some children may have severe complications including coronary artery aneurysms, myocardial dysfunction, and thrombotic events. On the other hand, TSS is a potentially lethal disease derived from the release of bacterial toxins. It is depicted by fever, rash, shock, vomiting and diarrhea, and treated by hemodynamic stabilization and antibiotics.[10]

Multisystem Inflammatory Syndrome is observed to affect older children with the mean age of 9 years but has no predilection for any gender.[10,11] The common symptoms encountered are fever, erythematous rash, abdominal pain or diarrhoea, conjunctivitis and lymphadenopathy.[10-12] Whitaker, et al have proposed three clinical patterns of MIS C presentation viz, those

with shock and cardiac involvement, those with fever and elevated inflammatory markers without features of Kawasaki Disease, and those who fulfilled diagnostic criteria for Kawasaki Disease.[11]

Table: 1

WHO, CDC & RCPCH Case definitions for emerging Hyperinflammatory condition in adolescent & children during COVID-19 pandemic

World Health Organisation	Centers for Disease Control and Prevention (USA)	Royal College of Paediatrics and Child Health (UK)
Children and adolescents 0–19 years of age with fever > 3 days **AND** two of the following: 1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet). 2. Hypotension or shock. 3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP), 4. Evidence of coagulopathy (by PT, PTT, and elevated d-Dimers). 5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain). **AND** Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin. **AND** No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes. **AND** Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.	An individual aged <21 years presenting with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); *Fever >38.0°C for ≥24 h, or report of subjective fever lasting ≥24 h *Laboratory evidence including, but not limited to, one or more of the following: an elevated CRP, ESR, fibrinogen, procalcitonin, d-dimer, ferritin, LDH, IL-6, elevated neutrophils, reduced lymphocytes and low albumin **AND** No alternative plausible diagnoses; **AND** Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms **Additional comments** Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection	1. A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional features . This may include children fulfilling full or partial criteria for Kawasaki disease. 2. Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus (waiting for results of these investigations should not delay seeking expert advice). 3. SARS-CoV-2 PCR testing may be positive or negative

Cardiac manifestations including myocardial involvement, cardiogenic shock, coronary artery aneurysms, acute cardiac decompensation caused by severe inflammatory state after SARS-CoV-2 infection are being reported in patients of MIS-C. Elevated markers of cardiac injury (Troponin, NT proBNP) or abnormal ECHO – decreased left ventricular ejection fraction/ coronary artery aneurysms are the common findings in such patients.[10-15]

The laboratory findings in MIS-C are markers of inflammation – leucocytosis, neutrophilia, high CRP, procalcitonin, ferritin, LDH, triglycerides, markers of coagulopathy – high D-dimers, fibrinogen, deranged PT/ APTT/INR, no evidence of other bacteriological cause and evidence of COVID-19 infection - SARS-CoV-2 RT PCR or COVID-19 antibody.[10-12] The peripheral smear of the patients with MIS-C were found to be consistent with microangiopathy – revealed schistiocytes and burr cells.[16]

The treatment modalities used in most of the cases in the available literature were steroids, IV immunoglobulin and vasoactive drugs. However in a few cases immunomodulatory drugs like IL-1 or IL-6 antagonists were also used.[10-15] A western New York guideline for management of MIS-C (under progress) recommends giving IVIG 2 g/kg and aspirin 20–25 mg/kg/dose every 6 h (80–100 mg/kg/day) for all patients with KD-like illness, evidence of excessive inflammation (ferritin > 700 ng/ mL, CRP > 30 g/dL, or multisystem organ failure), or cardiac involvement. Patients with KD-like illness in high-risk categories (infants, KD shock syndrome, CRP > 130 g/dL, admission echo Z score > 2.5 or aneurysms, Asian race) should receive IVIG 2 g/kg as single infusion with a three day pulse methylprednisolone. If the presentation is most consistent with KD and there is failure of first line treatment a second dose of IVIG or infliximab (a Tumor necrosis factor (TNF)-alpha inhibitor) could be considered.[17]

According to the available literature the mortality of MIS-C is 1.7% which is comparable to the death rate of adults between 55-65years with COVID-19 disease.[10]

MIS-C may be similar to KD/ KDSS/ TSS but it differs from the same as the children with MIS-C are older, sicker and have greater elevation of inflammatory markers as compared with those of classical KD. Feldstein et al, in their case series of 186 patients of MIS-C observed that approximately 5% of children with Kawasaki's disease in the United States present with cardiovascular shock leading to vasopressor or inotropic support as compared with 50% of the patients in their series.[13] Also, the cytokine profiles associated with the MIS-C particularly marked elevations in IL-10 were found to be distinct from previously reported cytokine profiles in KD, which tend to be associated with mild elevations of IL-1, IL-2, and IL-6.[16]

CASE SERIES:

Here we report 3 cases of Multisystem inflammatory syndrome with varied presentations but with similar investigation results and responded well to treatment.

Case 1: A 2 year 9 months old female child was admitted with complaints of fever for 5 days, vomitings for 2 days which subsided subsequently and poor oral intake. There was no H/o of any cough, cold, loose motions, pain abdomen, rash, joint pains, headache, seizures or urinary complaints. There was no H/o contact with suspected/confirmed case of COVID-19. On examination Weight: 9Kg, The child look sick, was febrile (101.4ºF), had strawberry tongue, pre-auricular and post-auricular swelling with redness and induration, erythema in palms and soles, abdominal, gluteal and perineal blanchable rash. The child was hemodynamically stable, maintaining SpO2 of 97% in room air. Systemic examination was normal except that the child was irritable. The child was admitted with above mentioned complaints and provisional diagnosis of Acute lymphadenitis/ ? Kawasaki Disease. She was started on Inj Augmentin, Inj Clindamycin, along with other supportive treatment.

Initial investigations revealed Hb-9.3 gm%, TLC-9540 / cu.mm, P91, L6, Plt 1.64 lac, CRP 241.8 mg/lt, ESR 32, SGOT/SGPT:101/76 IU/lt, Urea-12 mg/dl, Creat-0.32 mg/dl, Na 128 mmol/lt, Ca- 8.7 mg/dl, K 5.7 mmol/lt, Dengue NS1 negative. COVID PCR was negative. CXR showed right sided opacity. **(Fig 1 a)** USG neck revealed multiple enlarged cervical lymph nodes. After 48 hrs of antibiotics also, high grade fever continued, facial swelling, edema and redness over both upper eyelids increased and the child also developed diarrhoea. At this time the child had features of compensated shock (tachycardia, tachypnea, flash CFT, cold peripheries and blood gas showing metabolic acidosis and increased lactate), hence the child was shifted in PICU and started with HHHFNC and epinephrine infusion. Possibilities of Toxic Shock Syndrome, Kawasaki Disease, and MIS-C were considered. Repeat investigations revealed worsening counts (TLC 16570 with 83% Polys), falling platelets (1 lac), deranged LFT, further increase in CRP (258), and markedly Triglycerides & Ferritin (101/ 1022). **(Table 3)** Antibiotics were upgraded to meropenem, vancomycin with clindamycin considering Staphylococcal Toxic Shock Syndrome.

On day 4 of admission, ECHO showed mild LV dysfunction (Ejection Fraction 50%, No coronary dilatation), CPK-MB 53. IvIg was started in view of possibilities of Toxic Shock Syndrome/ Kawasaki Disease or Multisystem Inflammatory Disease. CBC: Hb 6.9 gm%, TLC 23570 / cu.mm, P85%, L13%, Plt 60000 /cu.mm, Blood culture and Urine C/S - sterile, LDH 408, D-dimer 1.4, COVID antibodies were positive. Packed red cell transfusion was given. As there was no significant improvement after IVIG (2 gm/kg), Methylprednisolone at dose of 5mg/kg/day in two divided doses was added.

By day 5-6 hemodynamics improved, tachycardia settled, adrenaline was tapered but there was increase in oxygen requirement and HFNC flow. CXR and HRCT chest was done. CXR showed B/L opacities. **(Fig: 1b)** HRCT chest revealed bilateral moderate pleural effusion with segmental / subsegmental basal atelectasis (? Passive changes) and presence of perihilar / central lung field opacities with air bronchogram and peripheral ground glass haze with dependent gradient. **(Fig 1c)**

Possible D/D considered were 1. ARDS 2. Fluid overload 3. Atypical pneumonia. Pulmonary CT angiogram was normal. Child also had an episode of melena on platelets count of 30,000 /cu.mm so was also given 2 unit of RDP. Furosemide infusion was started as the child had gained 10% of body weight since admission.

By day 7-8 the child started showing improvement in form hemodynamic stability, reduction of fever spikes, settling of loose stools and improvement in oral acceptance. Investigation revealed normal counts, improving platelets and LFT, settling down of all the inflammatory markers (CRP = mg/lt, LDH = I.U/lt, and Ferritin = ng/ml) and improved Chest X-ray. **(Fig 1d)** HFNC was stopped once patient was maintaining SpO2 in room air. Pediatric Cardiology opinion was again sought and repeat ECHO still showed LVEF 30-35%. The child was started on Tab Enalapril and Furosemide drops. I.v Methylprednisolone was given for 5 days and then switched to oral prednisolone. Tab Spironolactone was added in view of hypokalemia. Injection Meropenem and Vancomycin were given for 8 days and patient was discharged on oral prednisolone in tapering doses, Tab Enalapril, Furosemide drops and Tab Spironolactone.

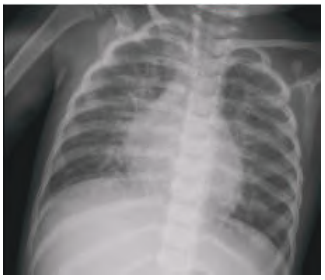

Fig 1a: CXR (Day 2 of admission)

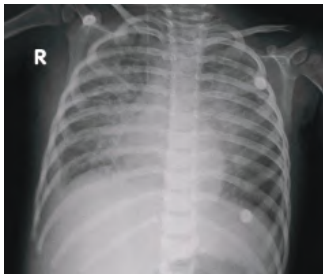

Fig 1b: CXR (Day 5 of admission)

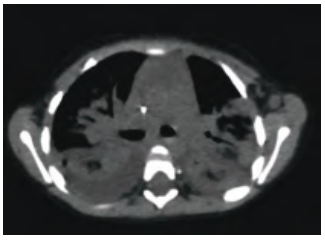

Fig 1c: HRCT (Day 6 of admission)

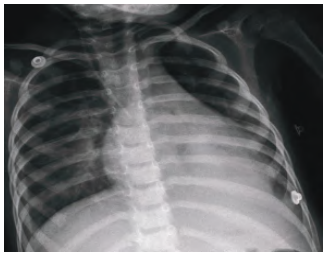

Fig 1d: CXR (Day 9 of admission)

Case 2: 12 yr old boy presented to ER with complaints of fever for 13 days which was remittent, documented upto 102*F, vomiting for 5-6 days initially, which later subsided, swelling of hand, feet and pain abdomen for 6 days and breathing difficulty for 3-4 days. There was no history of cough, loose stools, rash, bleeding from any site, decrease urine output, headache, irritability or lethargy. There was no history of contact with COVID-19 patient.

Initially, the child was treated at home and became afebrile, but fever again started coming and the child was admitted in a government hospital in view of persistent high fever, vomiting and swelling in the hands and feet. Investigations revealed: Hb 10.3 gm%, TLC 5400/cu.mm, P84 L10, HCT 30.5%, PLT 40,000, Typhidot Negative, Dengue Serology Negative, SGPT/SGOT 269/223 IU/lt, S. Albumin 2.7g/lt, KFT Normal, USG abdomen: mild ascites, B/L pleural effusion. He was managed with Inj Ceftriaxone, Inj Vancomycin, and Inj Artesunate along with other supportive treatment. During the course of stay he became hypotensive and was started on colloids and Dopamine infusion. In view of persisting high fever and no improvement in the general condition of the child despite treatment, the parents took discharge against medical advice and brought the child to our hospital for further management.

At admission, the child was febrile, tachycardiac, tachypneic, SpO2: 88-89% in room air, BP 107/73, with mild peri-orbital, facial puffiness and generalised flushing, Chest – decreased breath sounds in Rt infra-axillary and infra-mammary area, B/l fine basal crepts +, P/A – was soft, liver: 3cm below Rt SCM, splenomegaly, no tenderness, CVS – S1S2+ no murmur, CNS – GCS: 15/15, no meningeal signs. The child was admitted in PICU and started on O2 by mask, IV fluids, Inj Ceftriaxone, Inj Vancomycin, Syp Paracetamol and Inj Dexamethasone. Initial investigations revealed: anemia, leucopenia, thrombocytopenia (platelet 70000), high inflammatory markers (CRP 162 mg/L, Procalcitonin 6.17 ng/ml, Ferritin 9593 ng/ml, D-dimer 0.5mg/L, LDH 1092 IU/L, triglycerides 458mg/dl), deranged LFT with hypoalbuminemia, high CPK MB. **(Table 3)** Malaria Ag was negative, CXR revealed B/L peripheral airspace opacities – ?pulmonary edema. **(Fig 2a)**

Over next few hours, the respiratory distress of the child worsened, was not maintaining SpO2 on HHHFNC, hence was intubated and started on mechanical ventilation. PRBC was transfused and inj furosemide was given for pulmonary edema. In view of multisystem involvement and high inflammatory markers, Inj Methylprednisolone was added. Subsequent investigations revealed, Dengue IgM positive, Anti SARS CoV-2 antibody positive, Scrub typhus serology positive, Fibrinogen levels: 53.7mg/dl. Considering possibility of MIS-C, intravenous Immunoglobulin was started and Azithromycin was added in view of positive scrub typhus serology. The child improved with the above treatment, became afebrile, and was weaned off from ventilator after 48 hours to free flow O2. **(Fig 2c, 2d)** ECHO was normal (LVEF: 60-65%). The blood culture and urine culture were sterile. Ceftriaxone and Vancomycin were stopped after 3 days and Azithromycin was given for 7 days. The platelet counts improved (95,000) and inflammatory markers decreased. The child was discharged after 6 days on tapering doses of steroids.

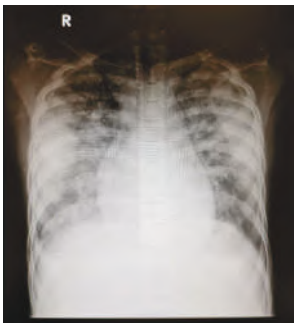

Fig 2a: CXR at admission

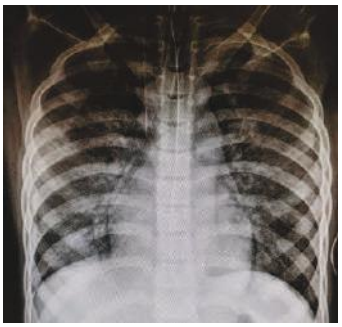

Fig 2b: CXR after Intubation

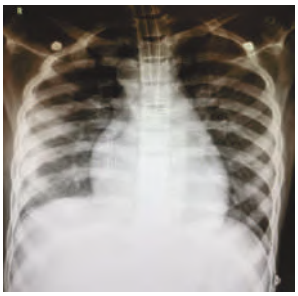

Fig 2c: CXR on Day 2 of admission

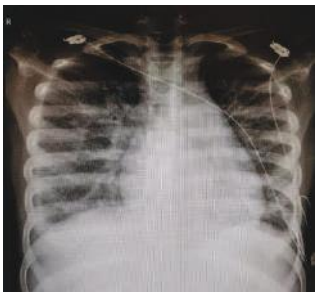

Fig 2d: CXR after Extubation

Case 3: A 6 year old female child was admitted with complaints of high grade fever for 4 days, pain and swelling in left ankle joint for 12 hours and pain in the right shoulder joint for a few hours. The child was not able to bear weight on the left leg. There was H/o loss of appetite. There was no H/o of diarrhoea, vomiting, loose motions, cough or cold, eye discharge or burning micturition. The child had history of fever 1 week back which lasted for 4 days and subsided with paracetamol only. On examination, the child was hemodynamically stable, no respiratory distress, SpO2: 99% in room air, no pallor/ icterus/ lymphadenopathy, S.E: was normal. The child was admitted with a provisional diagnosis of Septic Arthritis and started on Inj Ceftriaxone and Inj Flucloxacillin along with supportive treatment. Initial investigations revealed normal counts (TLC: 10,010/ cu.mm, P81%), CRP 157mg/lt, ESR 53, SGOT/ SGPT 58/59 IU/lt, Widal negative, Chikungunya serology negative, COVID rRT PCR negative, CXR- mediastinal widening. **(Fig 3a)** Over next 24 hours, pain and swelling also appeared in right ankle and was noticed to have tachycardia (HR: 140-150/min). The child was further evaluated for alternate diagnosis (MIS-C, Juvenile Rheumatoid Arthritis, Rheumatic fever). Subsequent laboratory investigations revealed high inflammatory markers, high d-Dimer and troponin, **(Table 3)** ASO titres negative, Rheumatoid Factor mild positive, COVID-19 antibody titre positive. CT Chest showed small peripheral wedge shaped patch of ground glass opacities in basal segment of left lower lobe **(Fig 3b)** and ECHO was suggestive of valvulitis. **(Fig 3c)** Later the child also developed rash in hand and feet. With COVID-19 antibodies positive and multiple systemic involvement, the possibility of MIS-C /KD was kept and treatment was initiated with IV Immunoglobulin and Inj Methylprednisolone. The child showed significant improvement within 24 hours of IV Ig as the swelling over the joints decreased, joint pain decreased and mobility improved. The blood C/S grew MRSA but since the child responded to treatment of MIS-C, no further intervention was done. The arthritis improved, although child had some pain while walking and repeat inflammatory markers showed significant improvement. The child was discharged on tapering doses of steroid. **(Table 4)**

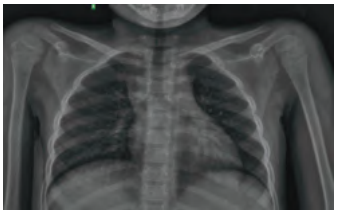

Fig 3a: CXR Mediastinal widening

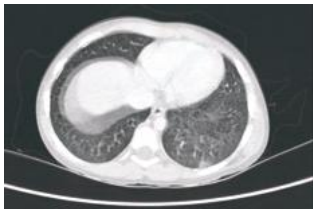

Fig 3b: CECT Chest wedge shaped ground glass opacity

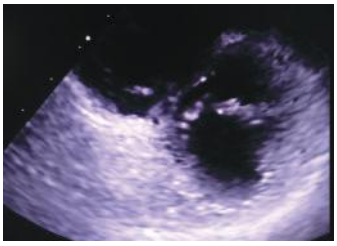

Fig 3c: ECHO: Nodularity in Mitral Valve

Table 2
Clinical features of patients with MIS-C

	Case 1	Case 2	Case 3
Age/Sex	2yr 9 months/ Female	12yrs/ Male	6yrs/ Female
Comorbidities	None	Intermittent Asthma	None
Fever	Yes	Yes	Yes
Rash	Yes	No	Yes
Strawberry tongue/ fissured lips	Yes	No	Yes
Pain abdomen	No	Yes	No
Loose stools	Yes	No	No
Lymphadenopathy	Yes	No	No
Extremity edema	Yes	Yes	Yes
Arthritis	No	No	Yes
Shock	Yes	No	No
Respiratory Failure	No	Yes	No
CHF	No	Yes	No

Table 3
Investigations of patients with MIS-C

	Case 1	Case 2	Case 3
TLC(5000 - 15000/ cumm)	9450	5830	10,010
Neutrophils (40-70%)	91.5%	55%	81.2%
Platelet (1.5L-4.0L/ cu.mm)	1.64L	70,000	2.32L
CRP (<5mg/L)	241	162	157
ESR (0-20)	32	-	53
Procalcitonin (<0.5ng/ ml)	79.18	6.17	-
Ferritin (12-73ng/ml)	1022	9593	1024
LDH (150-300IU/L)	408	1092	297
Triglycerides (<150mg/ dl)	101	458	-
PT/INR	14.5sec/ 1.25	45.6sec /4.20	10sec/ 0.84
D Dimer (0-0.5mg/L)	1.4	0.5	3.2
Fibrinogen (180-350mg/dl)	-	53.7	-
Albumin (3.5-5.2g/dl)	2.2	2.1	-
CPK–MB (0-25IU/L)	53	59	17
Troponin I (<19ng/L)	-	-	46

Table 3

Investigations of patients with MIS-C

ECHO	LVEF 30-35%	LVEF 60-65%	Nodularity in mitral valve
Blood Culture	Sterile	Sterile	Staph aureus (MRSA)
COVID-19 RT PCR	Negative	Negative	Negative
COVID Antibody	Positive	Positive	Positive

Table 4

Treatment given to the patients with MIS-C

Treatment	**Case 1**	**Case 2**	**Case 3**
PICU	YES	YES	NO
Respiratory Support	HHHFNC	Mechanical Ventilation	None
IV Immunoglobulin	1st dose: @ 2 gm/kg 2nd dose: @ 1 gm/kg	Single dose: @1 gm/kg	Single dose: @ 2 gm/kg
Steroid	Methylprednisolone @ 5 mg/kg/day for 5 days followed by oral Prednisolone @ 2 mg/kg/day in tapering doses	Inj Dexamethasone Stat dose @ 0.15mg/k Methylprednisolone @ 5 mg/kg/day (max: 100mg/day) for 3 days then tapering doses	Methylprednisolone @2mg/kg/day for 2 days followed by Oral Prednisolone @ 2 mg/kg/day in tapering doses
Antibiotics	Amoxy-clav Clindamycin Meropenam Vancomycni	Ceftriaxone Vancomycin Azithromycin	Ceftriaxone
Blood transfusion	PRBC transfusion Platelet transfusion	PRBC transfusion	None
Length of hospital stay	12 days	7 days	6 days

DISCUSSION:

We have described here three cases of Multisystem inflammatory syndrome in children (MIS-C) who had 3 different presentations at admission. First case presented as acute lymphadenitis, second one presented as febrile illness with hepatosplenomegaly and respiratory distress and third case as acute arthritis. All the three cases had fever, high inflammatory markers, cardiac involvement and were COVID-19 antibody positive. Two of them required ICU admission and respiratory support.

All the three patients were treated with IvIg and steroids (methylprednisolone). However there was a lot of dilemma regarding the dose of the medications. Various studies in literature have used different doses of IvIg and steroids and we also individualized the doses based on response to treatment. First case showed no improvement after first dose of IvIg (@ 2gm/kg so a repeat dose of IvIg (@1 gm/kg and methylprednisolone @ 5 mg/kg/day was given. In contrast second case responded well to single dose of IvIg @ 2 gm/kg and methylprednisolone @ 5 mg/kg/day. The third case received single dose of IvIg @ 2gm/kg and methylprednisolone @ 2 mg/kg/day. **(Table 4)**

Cardiac involvement in all the three cases were different – first case had cardiogenic shock and low left ventricular ejection fraction, second case had features of pulmonary edema and third case had tachycardia with ECHO showing features of mitral valvulitis.

Any alternate diagnosis was ruled out in first case, however second case had positive scrub typhus and Dengue IgM serology. Third case had a blood culture growth of Staph aureus (MRSA) but the child responded well to Inj Ceftriaxone, IV Ig and methylprednisolone.

Most of the clinical features and laboratory findings in our case series were similar to those published earlier. However, acute arthritis of large joints (ankle and shoulder) have not been described earlier.

CONCLUSION:

In the current scenario, MIS-C should be strongly considered as a differential diagnosis in the management of any child/ adolescent presenting with persistent fever and evidence of inflammation (clinical/ laboratory). However, MIS-C being a new disease entity, is creating lot of dilemmas in the diagnosis and management. More studies and analysis of a large data from children presenting with MIS-C would be required to understand the disease and in developing protocols for diagnosis and management.

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Laparoscopic Gastrointestinal Surgery in the COVID Era - Experience of a Tertiary Care Hospital

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INTRODUCTION:

SARS-CoV-2 infection was declared a global pandemic and India along with rest of the world went into a state of lockdown in March 2020. Healthcare field and especially the surgical field were faced with a need to prioritize their resources to treat the patients. Protocols were made and adapted to each country as per their local context. In the surgical field many organizations laid down guidelines on performing safe surgeries. Laparoscopic surgery especially came under scrutiny as it was an aerosol generating procedure and precautions that can be taken and modifications that can be done to ensure personnel safety were suggested.[1]

In an effort to continue to cater to the surgical load presenting in our hospital we also adapted to the situation and started incorporating modifications in the functioning, so as to ensure a safe environment for both our patients and healthcare workers. In this paper we look at the laparoscopic gastrointestinal surgeries done for a period of nearly 100 days post announcement of the lockdown and see the recovery outcomes of these patients.

METHODOLOGY:

The study is a cross sectional observational study conducted from April 1st to September 30th 2020 in the Department of Minimal Access Surgery, Gastrointestinal and Bariatric Surgery at our hospital. All consecutive patients who underwent emergency or elective laparoscopic surgery in the department during this period were included for the present study. Patients were followed up for one week post discharge from the hospital.

Data collection was done retrospectively from the case records of the patients. Data collected included mainly the demography and the type of surgery done and the diagnosis. This information was taken from the electronic case records. All patients who presented for the surgical procedure were advised one week quarantine pre procedure. After this they were subjected to COVID-19 rRT-PCR testing. Once negative, the patients were admitted to the Green zone of the hospital and then underwent the operative procedure. All the members of the anaesthesia and the surgical team took adequate precautions and used personnel protective equipment during the procedure as depicted in **Fig. 4**. Post discharge they were again asked to self-isolate to minimize contact and they were then reviewed one week following surgery. This was done mainly to review the wound and to assess their overall general condition following the operative procedure.

For patients who presented as an emergency and where the general condition of the patient did not permit waiting for the rRT-PCR results to come before the operative procedure, the following hospital protocol was adopted. These patients were admitted in the amber zone for the suspected cases and then the rRT-PCR sample was sent. But the test results were not awaited and the patients were taken up for the emergency procedure. To minimize contact with the rest of the patients, these patients were directly shifted to operation theatres specially designed for managing these suspect patients through a dedicated channel with the healthcare workers taking all the standard precautions of using the full Personal Protection Equipment (PPE).

Postoperatively after ensuring the recovery of patient from anaesthesia, they were again shifted back through the dedicated channel to the post-operative wards. They were not kept in the common recovery area with the other tested negative patients to prevent cross infection. Intraoperatively few of the modifications that were standardized for the institution were:

i) All patients requiring general anaesthesia were intubated using Video laryngoscopy to increase the distance and decrease the droplet spread. In addition, an impervious plastic sheet was used as a barrier between the intubating healthcare worker and the patient. This is depicted in **Fig. 1**

ii) The intraabdominal pressures and volumes were set a new low level.

iii) The fumes generated and aerosolized during the surgery were vented out through a separate suction tubing into a hypochlorite solution before it was evacuated through the central suction as shown in **Fig. 2.**

iv) Laparoscopic smoke filters were also used in few of the cases as shown in **Fig. 3.**

v) During intubation and extubation of the patient it was ensured that bare minimum people required were only allowed into the operating theatre.

vi) Personal protection equipment (PPE) donning and doffing areas were identified in the operation theatre and the process of donning and doffing was supervised to ensure no breach in the protocol of handling these cases.

Fig. 1

Videolaryngoscopy being performed by the anaesthesia team to intubate the patient who was SARS-CoV2 RT-PCR negative

Fig. 2

Figure showing the collection of the vented out fumes into the hypochlorite solution through a separate suction tubing.

Figure 3

PALL filter, attached to one of the 5mm ports, used to filter out the fumes generated during laparoscopic surgery.

Fig. 4

Personnel protection Equipment used by the members of the surgical team in a SARS-CoV2 negative RT-PCR case undergoing Laparoscopic Cholecystectomy.

RESULTS:

A total of 307 procedures were done in the Department of Minimal Access, Gastrointestinal and Bariatric Surgery during the time period of the study. This included the elective and emergency surgeries performed during the study period. The total number of cases also included both laparoscopic and open procedures done for varied diagnosis **(Fig 5)**.

Fig. 5

Flowchart showing the patients included for the study.

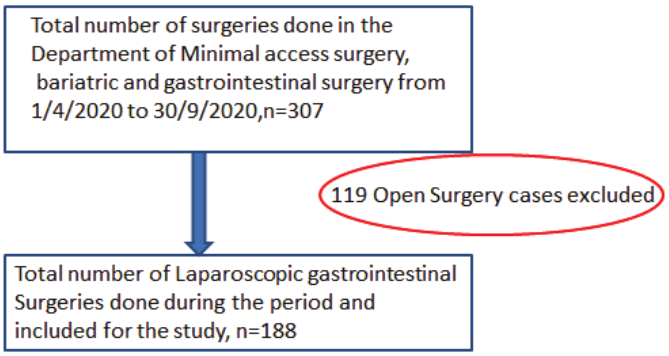

Table 1

Demographic characteristics of the patients who underwent surgery in the Department of Minimal access, Gastrointestinal and Bariatric Surgery

Characteristic	Total number, n=307
Age (Mean) in years	38.7
Gender, n (%) Male Female	166 (53.8) 141 (46)
Operative procedures, n (%) Laparoscopic Open	188 (61) 119 (38.6)

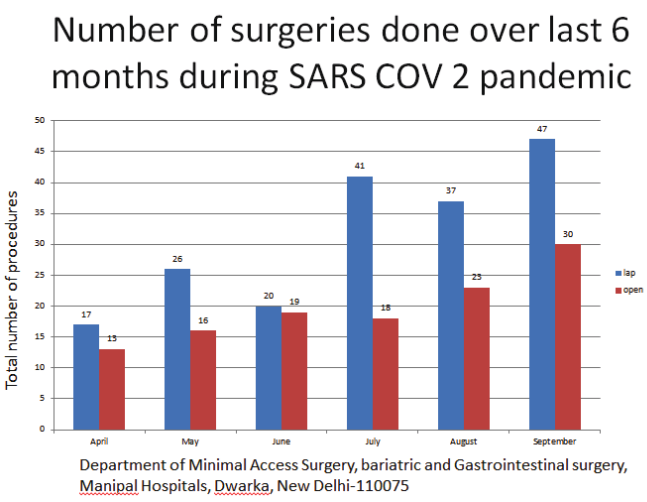

Fig. 6

Graph depicting the time trend of cases operated by the department over period of 6 months

Table 2

Description of operative procedure done laparoscopically for varied indications in study period

Name of the procedure done	Total number n=188, n (%)
Laparoscopic Cholecystectomy	118 (62.7)
Laparoscopic Appendectomy	24 (12.7)
Laparoscopic Ventral Hernioplasty	8 (4.2)
Laparoscopic Inguinal hernioplasty	22 (11.7)
Laparoscopic Hiatus hernia repair with Fundoplication	4 (2.1)
Laparoscopic Anterior resection of rectum	1 (0.5)
Laparoscopic Bariatric Surgery	5 (2.6)
Laparoscopic D1 resection with gastrojejunostomy	1 (0.5)
Laparoscopic Common Bile duct exploration	1 (0.5)
Laparoscopic Meckel's diverticulectomy	1 (0.5)
Laparoscopic mesenteric lymph node biopsy	1 (0.5)
Laparoscopic Omental harvest	1 (0.5)
Laparoscopic Varicocele surgery	1 (0.5)

As depicted in **Table 1**, nearly two thirds of the cases were done laparoscopically during the study period. The average age of the cases operated was 38.7 years. The males were slightly more than the females (53.8% versus 46%) in the operated cohort. Cholecystectomy was the most common procedure done during this period. This was done for a wide range of indications like symptomatic Cholelithiasis, post biliary pancreatitis, acute cholecystitis, post ERCP and stone extraction. Appendicectomy was the second commonest procedure done. Here again the indications ranged from acute appendicitis to Appendicular perforation with abscess formation. Other surgeries done during this period were surgeries for ventral hernia, inguinal hernia, hiatus hernia, surgeries for rectal cancer and neuroendocrine tumour. Five patients underwent metabolic surgery and one diagnostic procedure was also done laparoscopically.

All the patients were followed by for one week following surgery and none of the operated patients had any symptoms of SARS-CoV-2 on follow up. The patients recovered well and wound also healed well when assessed at one week following surgery.

DISCUSSION:

Laparoscopic Surgery versus open surgery, which is safer in terms of aerosol generation is a debate that goes on. Studies have been done which have shown that breathable aerosols and cell size fragments are generated during laparoscopy ranging in size from 0.1 to 0.25 micrometers especially during the use of thermal energy sources.[5]

An aerosol is defined as a suspension of solid and liquid particles in gas. In laparoscopy this gas is carbon dioxide. Few other viruses have been demonstrated in the laparoscopically generated smoke in studies done earlier. It is not clear if the SARS-CoV-2 virus has similar properties and its presence in the smoke generated has not been proven.[2]

The argument against the use of laparoscopic surgery during the COVID pandemic that was raised and discussed at multiple forums was based mainly on caution and not based on data showing the same.[3,4]

Closed circuit systems have been advocated to deal with the smoke generated.[2] This can ensure a safe disposal and prevent contamination of the operation theatre. Laparoscopic smoke filters have been shown to be effective in filtering certain viruses and upto a size of 0.02 micrometer. Both these systems were used in our study cohort of patients depending on feasibility and availability but no comparative study was done to assess efficacy of one method over the other.

In our study we have made an attempt to show that laparoscopic gastrointestinal surgeries can be performed safely if certain modifications and adaptations are made to the protocol followed. There is a need to continue doing the surgeries safely without postponing them otherwise the non-COVID patient burden would increase and lead to worsening of treatable conditions.

CONCLUSION:

Laparoscopic gastrointestinal surgeries can be performed safely in these times of the pandemic if the necessary precautions are taken and no deviations from the set protocol is ensured.

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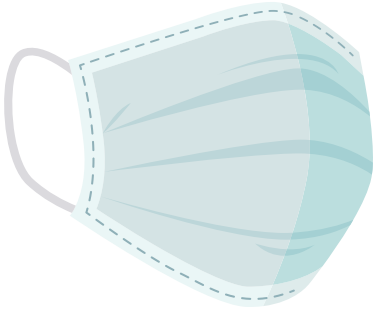

THE MASK

Wear me,
Flaunt me,
Use me, up to you.
But don't you avoid me,
I will surely protect you.

I am your savior,
I am your confidence,
You saved me from extinction,
I will help you till your end.

You help me, I help you.
You need me, I need you.

Wash me,
Hang me,
Throw me,
Reuse me,
But always do keep me.

Some had me matched.
Some had me layered.
Some stitched me at home.
Some bought me online.

N 95 for the doctors.
Surgical for everyone.
Clothed ones for public.

Corona virus,
Swine flu,
Cold virus,
Can't cross me.
Pull me down, pull me out,
But do remember my two walls in and out.

Keep me safe,
Keep me close,
Use me wise,
Let me shine.
I am the mask which you can never hide.

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Use of Extra-Corporeal Membrane Oxygenation in Patients with Cardio-Pulmonary Failure due to COVID-19 Disease – Our Experience

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ABSTRACT:

Introduction: As coronavirus disease 2019 (COVID-19) cases surge in India and worldwide, an urgent need exists to enhance our understanding of the role of extracorporeal membrane oxygenation (ECMO) in the management of severely ill patients with COVID-19 who develop acute respiratory and cardiac compromise refractory to conventional therapy. The purpose of this manuscript is to review our initial clinical experience in 5 patients with confirmed COVID-19 treated with ECMO.

Methods: The data for 5 patients who underwent ECMO for respiratory failure due to COVID-19 was retrospectively collected and analysed. The data captured included patient characteristics like age, sex etc, the need for inotropes, after how long did they need ECMO support, cannulation techniques, inotropic requirements, their treatments and outcomes.

Results: The mean age of patients was 48 years and there were 4 males and one female. None of the patient required ECMO on day of admission. The patients were initially supported with ventilation and prone positioning and other conservative therapies before resorting to ECMO. All patients were on V-V ECMO for support with Rt femoral vein and Rt IJV cannulation via percutaneous route. Four out of 5 patients could be successfully weaned off ECMO and 3 could be successfully discharged from the hospital. One patient died after successfully weaning from ECMO due to severe neutropenic sepsis

Conclusion: Analysis of these severe COVID-19 patients with respiratory failure, supported with ECMO suggests that ECMO may play a useful role in salvaging select critically ill patients with COVID-19. Additional patient experience and associated clinical and laboratory data must be obtained to further define the optimal role of ECMO in patients with COVID-19 and acute respiratory distress syndrome (ARDS). These data may provide useful information to help define the best strategies to care for these challenging patients

Keywords: ECMO, COVID-19, Cardio-pulmonary failure, Inotropes.

INTRODUCTION:

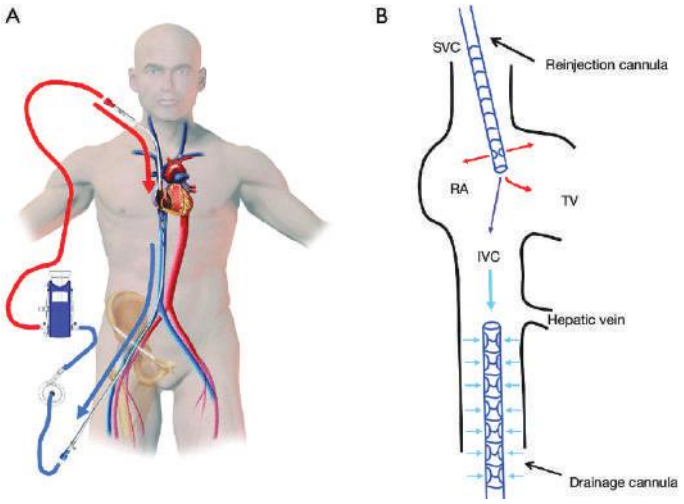
As of mid-November more than 50 million cases of COVID-19 have been reported worldwide. Maximum number of cases (more than 10 million) have been reported from United States of America while India stands second with 8 million reported cases and 1.5 lakh deaths.[1,2] Most deaths in patients with COVID-19 are due to severe respiratory failure, with a smaller group succumbing to combined pulmonary and cardiac failure.[2,3]

Extracorporeal membrane oxygenation (ECMO) is an advanced life support modality that was initially used to treat severe neonatal respiratory failure.[4,5] Over time, the use of ECMO has expanded, with ECMO presently utilized widely to treat multiple forms of severe acute respiratory, cardiac, or combined cardiorespiratory failure in neonates, infants, children, and adults. SARS-CoV-2, the virus which causes COVID-19, primarily attacks the lungs and causes acute hypoxemic respiratory failure in a subset of patients. Large case series from China and New York suggest that 5 – 14% of patients require intensive care and 2 – 20% will require invasive mechanical ventilation.[6-9] Nearly all of these patients will have the acute respiratory distress syndrome (ARDS) and thus require lung-protective ventilation (LPV).[9-10] Severe hypoxemia may be improved with the prone position, positive end-expiratory pressure (PEEP) optimization, neuromuscular blockade and inhaled pulmonary vasodilators.[11-15] Patients with refractory hypoxemia or hypercarbia as well as patients with right ventricular failure resulting from hypercarbia, acidemia or hypoxic pulmonary vasoconstriction may benefit from extracorporeal life support (ECLS) through venovenous (V-V) extracorporeal membrane oxygenation (ECMO). In addition, a small subset of COVID-19 patients may suffer from cardiogenic shock or massive pulmonary embolism and may be considered for venoarterial (V-A) ECMO.[16]

V-V ECMO involves removing a portion of venous blood and pushing it through a "membrane lung" which fully oxygenates the blood and removes carbon dioxide through counter-flow of a sweep gas, then returning that blood to the right atrium. **(Figure 1)** Replacing the function of the lungs allows for "resting" ventilator

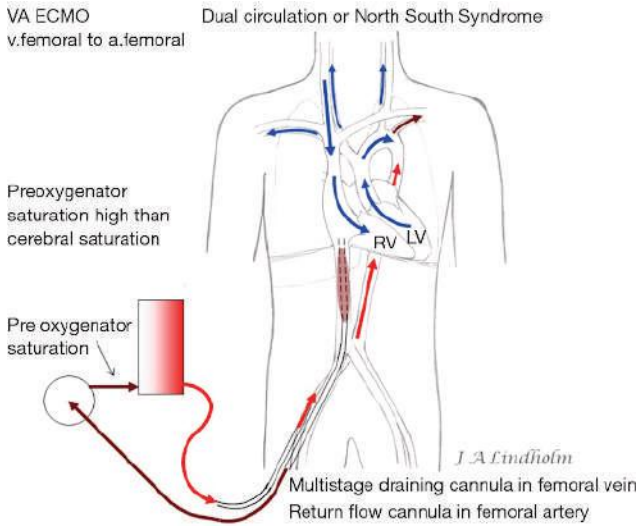
settings to provide lungs the time to heal without further ventilator induced damage.

Fig 1: Veno-Venous ECMO



V-A ECMO **(Figure 2)** involves removing a portion of the venous blood and pushing it through a membrane lung then returning it to the distal-aorta to distribute through the arterial circulation. This results in partial cardiopulmonary bypass thus supplementing the reduced cardiac output of the failing heart with oxygenated blood.

Fig 2: Veno-Arterial ECMO



MATERIAL AND METHODS:

A retrospective analysis of all patients who were admitted at our centre due to COVID-19 and underwent ECMO therapy for severe cardio-respiratory or respiratory failure was done. The data was collected in the form of patient characteristics like age, sex, body weight, body mass index, assosiated co-morbidities, any history of previous significant disease, date of admission and course in the hospital. The treatment that patient received prior to ECMO therapy and during entire course in the hospital was noted, when did the need for ECMO arose and the metabolic and vitals parameters of the patients was recorded during entire hospital course. The data was analysed in the form of mean and median in retrospective manner.

RESULTS:

The data of all the patients who required hospitalization at our centre between March 2020 and September 2020 was looked into. Total 5 patients were identified who needed ECMO therapy for severe respiratory failure. The first patient underwent ECMO in June 2020 and since then our experience has grown with this therapy. All the patients were put on V-V ECMO with femoral vein being used for taking out blood and Right IJV used for inlet of blood. None of the patient required V-A ECMO. A 24 FG cannula was used in all cases for taking out blood from Rt femoral vein and an 18 FG cannula was used to introduce blood from Rt IJV. The cannulation was percutaneous in all the cases.

The hemodynamic parameters were maintained for the patients and all had severe respiratory failure with Chest X-Ray flooding and need for ventilation. The mean age of patients was 48 years with oldest patient being 58 years and youngest being 38 years. There were 4 males and 1 female. The average time between hospital admission and need for ECMO was 6 days with one patient put on ECMO on the day of admission and maximum intervening gap being 16 days post admission. The rest of 3 patients required ECMO after 2 days, 3 days and 10 days respectively. All the patients were proven COVID-19 after admission and were COVID-19 positive at the time of institution of ECMO therapy. All the patients received optimum COVID-19 therapy before being put on ECMO therapy in the form of ivermectin, plasma therapy, wide spectrum antibiotics, Remdisivir, steroids, ventilation, prone position and other standard treatment. Only in the case where patient was put on ECMO on the day of admission due to severe respiratory failure, this was not possible. The vitals monitoring was done and patients were followed up. Three patients could be successfully weaned off ventilator after an average duration of 11 days (10-12 days). The only patient who could not be weaned, was on ECMO for 15 days. One patient died after sucessful weaning after 15 days due to severe progressive neutropenia.

The indications for putting the patient on ECMO were strictly followed in all cases and adequate and optimum trial of conservative management was given before putting the patient on ECMO therapy.

DISCUSSION:

ECMO as a treatment for viral pneumonia causing severe ARDS:

The best data for ECMO as a treatment for respiratory failure in viral pneumonias comes from H1N1 influenza pneumonia. A systematic review and meta-analysis including 494 patients who received ECMO (94% V-V) found overall mortality of 37% (compared to 46% for all-comers with severe ARDS in a recent large epidemiological study[17] with a median duration for ECMO of 10 days. The most recent randomized controlled trial of ECMO for severe ARDS included 21% of patients with viral pneumonia in the ECMO arm and 16% of patients with viral pneumonia in the control group. The survival rate of 65% in the ECMO arm did not represent a statistically significant difference from the control arm, though a

Bayesian analysis suggests there may be a benefit to ECMO. [18-20]

ECMO use for COVID-19:

The cannulation and management of patients on ECMO is a labor, equipment and cost-intensive process, and the decision to do so should not be taken lightly. In all cases and in particular in locations where caseloads and intensive care unit (ICU) occupancy is rising, ECMO should be reserved for cases refractory to the best traditional ARDS and cardiogenic shock management and with the best chance of survival. ECMO can only support the lungs and heart, and patients with chronic systemic disease and irreversible multi-system organ failure are less likely to benefit. Patients being considered for ECMO should be transferred to ECMO centers for management.

The Extracorporeal Life Support Organization (ELSO) maintains a live dashboard of all reported patients treated with ECMO for COVID-19 and issues guidelines for putting patients on ECMO therapy

V-V ECMO as a treatment for respiratory failure caused by COVID-19:

Patient selection for ECMO is critical. Traditional ARDS therapies (Lung protective ventilation, neuromuscular blockade for significant ventilator dyssynchrony, patient proning, inhaled pulmonary vasodilators) should be maximized prior to initiating ECMO. Early transport to ECMO centers should be considered [21]

- if PaO2/FiO2 is < 60 mm Hg for > 6 hrs or < 50 mm Hg for > 3 hrs and/or
- pH <7.20 for > 6 hrs + PaCO2 > 80 mmHg for > 6 hrs (while targeting plateau pressure <30 cm water) [21-23]

V-A ECMO as a treatment for cardiogenic shock caused by COVID-19:

COVID-19 is primarily a respiratory disease, but does have cardiovascular manifestations as well and can occasionally be complicated by cardiogenic shock.[16,24,25] COVID-19 has been associated with myocarditis, septic or stress cardiomyopathy, acute coronary syndrome as a result of a potential hypercoagulable state as well as pulmonary embolism.

Indications for V-A ECMO in the setting of cardiogenic shock from COVID-19 should not differ from indications in other settings.[22,26-28] V-A ECMO should be initiated prior to the development of irreversible multi-organ failure. Occasionally patients on V-V ECMO for respiratory failure will develop cardiogenic shock and require V-A support and can be transitioned to veno-arterial (V-A) ECMO.

Indication:

Refractory cardiogenic shock with persistent tissue hypoperfusion (systolic blood pressure < 90 mm Hg, cardiac index < 2.2 L/min/m2 while on noradrenaline > 0.5mcg/kg/min, dobutamine 20 mcg/kg/min or equivalent)[21,25]

DISCONTINUING ECMO:

The possibility of discontinuing ECMO for futility should be discussed with the family prior to cannulation.[22,28,29] The absence of hope for healthy survival should be considered as an indication for withdrawing ECMO, and is demonstrated by severe brain damage, severe irreversible multi-organ failure, or absence of heart or lung recovery without a durable option for replacement (ventricular assist device or transplant). The optimal timing for determining absence of recovery will vary by centre, but no cardiac function for 3-5 days on V-A ECMO would meet the definition of futility in many ECMO centers. Establishing futility in pulmonary recovery for patients on V-V ECMO is challenging. A definition of futility after 2-3 weeks of no lung function has been challenged in recent years after observation of favourable outcomes after prolonged ECMO runs for patients with ARDS.[30-31]

CONCLUSION:

Our early experience and analysis of 32 patients from 9 hospitals reveals that ECMO plays a role in the stabilization and survival of select critically ill patients with COVID-19. COVID-19 related cardiopulmonary failure such as ARDS and cardiogenic shock or massive pulmonary embolism can be successfully supported with ECMO. Judicious patient selection is important to enable maximal benefit and optimized outcomes with this limited resource during a pandemic. Additional gathering and analysis of data will inform appropriate selection of patients with COVID-19 and provide guidance as to best use of ECMO in patients with COVID-19, in terms of timing, implementation, duration of support, and best criteria for discontinuation. A tremendous amount of information still needs to be learned about the role of ECMO in treating these critically ill patients.

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Outcome of COVID Positive Pregnant Patients under Labor Room Protocol

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ABSTRACT:

As we are all aware of this recent pandemic, severe acute respiratory syndrome – Coronavirus-2 (SARS-COV-2) has infected pregnant patients worldwide. Its effect on mother and baby are still unknown. Earlier studies suggest increased chances of pre-eclampsia, preterm labour, respiratory distress in mother and sudden death in the fetus. As mother is in an immunocompromised state, her chances of developing respiratory disease are more. Understanding the disease, making labour room protocols, providing antepartum, intrapartum and post-partum care, and understanding the outcomes were the mainstay of this study. Screening was done for all patients. Out of 18 patients, none developed severe disease. One patient was shifted to ICU for post-partum eclampsia. None of the babies needed NICU admission because of COVID. Mothers and babies were kept in isolation. None of the health care worker got infected. No mortality was noted in either mothers or newborns.

INTRODUCTION:

Coronavirus are a group of RNA viruses which belong to the subfamily of Orthocoronaviridae. Mild illness causes cough and cold but lethal varieties can cause SARS, MERS and COVID-19. Coronavirus contains a positive sense, single stranded RNA genome. Human corona virus infects the respiratory tract. The disease which had its outbreak in Wuhan, China is now seen in each and every city of the world infecting young, old and pregnant equally. The effect of COVID-19 infection on pregnancy is not completely known because of lack of reliable data. During the pandemic, prenatal visits were postponed but deliveries could not be delayed and the delivery rooms worked as usual. There is no data suggesting increased risk of miscarriage or pregnancy loss due to COVID-19. It is still unclear whether conditions arising during pregnancy like gestational diabetes, cardiac failure, hypercoagulability or pregnancy induced hypertension represent additional risk factors for pregnant women as they do for non-pregnant women.

The Royal College of Obstetrics and Gynecology (RCOG) says that 4.9 pregnant women per 1000 were admitted to hospital with COVID-19 and 1 out of 10 required intensive care.[1] Some data says that there may be an increased incidence of preterm labour but no definite data has yet been published.[2] Studies till date have not found any vertical transmission from mother to baby.[2,5,6,7] But more clarity and studies are required. Viral pneumonia is one of the leading causes of pregnancy deaths worldwide.[8] According to UNFPA (United Nations Population Fund) number of unintended pregnancies will increase as lockdown continues and services for contraception will not be easily available to the general public.[3] Online consultations are considered to be best for pregnant patients till they can avoid visiting the hospital. RCOG recommends that appointments can be deferred by 7 days after start of symptoms of COVID-19 or 14 days if another person in the house has symptoms. All confirmed cases should notify the doctor and hospital in advance of their visit if need arises. Universal screening at New York Presbyterian Allen Hospital and Columbia University Irving medical center found that out of 215 pregnant patients, 4 (1.9%) had symptoms and were positive for COVID- 19 and 29 (13.7%) were asymptomatic but tested positive for the virus.

Obstetrical indications for caesarean would be similar for COVID positive and negative patients.[5] Few articles published revealed that COVID-19 can cause fetal distress, miscarriage, respiratory distress and preterm delivery in pregnant woman but does not infect newborns.[2] There has been no report of vertical transmission in pregnancy, and it has been found that clinical symptoms of COVID-19 in pregnant women are not different from those of non-pregnant women.[2]

COVID SCREENING AND PPE PROTOCOL:

Primary screening of all delivery patients was conducted with COVID-19 rRT-PCR using nasopharyngeal swab. All patients in OPD and emergency were considered suspected cases and Level 1 protection was used in OPD. All suspected and positive cases were taken to the isolation delivery room and contact with relatives and other patients was restricted. Level 3 protection was used in the delivery room. For caesarean section, an OT specially dedicated to positive patients was used. Choice of anesthesia was regional unless there was an indication to give general anesthesia. None of the patients became sick or needed ICU care. Post-delivery all patients were followed upto 2 weeks. All were disease and symptom free. Testing for the support person was not used. Patients isolated in the COVID ward, were discharged directly from there. Babies were handed over to the relatives explaining all precautions related to breast feeding. Initially COVID testing was done at 36-37 weeks from OPD but later on it was stopped as it did not help in long run. rRT PCR testing was avoided till 1 day prior to admission as validity taken was for 48 hrs.

ANTENATAL CARE:

During the pandemic, due to lockdown most consultations were done online. Near term patients came to hospital for checkup, ultrasound and non-stress test as and when required. We tried to reduce the number of their visits to the hospital. Patients were advised for nuchal scan, baseline antenatal investigations, anomaly scan and in case of high risk an early doppler at 28 weeks, rest were advised to come for follow up directly in third trimester. High risk pregnancies were advised to visit more frequently. COVID symptomatic patients were advised for online follow-up with physician and to report to the emergency room in case of aggravation of symptoms. Video calls were used for inpatients besides routine visits for consultations.

INTRAPARTUM CARE:

In our setup mother was admitted in a separate isolation COVID ward. Epidural analgesia was recommended. Electronic fetal monitoring was done in all admitted patients. Birthing pools or water birth was avoided due to high risk of transmission of COVID-19. In the labour room a transparent curtain was used as protection barrier between mother and HCP apart from PPE kits. Baby was resuscitated in the same room maintaining at least 2 meters distance from the mother. Due to restriction of infrastructure and space one labour room was separately used for COVID positive and suspected cases. In case of unbooked patients or multiple patients other side rooms were used and then fumigated. Delayed cord clamping was continued.

POST-PARTUM CARE AND BREAST FEEDING:

Post-natal care depends on multiple factors – hospital facility, maternal support, testing facility and separation facility in the hospital. Low molecular weight heparin was given subcutaneously to all mothers for 7-10 days post-partum. Babies were kept in a separate COVID positive/ suspected NICU. High risk mothers were kept in high risk ward or our COVID positive LR for post-partum care and rest were sent to COVID positive ward after 2 hours of observation. Expressed breast milk was preferred in all cases or else mother was asked to use mask and then feed the baby after following standard universal precautions. COVID test was done for all babies.

Only two babies delivered out of a twin gestation came to be positive; twin 1 on day 1 and twin 2 on day 2. COVID test was negative in both cases on repeat testing and babies were stable. When mother was discharged, baby was handed over to the relative explaining all precautions to prevent transmission from mother to baby. Though transmission of virus in breast milk has not been found as per the available literature, top feed was given to all our new borns. On discharge direct feeding with all universal precautions by the mother including mask and hand hygiene was explained. Mothers were advised to keep the baby at least 2 meters away with a curtain or in a separate room. Option of expressed milk were also given.

During the pandemic the hospital conducted graded, staged, comprehensive and continuous training of all staff as per protocols issued by government. Protocols were made for labour room and OT to deal with COVID positive patients. In the initial phase when our hospital was not designated for COVID, COVID positive patients were shifted to dedicated hospitals but later they were delivered in the institute only with all precautions and keeping separate beds for positive patients.

Figure 1

Flow Chart for Labour Room (Old)

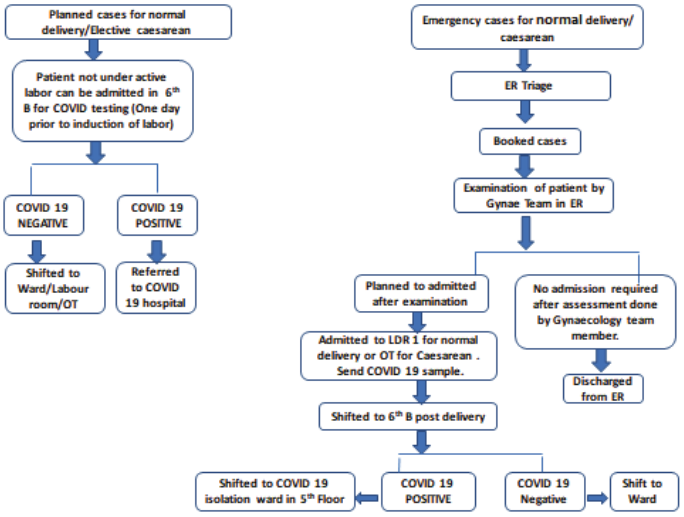
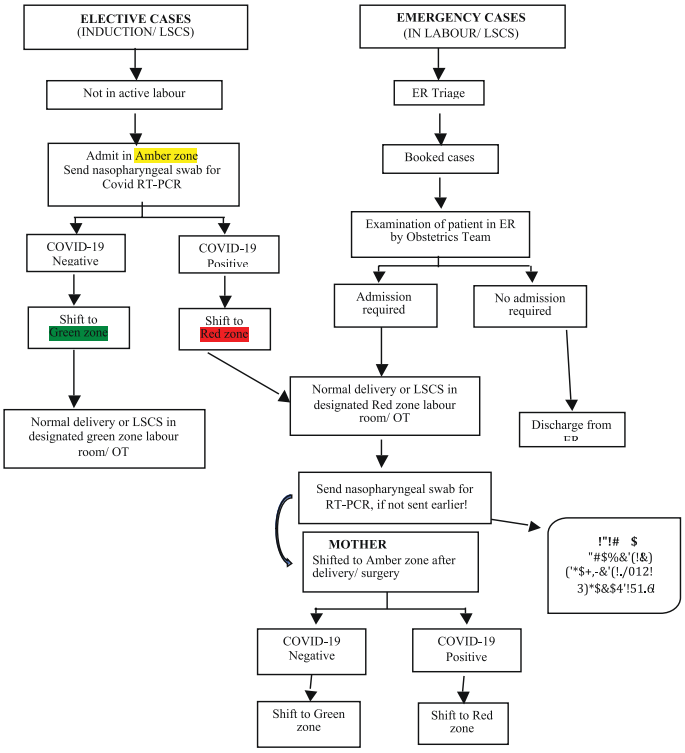


Figure 2

Flow Chart for Labour Room (New):



RESULTS:

In total 372 deliveries were conducted between April 2020 and September 2020. Out of these 198 were COVID negative (95.2%) and 10 were COVID positive (4.8%) on admission. 164 patients were admitted with unknown COVID status and tested later on; out of these 156 came negative (95%) and 8 positives (4.9%). Total 18 patients were COVID positive (4.8%). 6 patients out of 18 had normal delivery (33.3%) and 12 had caesarean section (66.7%). Indications for caesarean were breech (1), twins (2), maternal request (2), doppler changes (2), antepartum hemorrhage (1), eclampsia (1), previous caesarean with scar tenderness (1), heart disease in fetus (1), precious pregnancy (1). 9 patients were less than 37 weeks of pregnancy (50%) and 9 more than 37 weeks (50%). 3 out of 6 patients who delivered vaginally took epidural analgesia (50% normal delivery rate with epidural analgesia). 10 patients were given spinal anesthesia for caesarean and 2 were given general anesthesia for eclampsia and preterm antepartum hemorrhage with breech respectively.

2 mothers who tested positive before admission were delayed for delivery. After 14 days they both were negative. Both had successful outcome with healthy babies. One was an elective caesarean who was postponed for 14 days and she was negative. Another patient was 36 weeks with oligoamnios in early labour, she was admitted for steroid cover and observation. She had fever and was treated for COVID. Henceforth her symptoms improved and was left for spontaneous labour. Her further ultrasound showed liquor within range and delivery was deferred till 38 weeks. Both mother and baby were discharged in stable condition.

One mother came to labour room with history of seizures. Her BP was normal on admission but after caesarean she was shifted to ICU and had postpartum eclampsia and was given magnesium sulphate. Another patient who was admitted for delivery had flu like symptoms, anosmia and fever but had no respiratory distress. Two antenatal patients had flu like symptoms but only one required admission.

DISCUSSION:

Effective separation of COVID-19 patients from non-infected cases would be the key to success for prevention of cross-infection. 50% patients who came to be COVID positive came with pre term labour pains in our setup. More data and results will be needed in future to comment on this analysis. Maternal COVID status should not be an indication for early delivery. The timing and mode of delivery should solely be determined by the obstetric indication and maternal respiratory status (e.g., progressive detoriation with increasing need for oxygen supplementation, escalation of ventilatory support due to increasing fetal size with splinting of diaphragmatic movement and restriction of chest expansion in compromised infected lungs, resulting in respiratory failure). Infection rate is not affected by Normal delivery or caesarean.[9,7,8,10] Vertical transmission was not seen in our cases. Most of the patients at the time of delivery were asymptomatic.[6] Because of false positivity and early incubation period patient can be negative at the time of testing. No ICU admission was required because of the disease per say. Hospital and labour room protocols play a large role in prevention of spread of infection between health care workers and other patients. Some issues are still unclear with regard to maternal isolation, new born isolation, breast feeding, vertical transmission. More data and research is needed for the same.

CONCLUSION:

COVID infected pregnant patients are increasing in the present scenario of sudden surge in cases. Hence all hospitals need to streamline their labour room protocols. A booked patient in labour with an unknown COVID status cannot be refused admission. But health care workers need to take full precautions to prevent the disease from spreading. Testing all patients makes life easy for the patients, doctors and hospital and helps in preventing the disease from spreading and giving proper care to both mother and baby. Potential benefits of a universal testing approach include the ability to use COVID-19 status to determine hospital isolation practice and bed assignments, inform neonatal care and guide the use of personal protective equipment.[4] Such clinical data provides an important opportunity to protect mothers, babies and health care teams during these challenging times. We all look forward to some definitive results about pregnancy and newborn in future.

ACKNOWLEDGMENT:

We would like to thank our management and Infection Control Team, Medical team looking after COVID patients, Labour Room Team, OT team, OPD, ICU and Ward for managing all patients so efficiently. The government rules which changed very quickly and needed the private hospitals to comply as soon as possible was a difficult task for the management and health care workers. Despite all the hassles, things worked out well, making the environment amicable for both staff and doctors. We would like to thank all doctors who have supported this compilation by sharing the patient data and helping in completing the study.

Conflicts Of Interest: The authors have no conflicts of interest.

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Chest Imaging in Corona Virus Disease (COVID-19) - (Our Experience)

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INTRODUCTION:

Coronavirus disease (COVID-19) began in central China, in the city of Wuhan, the capital of Hubei province, in December 2019. It is zoonotic in nature and belongs to coronavirus group[1], which includes Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). COVID-19 was declared as a global health emergency by the World Health Organization (WHO) on the 30th January 2020. It had wide-spread human to human transmission worldwide and by mid October 2020 had resulted in more than 3.89 crore cases in the world with more than 10.99 lakh deaths. In India there have been more than 73.67 lakh cases of COVID-19 and 1.12 lakh deaths as on mid October 2020.

The commonest clinical presentation is cough and fever with other non-specific symptoms ranging from dyspnea, headache, muscle pain, weakness, fatigue and anosmia. Severe disease outcome has been reported from India with a declining mortality of less than 2% by mid October 2020. In India the recovery rate of Corona Virus Disease is highest in the world and leading the table with more than 85% recovered patients. It becomes imperative to document the various imaging findings including the sequelae that we have encountered in our institution till date during this pandemic.

Chest Radiograph and CT scan are the commonly used imaging modalities for evaluation of COVID-19. Chen N. et.al.[7] in their initial prospective study revealed bilateral lung field opacities in 40 of 41 (98%)[2] patients with lobular or segmental areas of consolidation as the typical findings, and ground glass opacities, with/without consolidation, rounded morphology and peripheral predominance are also seen.[1] Distinctive patterns in chest radiographs and CT scan were also observed in our study in the early stage of disease. Other studies have also evaluated linear temporal disease course and correlation of severity with duration since onset of symptoms and disease load[3]. There are also studies proposing CT scan of chest as a diagnostic modality with prompt recognition of the infection, rapid patient isolation and timely treatment being crucial in a public health perspective for containment of the disease. CT scan is more accurate in assessing Severity Index of pulmonary involvement in COVID-19 pneumonia and also useful in cases with strong clinical suspicion of COVID-19 pneumonia and repeated negative laboratory diagnostic tests.

OBJECTIVE:

We characterized the CT chest findings in Laboratory confirmed patients of COVID-19 at our institution and found that the X-ray and CT chest findings to be in concordance with other published studies. X-ray and CT chest are the mainstay imaging modalities for COVID-19 patients. They help to assess the CT severity index of the disease for optimal treatment, planning as well as progression/regression of the pathological process. The role of HRCT chest in clinically suspected COVID-19 patients with repeated negative laboratory tests can't be undermined.

In our study we have shown the time interval from disease onset/admission to the more common Chest CT findings depicting the time course of the infection and severity of the disease at presentation. Additionally, with the passage of time and more patients recovering from the infection, this study is able to document the sequelae of COVID-19 on follow up CT chest.

MATERIALS & METHODS:

It was deemed appropriate to waive the written informed consent from patients for this study as de-identified data was considered for evaluation and there was no risk of patient privacy. All patients considered in this study were positive for COVID-19 with real-time reverse transcriptase polymerase chain reaction (rRT-PCR). A total of 1050 COVID-19 positive patients were admitted in the wards, while another 310 patients required ICU care from the beginning of April 2020 to the mid October 2020. A total of 1915 Chest X-rays and 356 CT chest scans were done for these patients. All the patients were imaged with Philips, Ingenuity Core 128 slice CT scanner, Portable X-Ray (Philips Mobile diagnost M50) and fixed radiography with Philips Dura-diagnostic. The images were randomly reviewed by a consultant radiologist. Diagnostic consensus and clinical findings were obtained for all patients and no normal controls were used. Random follow up scans were performed with time interval deemed appropriate according to clinical requirements.

Plain radiography was used for evaluating all patients with fever and breathlessness and considered as mainstay imaging tool at our center for COVID-19 positive/suspected patients. The reporting format proposed by The British Society of Thoracic Imaging (BSTI) was used, depicting

a. Classic/probable COVID-19: lower lobe and peripheral predominant multiple opacities that are bilateral (>>unilateral) **(Fig.1a)**

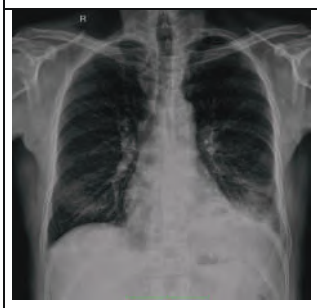
b. Indeterminate for COVID-19: findings do not fit the above described classic or non-COVID descriptors **(Fig. 1b.)**

c. Non-COVID: pneumothorax / lobar pneumonia / pleural effusion(s) / pulmonary edema / other

d. Normal chest radiograph: COVID-19 not excluded.

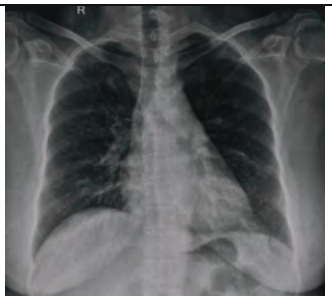
The categories of non-COVID and Normal chest radiographs warranted further investigations and did not negate the possibility of COVID-19 infection.

Fig. 1a. Classic/probable COVID-19



51 Yr. Male, on 4th day, with bilateral, lower lobe predominant, multiple illdefined opacities.

Fig. 1b. Indeterminate for COVID-19



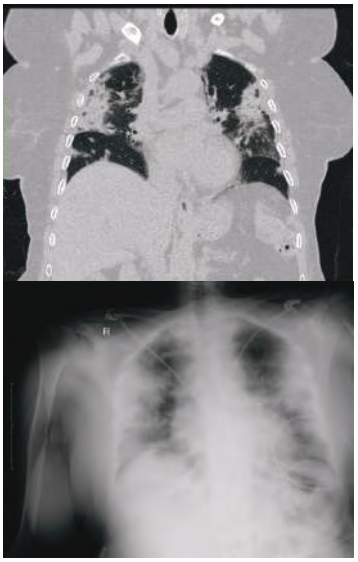
51 Yr. Female on 2nd day, with ill defined, poorly marginated haze in the para-cardiac right lower zone.

CT scan chest was used as standalone imaging tool for characterization of pathological lung lesions in the form of (1) presence of ground glass opacity (2) presence of consolidation (3) uni-laterality / bi-laterality of ground glass opacity and consolidation (4) number of lobes affected where either ground glass opacities or consolidation were present. Degree of involvement of each lobe was done by measuring "Total Severity Index" as detailed by (a) presence of nodules (b) presence of pleural effusion (unilateral / bi-lateral) (c) presence of mediastinal lymphadenopathy (defined as lymph node size of > 10mm. in maximal short axis diameter) (d) presence of airway abnormality (including airway wall thickening, bronchiectasis, and endobronchial secretions) (e) axial distribution of disease (characterized as no axial distribution, central "peri-bronchovascular" predominance of disease, or peripheral predominant disease f) background of underlying lung disease such as emphysema or fibrosis. Opacities were classified as (1) linear opacities (2) opacities with a rounded morphology (3) opacities with a reverse halo sign (4) opacities with a crazy-paving pattern and (5) opacities with intra-lesional cavitation.

Ground-glass opacification was defined as hazy increased lung attenuation with preservation of bronchial and vascular markings, whereas consolidation was defined as opacification with obscuration of markings of vessels and airway walls[4].

CT Severity Score (CTSS) – CTSS was deemed as a quick and objective evaluation of the severity of pulmonary involvement in COVID-19[5]. The anatomical structure, with 18 segments of both the lungs was divided into 20 regions; in which the posterior apical segment of the left upper lobe was divided into apical and posterior segment, while the antero-medial basal segment of left lower lobe was subdivided into anterior and basal segmental regions. Each of the 20 segments was subjectively evaluated for degree of involvement, which was classified as none (0%), minimal (1%–25%), mild (26%–50%), moderate (51%–75%), or severe (76%–100%). No involvement of a segment corresponded to a score of 0, minimal segmental involvement scored 1, mild, moderate and severe segmental involvement scored 2, 3 & 4 respectively, whereas opacification of entire segment was considered as critical and scored 5. An overall lung total severity score was reached by summing the segmental scores (range of possible score varied from 0% to100%).

Fig. 1c. Typical appearance, Correlation of chest CT scan and Radiography features Peripheral, multifocal, bilateral GGO +/- consolidation.

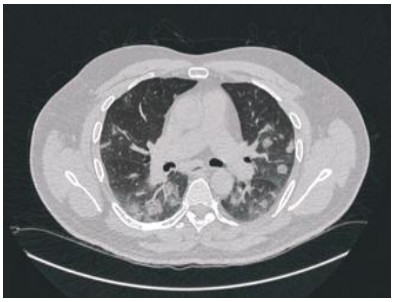


75 Yr. Female, on 10th day, severe disease with high grade fever and breathlessness, comparison on CT scan and X-Ray with multifocal GGO and consolidation depict the severity of disease, allowing use of either for follow up evaluation.

CHEST CT SCAN:

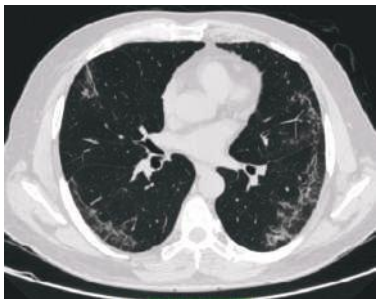
The Radiological Society of North America (RSNA) has released a consensus statement endorsed by the Society of Thoracic Radiology and the American College of Radiology (ACR) that classifies the CT appearance of COVID-19 into four categories for standardized reporting language[6,7].

Fig. 2a. Typical appearance
Peripheral, bilateral GGO +/- consolidation, rounded morphology +/- consolidation or visible intra lobular lines ("crazy paving" pattern)



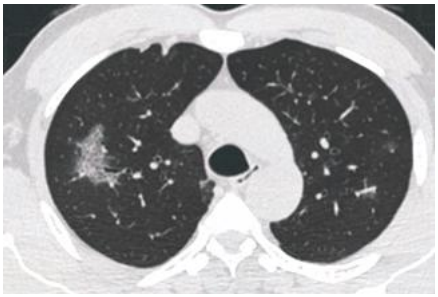
65 Yr. Male, on 7th day, High grade fever and breathlessness, multifocal, bilateral, peripheral predominant, rounded areas of consolidation.

Fig. 2b. Typical appearance
Multifocal GGO of rounded morphology +/- consolidation or visible intra lobular lines (“crazy paving” pattern)



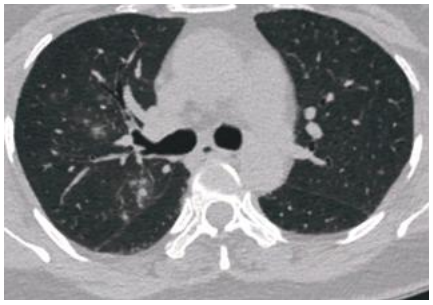
62 Yr. Male, on day 12th day, clinically stable with mild exertional breathlessness, with peripheral predominant morphology – crazy paving pattern.

Fig. 4. Atypical appearance
Isolated lobar or segmental consolidation without GGO, discrete small nodules (e.g. centrilobular, tree-in-bud), lung cavitation, smoother interlobular septal thickening with pleural effusion



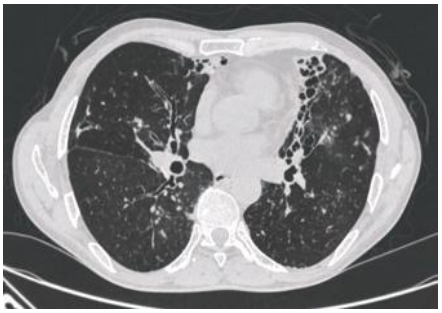
43 Yr. Male, on 10th day, ill-defined areas of ground glass density and focal intra lobular septal thickening.

Fig. 3a. Indeterminate appearance
Absence of typical CT findings and the presence of multifocal, diffuse, perihilar, or unilateral GGO +/- consolidation lacking a specific distribution and are non-rounded or non-peripheral location.



51 Yr. Female, on 2nd day, (same patient at Fig. 1b. with multifocal ill-defined, central distribution areas of ground glass distribution.

Fig. 5a. Chronic phase
Sequelae of infective aetiology
fibrotic densities in lobar / diffuse sub-pleural localization, tubular bronchiectatic changes, Pleural thickening / tag



64 Yr. Male, after 4 weeks, with fibrotic linear densities, tubular and cystic bronchiectatic changes.

Fig. 3b. Indeterminate appearance
Few very small GGO with a non-rounded and non-peripheral distribution

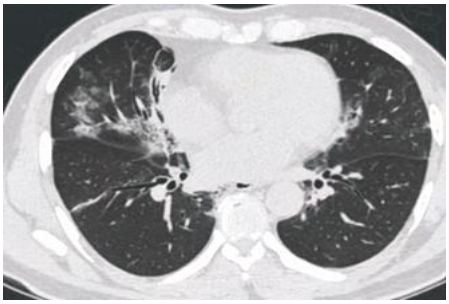
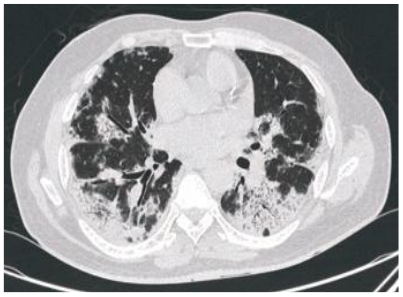
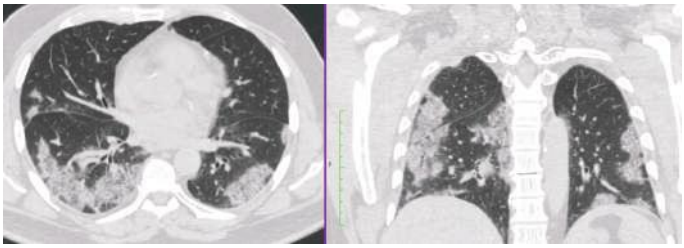


Fig. 5b. Chronic phase
Isolated or segmental consolidation, peripheral sub-pleural localization, fibrotic densities, tubular bronchiectatic changes.



55 Yr. Male, after 3 weeks, bilateral peripheral predominance consolidation, linear densities, tubular bronchiectatic changes.

Fig. 6a. Typical CT appearance in repeatedly RT-PCR negative patient.



45 Yr. Male, clinical suspicion having, repeatedly (twice) negative RT-PCR evaluation on Axial and Coronal (recon) images, multifocal peripheral predominant consolidation with ground glass density and intra-lobular septal thickening "crazy paving" typical characteristic findings of COVID-19 was found to be COVID-19 RT-PCR positive on day 10 of fever.

The CT Chest findings in our study are largely in concurrence with the various studies, defined as pattern of ground glassing and alveolar densities with consolidation, mostly seen in the bilateral distribution with peripheral predominance, and are proposed as the hallmark pattern of disease. **(Fig. 2a, b & c.)** This closely matches with the radiological response to acute lung injury, the initial infectious or inflammatory injury results in ground glass density; that may coalesce into dense segmental consolidation and progress to evolve and organize into linear septal thickening with preference for the lung periphery; seen as "crazy-paving" or "reverse halo sign". **(Fig. 3a, b & Fig. 4)** Our study shows predominance of consolidation, bilaterality, greater multi-lobar / total lung involvement, linear opacities and peripheral distribution in days following symptom initiation **(Fig. 5)** and chronicity follows the disease pathophysiology with organization of the pathological process in later stage. The findings on Chest CT scan significant lymphadenopathy, pulmonary nodules, cavitary changes and pleural effusion are also noted in the evaluation. The role of clinical suspicion cannot be underscored in the present scenario, as seen in repeated RT-PCR negative patients with classical HRCT appearance of lung findings **(Fig. 6)**. It is worth mentioning about two cases with repeated negative RT-PCR test for COVID-19, were subjected to Chest CT on strong clinical suspicion, which revealed classical Corona virus disease imprints in HRCT chest. A repeat RT–PCR test on 3rd occasion for these patients revealed positive results for COVID-19.

The observed time distribution of disease pattern follows more common normal radiological appearance in the early period (0-2 days), consolidation and disease bilaterality, being noted in the intermediate period (3-5 days) and peripheral distribution with linear opacities seen in the late stage (6-12days) of disease progression. There is predominance of ground glass opacities, alone in the early stages, followed by crazy-paving and increased consolidation. The imaging study positivity is related to the time interval since disease onset.

The perceived pulmonary inflammation: CT Severity Score (CT-SS) is higher in patients with severe illness. The severity score for identifying severe disease is above 50%. There may be an imperceptible selection bias due to the more severe patients being imaged sooner, while the asymptomatic / milder patients being imaged later / not imaged at all in the early course of illness.

The CT chest findings are seen to settle down with fibrotic changes and bronchiectasis over a period of time.

CONCLUSION:

Chest radiography helps a lot in the early detection and serial evaluation for basic severity staging of COVID-19. However the role of CT scan far surpasses the sensitivity in disease stratification and concurs that the frequency and severity of Chest CT findings are related to disease course and severity. Chest CT evaluation and reporting following the Radiological Society of North America chest CT classification for reporting COVID-19 pneumonia, has found moderate to substantial inter observer agreement and is appropriate to follow. The temporal evaluation is paramount, not only to understand the pathophysiology and natural history of the infection but also helps us to predict the patient's disease progression and expected potential complications. Further evaluation is mandated in determining the chronic phase of this disease / potential long term sequelae depicted on chest CT.

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INFORMATION CORNER

List of Webinars being conducted across specialties under the Department of Academics & Research in the last 3 months

Topic Name	Topic Name
Leading a normal life with Epilepsy	Social and Mental Wellbeing during COVID-19
Early Anomaly scan	Painless Labor
Six Monthly Antibiogram - Antibiotic Consumption data for 2019	Acute Chest Pain in ER- Pitfalls & Diagnostic Dilemma
Dermatology in our DNA	Lumbar Pain
Understanding Hepatitis- Neonatal Cholestasis and Hepatitis B in Adults	Management of Acute Liver Failure- Current perspective
Emerging trends in Liver transplant	ERGONOMICS
Diet in COVID	Stress Management
Red flag signs of stroke	Diet & Nutrition
Work Life Balance	Hepatitis
How to control BP	Happy Liver Happy life
Joint Pain in old age	Yoga for Old
Critical care in Obstetrics- Workshop	Social & mental wellbeing during COVID times
Journey of Feeding from liquids to solids and common problems	Coping with cancer- Treatment, diet and exercise
Laparoscopic surgery in Gynecology	Hernia during COVID times
Multiplex PCR for Genital Infections	Protecting yourself in pandemic
Minimally invasive cardiac surgery	Paradigm shifts in Breast Cancer Management
Alzheimer's Disease. Is it preventable?	Obesity and COVID-19
Urological problems in old age	Liver transplant
Role of Fetal medicine in Modern Obstetrics	Role of TAVR in present scenario
Healthy tips for healthy heart in COVID times	Going beyond NT Scan
Management of Hepatocellular Carcinoma	Evaluation of memory loss in the elderly
Health problems during monsoon	PCOD- Is it treatable?
Prostate Imaging - Guide to surgery, treatment and management	Pediatric Chest CT- What we should know - A multidisciplinary approach
Radiological services and customer satisfaction in corporate hospital	Breast Cancer Awareness Month - Be Breast Aware
How to recognize and manage the heart attack	Healthy Heart Management
Lifestyle management	Bone and Joint care
Mental health for all	General Eye health and common eye diseases
Women health- Taking control	Arthritis – The Aches of Common People
Menopause and it's complications/ no pause after menopause	Aneuploidy screening - facts & myths - what a gynecologist should know?
Managing obesity and stress in the new normal	Fatty Liver
End of Life Care: The Indian Perspective	Q&A on Spine Health
Colic problems in newborns	Brain tumor
Love your Bone – Bone will Love you	Imaging and management of acute pelvic pain

Healthcare Maintenance Issues in Children and Adolescents with Inflammatory Bowel Disease

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Keyword: IBD (Inflammatory Bowel Disease)

INTRODUCTION

The incidence of IBD in children continues to increase. Inflammatory bowel disease (IBD), as well as treatment-related medical or surgical interventions, can adversely affect linear growth, pubertal development, and nutritional status. A multidisciplinary approach that involves the general practitioner and paediatric gastroenterologist is needed to routinely monitor growth, bone health, vitamin and mineral deficiencies, vaccination status, and endoscopic surveillance. It is also important to monitor for extra intestinal manifestations of IBD that may affect the liver, joints, skin, and eyes. The chronic nature of the inflammatory process observed in these children and the waxing and waning nature of their clinical symptoms can be especially disruptive to their physical, social, and academic development.[1]

GROWTH

Impaired linear growth can precede gastrointestinal symptoms and may be the only presenting sign of IBD. Nutritional deficiencies, physical inactivity, inflammatory cytokines, and corticosteroid use negatively impact bone growth and bone formation. Measurement of height, weight, and body mass index (BMI) should be determined at every maintenance visit. Blood pressure should be obtained at least annually in all children with IBD and more frequently in patients receiving renal toxic medications including aminosalicylates and corticosteroids and more potent immunosuppressive therapies (cyclosporine and tacrolimus). Subtle changes in weight gain, linear growth, or growth velocity can be early signs of a clinical relapse. Annual urinalysis and yearly to twice-yearly measurement of serum creatinine is recommended in children and young adults receiving aminosalicylate therapy

VACCINATION

Live vaccines are not recommended for IBD patients taking certain medications such as: prednisone, azathioprine, 6-mercaptopurine, methotrexate, adalimumab, infliximab, tacrolimus etc. or any other medications that weaken the immune system.[2] This also includes patients who took these medications within the past three months or plan to take them in the next four to six weeks. If parents cannot recall a history of natural infection, Varicella vaccine should be administered to children. If the patient and/or parents are unsure, Varicella antibody titres should be checked. If patients do not have a history of Varicella infection or Varicella immunization, they should be vaccinated before starting immunosuppressive therapy. It is recommended that patients wait at least 1 month after discontinuing corticosteroids before immunization with Varicella vaccine. Patients should also be tested for latent hepatitis B or sero-negativity (HBsAg negative) because treatment with anti-TNF agents has been reported to result in HBV reactivation. If the child is not immune to hepatitis B, the hepatitis B vaccine may be given.

Live virus vaccines include: not recommended

- Rotavirus
- Intranasal flu vaccine —The nasal spray version is a live virus vaccine. The injected vaccine (shot) is not a live vaccine.
- Measles, Mumps, Rubella (MMR)
- Chicken pox
- Yellow Fever
- Oral Polio—The version taken by mouth is a live virus vaccine. The standard injected vaccine (shot) is not a live virus vaccine.

Inactivated Vaccines

Inactivated vaccines are recommended for all patients with IBD, regardless of the medications they are taking. Inactivated vaccines are not live and include:

- Diphtheria (DTaP, TDap)
- Haemophilus influenza (HiB)
- Hepatitis A
- Hepatitis B
- Human Papilloma Virus (HPV)
- Meningitis (Meningococcus)
- Pertussis (DTaP, TDap)
- Pneumonia (Pneumococcus) (Prevnar-13, Pneumovax-23)

- Tetanus (DTaP, TDap)
- Polio: The version given as a “shot” or injection is an inactivated vaccine.
- Flu vaccine (Influenza): The version given as a “shot” or injection is an inactivated vaccine. It is recommended annually.
- Typhoid vaccine
- Rabies Vaccine

VACCINATIONS FOR FOREIGN TRAVEL

Inactivated vaccines such as Typhoid, Hepatitis A and B, Japanese encephalitis, Rabies, Cholera, Polio, and Meningococcal can be safely administered to paediatric patients with IBD and the primary care provider should follow the usual recommended schedule.

VITAMIN AND MINERAL DEFICIENCIES

Children with Crohn’s disease (CD), especially those with significant small bowel involvement, are at risk for the development of macro- and micronutrient deficiencies.[3,4] Chronic occult blood loss can lead to iron deficiency. Iron studies to be done annually. The dose of elemental iron and the preferred route of administration required in patients with IBD are controversial. Oral supplementation is inexpensive and relatively safe. In patients with an elevated C-reactive protein, intravenous iron should be the preferred route.

Patients with CD involving the small bowel, especially those with extensive disease or resections involving the terminal ileum and on anti-folate medications should have periodic assessment of serum vitamin B12 and folate levels and supplements added in case of deficiencies found.

Vitamin D status (serum 25-OH D) should be checked at least once yearly to maintain levels above 30ng/mL and supplements should be prescribed accordingly. The International Society for Clinical Densitometry recommends that children with IBD undergo a total body (excluding the skull) dual energy radiograph absorptiometry (DEXA) screen at diagnosis and at 6-month intervals if abnormalities are found.[5,6]

Physicians caring for children with IBD should also routinely perform a dietary assessment, paying especially close attention to the consumption of vitamin D–containing foods including dairy products, fortified cereals, and oily fish.[7]

High fibre intake and processed fatty foods may cause increased symptoms and thus, should be avoided. Eating lots of red meat or processed meats may be associated with an increased risk of colon cancer, so a well-balanced diet is recommended.

EXTRA INTESTINAL MANIFESTATIONS

Additional questions should address potential extra-intestinal manifestations of IBD including skin lesions (possibly consistent with erythema nodosum and/or pyoderma gangrenosum), changes in skin colour or pruritus (suggestive of an evolving liver process such as primary sclerosing cholangitis or autoimmune hepatitis), arthritis and arthralgias, and any eye or visual changes (indicative of episcleritis or uveitis)

SCREENING FOR LATENT TB

Adult patients treated with anti-TNF therapy are at increased risk for reactivation of latent TB infection. The data regarding which method of screening for latent TB is superior is controversial. A positive purified protein derivative (PPD) as a marker of latent infection may be unreliable as results are reader dependent. Results may also be invalid in patients who received BCG immunization. Therefore, both PPD and Quantiferon TB GOLD are recommended for screening before starting anti-TNF agents in children given the lack of superiority of either test. Indeterminate Quantiferon TB GOLD results may occur in patients with lower weight-for-height z scores, higher platelet counts, and lower serum albumin levels as well as higher disease activity as measured by the Paediatric Crohn’s Disease Activity Index. Furthermore, many studies reveal that children <5 years of age are more likely to have indeterminate results. Despite this, the Quantiferon TB Gold is generally more reliable than a reader dependent PPD. Annual TB monitoring is recommended when on Anti-TNF drugs.

CANCER SCREENING

Other than an assessment for skin cancer during routine physical examinations, colon cancer screening is routinely recommended. As such, patients with IBD should undergo screening colonoscopy examinations with surveillance biopsies every 1 to 2 years, beginning approximately 7 to 10 years after their initial diagnosis. Patients with concomitant primary sclerosing cholangitis are at further risk for the development of cholangiocarcinoma and colon cancer, these patients should begin a screening colonoscopy program, with studies performed every 1 to 2 years, beginning at the time of diagnosis.

PSYCHOSOCIAL HEALTH

The psychosocial effect of IBD on the growing and developing child is considerable. The unpredictable and fluctuating clinical course experienced by many children with IBD often affects quality of life and the ability of children to participate fully in school functions, including standardized testing, proms, or competitions.

Similarly, families of children with IBD often find it difficult to schedule vacations, orchestrate sleep-overs with their friends, or sign their children up for summer camp. Paediatric patients with IBD are also at increased risk of anxiety, family conflict, medical adherence issues, altered self-image, and isolation. IBD is associated with poor sleep quality, Practitioners should routinely ask about psychosocial changes and stress, screen for depression, and inquire about sleep hygiene. **(Fig. 1)**

MESSAGE acronym for depression screening

M	Mood (depressed or irritable) and Motor (hyper or hypo)
E	Energy (fatigue)
S	Sleep (insomnia or hypersomnia)
S	Suicide and Self Esteem
A	Anhedonia (lack of pleasure)
G	Guilt
E	Eating (change in appetite)

Fig. 1

CERVICAL CANCER

Women with IBD are at greater risk of cervical cancer. The American Academy of Paediatrics now recommends HPV vaccine for all children (girls and boys) as part of the routine schedule of vaccinations. The HPV vaccine is safe for IBD patients taking medications that suppress the immune system. It requires three doses, and can be started as early as nine years old.

CONTRACEPTION

Women with IBD can use any form of contraception to avoid pregnancy, including oral contraceptives or the pill. Some evidence from clinical studies suggest that taking oral contraceptives can make Cohn's disease worse, but it is important to note that most of the women who experienced this problem were also smokers.

CONCLUSION

There are many aspects to maintaining optimal health care maintenance for paediatric patients with IBD. Given the systemic nature of the disease, the related extra-intestinal manifestations, and the risks associated with the various immunosuppressive therapies used to treat IBD, patients and their providers must remain vigilant about all aspects of physical and psychological health. A multidisciplinary team approach that is proactive is likely to ensure better outcomes for paediatric patients with IBD.[8]

TABLE 1 Summary Checklist for the General Practitioners Caring for a Pediatric Patient With Inflammatory Bowel Disease

Intervention	Frequency
Measurement of height, weight, BMI, linear growth	Every visit
Bone health	
a) Bone age determination	At diagnosis if growth retardation is present At diagnosis and 6-mo intervals if abnormal
b) DXA	Prompted by downward crossing of height or weight percentiles, amenorrhea, long-term glucocorticoid therapy, and clinically significant fractures
Minerals and vitamins	
a) Serum iron, ferritin, folic acid, vitamin D 25-OH, vitamin B12	At least yearly
b) Serum zinc level	At time of diagnosis
Vaccines	
a) Hepatitis A, hepatitis B, varicella*	Titers should be checked at time of diagnosis. If insufficient, revaccinate. (*only if not immunosuppressed)
b) Gardasil and pneumococcal vaccine	Within the first year of diagnosis, if not already given
c) Influenza	Yearly
Annual health care screening	
a) Latent TB infection	At diagnosis if starting anti-TNF
b) Ophthalmologic examination, including visual acuity, slit lamp examination, intraocular pressure measurements and examination of anterior and posterior chambers	Annually
c) Full-body skin examination	Annually

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Postoperative COVID-19 Infection after Cardiac Surgery: Challenges and Management

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ABSTRACT:

World is challenged by Corona virus pandemic. Cardiac surgery itself carries a high risk for cardiac patients and cardiac patients infected with corona virus are likely to have more complications due to COVID-19 disease. Here we describe a case report in a 60 yr old patient undergoing coronary artery bypass grafting who was found to be COVID-19 positive in postoperative period.

Key Words: Cardiac surgery, COVID-19, RT-PCR.

INTRODUCTION:

The outbreak of the novel coronavirus and coronavirus disease (COVID-19) was labelled as an International Public Health Emergency in January 2020.[1,2] As of date more than 42 million cases had been reported worldwide with more than 1.1 million deaths. India (nearly 8 million cases) and United States (>9 million cases) are worst affected countries with this pandemic. Caused by COVID-19 virus, also known as SARS-CoV-2, transmitted mainly by air droplets and contaminated surfaces with variable incubation period of 5 days to 2-3 weeks, the presentation varies from asymptomatic cases to life-threatening fatal outcomes. The infected patients can have unexpected progression to acute respiratory distress syndrome, renal failure, cardiac injury, and death. COVID-19 control has been extremely critical and demanding, having unfolded serious challenges to disease prevention and public health protection.

The disease has posed serious challenges to front-line health care workers, surgical and medical specialities with risk of infecting themselves as well as management of patients. Anaesthesiologists and critical care specialists are more at risk as they are associated with airways and aerosol generating procedures. The pandemic has affected cardiac surgery units in multiple ways with limited number of available ICU beds and ventilation sites, the need to postpone or cancel elective and/or complex cardiac interventional procedures, coronavirus patients needing urgent cardiac operations, patients developing COVID-19 post cardiac surgery, in-hospital transfer of emergency patients, emergency management of cardiac patients like primary revascularization without time even for corona virus testing, working with heavy PPE suits to infected health care providers with consequent shortage of medical and nursing practitioners, restrictions in clinical meetings, and cancellation of training and continuing medical education.[3,4] Amidst these challenges and fear, now patients are approaching hospitals for medical and surgical treatment with decline in surge of corona cases. Here we describe a case report of a cardiac patient undergoing coronary artery bypass grafting (CABG) who was found to be positive for corona virus in post-operative period.

CASE REPORT:

A 60- year old male patient was admitted to hospital with acute coronary syndrome with non-ST elevation myocardial infarction with diabetes mellitus. His echocardiography showed ejection fraction of 25-30% (45% previously). Coronary Angiography revealed significant triple vessel coronary artery disease. Patient was planned for CABG. His pre-operative COVID-19 RT PCR report was negative a day before the procedure. After thorough investigations, off pump CABG (3 grafts) was done with uneventful intraoperative course.

Post-operatively patient developed high-grade fever on second postoperative day (POD). Vitals were stable with no requirements of inotropes/vasopressors, and blood gases within normal limits. Blood and Urine cultures were sent. Antibiotics were upgraded empirically to Inj Meropenem, Inj Teicoplanin and Inj Levofloxacin. Patient remained febrile on subsequent days. His total leucocyte count and procalcitonin were within normal limits. Chest X-Ray also showed no signs of lung congestion or consolidation. Patient was otherwise awake with regular breathing pattern, stable vitals and hence put on gradual weaning mode of ventilator. As patient remained febrile and didn't respond to escalated antibiotics, repeat COVID RT-PCR was done which was found to be positive on 4th POD.

He was shifted to HDU (Fully equipped ICU dedicated for COVID-19 positive patients) for further management. Patient was extubated on 5th POD. Intravenous Inj Remdesivir along with other supportive treatment was started on 6th POD for 5 days (200 mg I/V on first day and then 100 mg I/V on next four days). Pt received convalescent plasma on POD 6 and 7. Patient became afebrile on 6th POD. His RT-PCR for COVID-19 done subsequently every 72 hours reported positive. His clinical condition was improving. All blood and urine cultures were negative. Patient was discharged in clinically good and stable condition on 14th POD with advice to take due precautions as his COVID-19 status remained positive.

DISCUSSION:

During this COVID-19 pandemic, initially there was an international call to postpone all elective surgeries. However, postponing surgery may impact patients' daily activities and increase the risk of deterioration of their cardiac condition. The patient population coming for cardiac surgery may be asymptomatic corona positive, recovered patients from corona virus and preoperative COVID-19 negative turning corona positive in postoperative period, mostly either false negative previous RT-PCR or new infection. During pandemic, elective cardiac surgery in an otherwise stable patient can be deferred in COVID-19 positive cases. New question of when to operate patients with COVID-19 has emerged, therefore the risk of adverse outcomes due to having COVID-19 should be weighed against the risk of morbidity due to delay in surgery.

The retrospective cohort study published recently in the Journal of Cardiac Surgery by Barkhordari et al. described the outcomes in 25 patients with asymptomatic COVID-19 infection undergoing emergent or urgent cardiac surgery in Tehran, Iran.[5] Most of the operations were performed on bypass (84%), with the majority of patients receiving coronary artery bypass grafting. The authors found that the patients postoperatively had a median duration of intubation and intensive care unit (ICU) stay of 13 hours and 3 days, respectively. The overall mortality rate and ICU readmission rate were both 16% each. Of note, those requiring readmission to the ICU fared poorly, with a mortality rate of 75%. The authors concluded that while asymptomatic COVID positive patients had early postoperative respiratory outcomes comparable to their pre-COVID cohort, those that required ICU readmission fared extremely poorly. Due to this risk, the authors recommended cardiac surgeries in the asymptomatic COVID-19 positive population to be postponed unless deemed emergent. Lei et al. in a retrospective study of 34 patients undergoing elective non-cardiac surgery while COVID-19 positive, observed that 44.1% required ICU level care postoperatively, with a mortality rate of 20.5%.[6]

Another consideration is whether a minimally invasive cardiac intervention can be beneficial in corona virus pandemic though at present it's unclear if COVID-19 has played a role in the decision to perform cardiac interventions minimally invasive or open. For instance, whether a patient would benefit from an open surgical versus percutaneous aortic valve replacement, is debatable and at least in some cases percutaneous approach might be beneficial.

According to WHO, repeated testing is the key strategy for containing the COVID-19 pandemic at the moment. The methods used so far for COVID-19 diagnosis are RT-PCR tests and serological tests. As of now, RT-PCR is regarded as the gold standard for diagnosing the infection. Specificity of RT-PCR is almost 100 percent. The performance of RT-PCR is not that good in terms of sensitivity and as many as 15-30% results are "false negative" in varying reports. Low sensitivity has been attributed to the defect in the sample which may arise at any stage during sample collection, transport, preservation or processing. Another, consideration is how adequately the sample has been collected. Another potential clinical scenario involves a patient who had recovered from COVID-19, is asymptomatic but now with a repeat positive PCR. In "Symptom Based Strategy to Discontinue Isolation for COVID-19," the Center for Disease Control note that "replication competent virus has not been successfully cultured more than 9 days after onset of illness," and "among those who continue to have detectable RNA, concentrations of detectable RNA 3 days following recovery are generally in the range at which replication competent virus has not been reliably isolated by CDC."[7] This might give provide a timeline as to when to safely operate on a patient who has recovered from COVID-19 with a persistently positive PCR test. Our patient was COVID-19 positive at the time of discharge so with this CDC observations this patient might not be having active COVID-19 infection or spreading infection in community. However, this requires further study and at present can't downplay the concerns that a persistent positive test may reflect a re-infection.

Treatment of corona virus is primarily supportive. Mild cases recover spontaneously. Various drugs like hydroxychloroquine, ivermectin have been used with no consistent results. Drugs like Favipiravir has been approved for mild cases of COVID-19 infection. The main advantages of Favipiravir are that it is administered orally and that it can be given in patients who are symptomatic but not ill enough to be hospitalized. As most COVID-19 patients (85%) have mild to moderate disease and can be treated at home, this drug could potentially be used in large numbers of patients. As with any antiviral, it should be stressed that Favipiravir should be administered early after the onset of symptoms to be effective in reducing viremia. Inj Remdesivir has been used in moderate to severe cases again without consistent results though trial had shown decrease in duration of corona virus disease with Remdesivir therapy. In trial, clinical benefit of Remdesivir was seen in patients requiring supplemental oxygen but who did not require oxygen delivery through a high-flow device, non-invasive ventilation, invasive mechanical ventilation, or ECMO[8]. In this subgroup, those who received Remdesivir had a shorter time to recovery. In a post-hoc analysis of deaths by day 14, Remdesivir appeared to confer a survival benefit (OR for death 0.22; 95% CI, 0.08–0.58). In those patients not improving after 5 days of Remdesivir therapy, treatment duration had been increased up to 10 days. Inj dexamethasone has been found to be effective in severe cases. 32 participants with severe COVID-19 (2104) given 6 mg dexamethasone once daily had an 8-26% lower mortality than 4321 participants given standard care. The WHO Study panel made a strong recommendation for systemic (i.e. intravenous or oral) corticosteroid therapy (e.g. 6 mg of dexamethasone orally or intravenously daily or 50 mg of hydrocortisone intravenously every 8 hours) for 7 to 10 days in patients with severe and critical COVID-19, and a conditional recommendation not to use corticosteroid therapy in patients with non-severe COVID-19. Oxygen therapy and ventilatory support is required to maintain oxygenation. ECMO may be required in cases where

oxygenation can't be maintained even on ventilatory support. Vaccines are in various stages of development but as yet no WHO approved vaccine is available.

CONCLUSION:

Patients with suspected or confirmed COVID-19 infection, who undergo cardiac surgery procedures, represent numerous challenges for the cardiac anaesthesia and surgery team. They require an extremely careful approach during perioperative anaesthetic care. The COVID-19 pandemic and the decision making process of when to perform urgent procedures in corona positive patients and patients who had recovered from corona virus but are persistently corona positive, will not likely disappear in the near future. Not much is known at present about the post-COVID sequelae like residual lung fibrosis and its effect on outcome of cardiac surgical patients. Multi-disciplinary discussions and clinical experience will continue to be important to decide individual risk and benefit profiles and management of patients in corona virus pandemic.

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Post COVID Lung Fibrosis

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ABSTRACT:

To date, there are more than 19 million infected people and about 700,000 deaths reported worldwide. COVID-19 leads to a wide spectrum of respiratory diseases ranging from mild upper respiratory tract symptoms to severe acute respiratory distress syndrome (SARS). Almost all COVID-19 related serious consequences feature pneumonia.[1] There are currently no effective vaccines, and treatments are mostly experimental. Data from previous coronavirus outbreaks such as SARS-CoV (2003 outbreak) and emerging epidemiological data from the current global COVID-19 pandemic suggest that there could be substantial tissue fibrotic consequences following SARS-CoV-2 infection, responsible for severe and in some cases fatal lung lesions.[2] The role of anti-fibrotic drug therapy in patients with ongoing SARS-CoV-2 infection or in patients cured of residual pulmonary fibrosis is still unclear and the scientific rationale for initiating, continuing, or discontinuing therapy is poorly defined. In our case reports we describe the advantages of early initiation of corticosteroids along with other experimental therapy in patients of COVID-19 with severe pneumonia and thereby continuing low dose steroids with oxygen support to prevent the worsening of the clinical situation as well as to prevent the progressive pulmonary fibrosis.

INTRODUCTION:

SARS-CoV-2 infection can have a completely asymptomatic or mild symptomatic course, but in some cases, it can also cause systemic hyper-inflammation, pulmonary fibrosis and scarring with lung collapse, multi-organ dysfunction, and patient death.[3] The mechanisms through which severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes lung damage are only partly known, but plausible contributors include a cytokine release syndrome triggered by the viral antigen, drug-induced pulmonary toxicity, and high airway pressure and hyperoxia-induced acute lung injury secondary to mechanical ventilation. The burden of fibrotic lung disease following SARS-COV-2 infection is likely to be high, given the scale of the pandemic, and will probably increase further. Most patients infected by SARS-COV-2 present with bilateral ground glass opacities with or without consolidation, and with preference of lower lobes radiologically.[4] The most serious phase of COVID-19 infection is characterized by a sudden and excessive release of pro-inflammatory mediators, which leads to lung damage with extensive fibrosis and rapid onset of respiratory distress syndrome.[5] Studies have shown that bilateral interstitial pneumonia caused by COVID-19 is associated with the presence of fibrotic tissue caused by excess collagen (fibrosis) in the lung crevice with associated hyper-inflammation. Long term lung impairment may develop following virus clearance, and in particular fibrotic interstitial lung disease, which is a progressive disease with decline in the lung function, worsening symptoms and quality of life, development of respiratory failure and eventually death with lung transplantation being the only treatment option.[6]

CASE 1:

A 39 year old male, k/c/o Diabetes Mellitus with positive COVID-19 RT-PCR presented with history of cough, intermittent fever and shortness of breath for 1 week. On examination patient was conscious, oriented, febrile, tachypneic, restless, had hyperglycemia (RBS – 447 mg%) and desaturating in room air. Examination of chest revealed bilateral crepts. Abdomen and CVS examination was unremarkable. Investigations revealed raised TLC (14,400/cu.mm), KFT normal, LFT normal, CRP 155.20 mg/lt (normal < 5), Procalcitonin normal, and LDH 372 I.U/lt (100-250). Chest X-ray revealed a patchy opacity in the periphery of left lower zone with coarse reticular opacities. Patient was admitted in ICU and managed with i.v antibiotics – Piperacillin/ Tazobactam, Azithromycin, inj. Dexamethasone, oxygen and non-invasive ventilation. Inj. Remdesivir (antiviral RNA polymerase inhibitor) was also given as many clinical trials have suggested it as an effective therapy against SARS-CoV-2.[7] CT chest revealed bilateral patchy ground glass opacities with peripheral opacities involving bilateral middle and lower lobes. Patient was given convalescent plasma therapy and his clinical condition improved gradually and radiological picture started improving marginally. Patient was shifted to the ward after stabilization and was continued with supportive care along with oxygen and DVT prophylaxis.

Patient was discharged (after negative COVID test), on oral hypoglycemics, steroids, nebulization, aspirin, Novel oral anticoagulant (Rivaroxaban) and low flow oxygen support for 15 to 18 hours in a day. Patient was reviewed in OPD and he was kept on tapering dose of steroid with gradual weaning of oxygen. His serial CXR showed improvement along with normalization of oxygen saturation in room air.

CASE 2:

A 57 year old female with history of hypertension and positive COVID-19 RT-PCR presented with complaints of fever for 3 days and breathing difficulty. There was no H/o any chest pain, loose stools, vomiting, pain abdomen or urinary complaints. On examination, patient was conscious, oriented, tachypneic,

febrile and desaturating in room air. Examination of chest revealed bilateral crepts. Abdomen and CVS examination was unremarkable. Investigations revealed raised TLC (18,800 /cu.mm), CRP 83.56 mg/lt (normal < 5), D-Dimer 2.0 mg/lt (0.0-0.5), LDH 755 I.U/lt (100-250), Plasma IL-6 83.98 (<7.00), S. Ferritin 908.3 ng/ml (18.0-340.0), Procal negative. Chest X-ray revealed prominent bronchovascular markings in both lung fields, confluent air space opacities in the middle and lower zone bilaterally with both CP angles obscured. Patient was admitted in the ICU and started on i.v antibiotics – Teicoplanin, Pregabalin, inj. Dexamethasone, Novel oral anticoagulant (Rivaroxaban) and inj. Tocilizumab (IL-6 receptor inhibitor). Transfusion of 2 units of convalescent plasma was also planned the subsequent day. Patient was started on HHHFNC @50 L flow, 0.5 FiO_2 with overnight CPAP of 8. Her IL-6, CRP and LDH levels were seen in a decreasing trend over the next few days. CT thorax revealed peripheral areas of patchy consolidation, ground glass opacities and septal thickening with fibrotic changes involving both lungs consistent with resolving atypical pneumonia. Patient was shifted to the ward after stabilization, gradually weaned off O_2 over next few days as the general condition improved. Last chest x ray before discharge revealed only few reticular opacities in bilateral lung fields with significant clearing of lung opacities as compared to previous x rays. Patient was discharged on oral steroids, nebulization, aspirin, Novel oral anticoagulant (Rivaroxaban) and low flow oxygen support for 15 to 18 hours in a day. Patient was reviewed in OPD and she was kept on tapering doses of steroid with gradual weaning of oxygen and her serial CXR showed improvement along with normalization of oxygen saturation in room air.

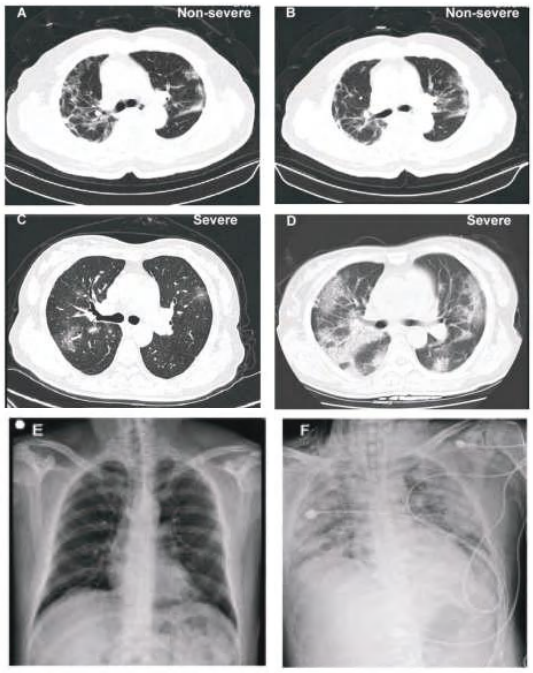

Fig. 1:
Representative Chest Radiographic Manifestations in a non-severe & severe case with COVID-19

DISCUSSION:

Although many patients who develop ARDS survive the acute phase of illness, a substantial proportion die as a result of progressive pulmonary fibrosis.[8] Fibrosis could be viewed as a consequence of a disordered wound healing process and may be directly related to the severity of an inciting event.[9] Coronavirus infection could directly promote lung fibrosis by at least two mechanisms – first, the nucleocapsid protein of SARS-CoV-2 is known to directly enhance transforming growth factor-beta (TGF-beta) signaling, which is a powerful pro-fibrotic stimulus.[10] Second, coronaviruses induce a downregulation of angiotensin-enzyme-2, reducing angiotensin II (Ang II) clearance in the lungs. Ang II could then upregulate TGF-Beta and connective tissue growth factor.[11]

Additional factors that could predispose individuals to severe lung injury include advancing age[12] (individuals with median age of 65 years), illness severity including comorbidities such as hypertension, diabetes and coronary artery disease.[13] Laboratory findings of lymphopenia, leukocytosis and elevated Lactate dehydrogenase (LDH) correlate with increased disease severity.[14] The increase of LDH reflects tissue destruction and is regarded as the most important prognostic markers of lung injury.[15] The increase of high sensitivity CRP (hs-CRP), a well-established marker for poor prognosis in sepsis and ARDS, reflects a persistent state of inflammation.

Anti-fibrotic therapies are exclusively used in chronic fibrotic disorders – mostly in IPF but also for progressive pulmonary fibrotic disease in disorders other than IPF.[16] Outcomes have generally been evaluated at 1 year follow-up, with changes in forced vital capacity (FVC) being the uniform primary endpoint. The viral protease inhibitors: Favipiravir and Remdesivir, are antiviral agents currently used in many clinical trials in a bid to find an effective therapy against SARS-CoV-2.[17] There is evidence of potential use of pirfenidone, azithromycin and prednisolone in the management of pulmonary fibrosis post-H1N1 ARDS, based on a data from a case report of three patients (young males aged 40-49 years).[18] Immunosuppressive agents that are currently under consideration include the IL-1 receptor blocker Anakinra, which has demonstrated improved survival benefits and IL-6 receptor blocker Tocilizumab, which is currently registered for a multicenter clinical trial in COVID-19 patients.[19,20] Re-emerging convalescent plasma (CP) therapy is an ideal strategy, which gains paramount importance.[21,22] However, this strategy requires some crucial validation with respect to ethical consideration, criteria for donor selection, titer quantification, dose optimization, limitation factors, chances of occurrence of transfusion events etc.[23]

Assessing the long term consequences of COVID-19 thus appears crucial. We therefore stress on the importance of: (a) setting up specific follow-up strategies in COVID-19 patients showing pulmonary involvement to assess the possible progression towards lung fibrosis; (b) treating at risk patients early, with therapies preventing the development of future lung fibrosis. By doing this, we can hope to deliver appropriate clinical care and urgently design interventional trials to prevent a second wave of late mortality associated with this devastating pandemic.

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Vascular Sequelae of SARS-CoV-2 infection: Non-pulmonary Morbidity in SARS-CoV-2 Infection Survivors – A Case Report

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Key words: Arterial thrombosis, gangrene, peripheral limb ischemia, SARS-CoV-2 infection

INTRODUCTION:

SARS-CoV-2 infection has led to a pandemic and we are seeing patients in different stages of infection, recovery and residual disability left behind by the infection. Various aspects of the infection are dealt by the pulmonologists, intensive care physicians and internal medicine physicians. But there is an aspect of this infection which needs early intervention and management by the vascular surgeon and that is being discussed through these two case reports. Patients who recover from SARS-COV-2 infection are survivors but they have to live with the residue left behind by the disease and treatment. Peripheral limb gangrene has been noted to be one such effect. These two case reports show how these conditions were managed at our hospital.

CASE 1:

38 year old diabetic male was admitted with fever, cough, body aches, headache and sore throat for 4-5 days and fresh onset breathlessness since 2 days. On admission, 0_2 saturation was noted to be 74% on room air. Examination of the chest revealed bilateral crepitations in the lung bases. Patient was tachypneic, febrile and in metabolic acidosis. He was also noted to be in diabetic ketoacidosis at this stage. He was admitted in ICU and started on non-invasive ventilation (NIV). As patient continued to be hypoxic, he required intubation and ventilatory support. He was detected to have Severe COVID-19 pneumonia and was managed with prone ventilation and then ECMO. He developed a spontaneous hemopneumothorax on day 7 of admission and required intercostal drain placement. The heparin infusion was stopped and patient was given FFP, platelet and packed red blood cell transfusion.

Gradually patient improved but developed peripheral digital gangrene of both upper and lower limbs. Vascular surgery opinion was taken at this stage. The patient was evaluated and found that the peripheral pulses of the patient was palpable but he had developed upper and lower limb digital ischemia with gangrene. The patient was managed conservatively with anticoagulation and the ischemic area started demarcating and there was no further extension of the ischemic area. Patient improved clinically and at the time of discharge from the hospital required home care for the pressure sores, physiotherapy and nutritional support. **(Fig. 1 & 2)**

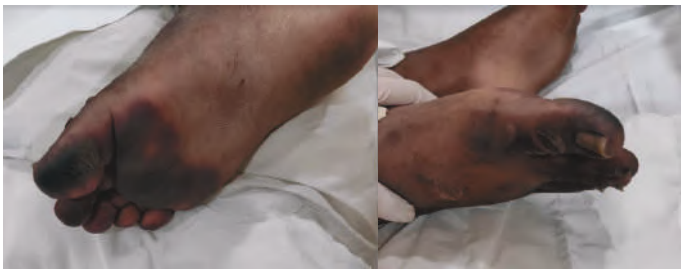

Fig. 1
Peripheral foot Ischemia

Fig. 2
Upper limb Ischemia

CASE 2:

55 year old male, diabetic presented with complaints of fever on and off for one week, dry cough for 3-4 days and shortness of breath for one day. Patient was tachypneic and on auscultation had bilateral crepitations. His 0_2 saturation in room air was 87%. Chest X-ray revealed a left side opacity and blood investigations revealed leucopenia and lymphopenia. Initially the patient was managed in the ward with oxygen supplementation, but later he was shifted to the ICU as his oxygen requirement increased. In the ICU, the patient was initially managed with HHHFNC and CPAP support alternatively. In spite of all the supportive therapy patient's condition worsened and had to be intubated and put on ventilatory support. In view of refractory hypoxemia not responding to

conventional therapy patient was ventilated in prone position. Tracheostomy was done in view of expected prolonged duration of mechanical ventilation. Patient later developed a spontaneous pneumothorax and intercostal drain was placed.

Gradually he was weaned off the ventilator and tracheostomy was de-cannulated. He then developed secondary bacterial infection and required high dose vasopressors. Following this he developed bilateral lower limb gangrene. Vascular Surgery opinion was taken at this stage. On evaluation, the patient could not be anticoagulated due to his general condition and had developed a wet gangrene of the left lower limb and dry gangrene of the right foot. He required right sided mid tarsal amputation and left below knee amputation.

Clinically patient improved and he was discharged from hospital on day 46 following admission. He was managed with regular dressings for the bilateral lower limbs. The left below knee amputation stump healed well and the right foot required a Split thickness skin grafting which was done a month later. He is presently being rehabilitated to lead a near normal life. **(Fig. 3, 4, 5)**

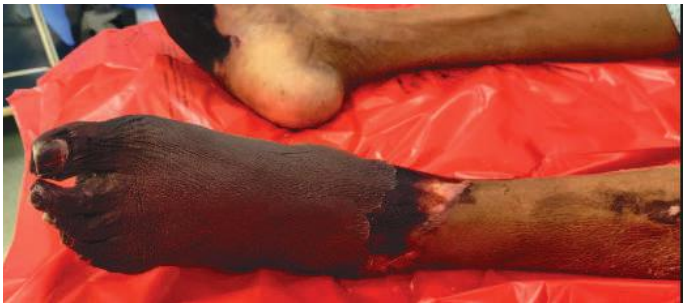

Fig. 3
Bilateral lower limb ischemia with gangrene

Fig. 4
Bilateral lower limb ischemia with gangrene

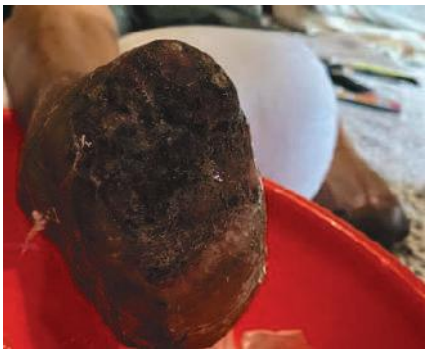

Fig. 5
Post op healed right mid tarsal amputation stump and left below knee amputation stump

DISCUSSION:

Peripheral limb ischemia in the SARS-COV-2 viral infection survivors is a reported entity in other case reports.[1-3] Through these two cases we present our experience in managing these patients. Both these patients had been on anticoagulation and it had to be stopped due to bleeding into the chest. Both these patients also required high dose of vasopressors. These two factors could have contributed to the development of the peripheral limb gangrene. The SARS-CoV-2 infection is also known to cause a prothrombotic state, causing arterial thrombosis even in patients on anticoagulants. All these factors combined could have led to the peripheral limb ischemia in these two patients.

SARS-CoV-2 infection primarily effects the lungs. It is a single stranded RNA virus which has been shown to bind to the angiotensin converting enzyme 2. This is present in nearly all human tissues, including the endothelial cells of the small to large arteries and veins. ACE 2 helps to convert angiotensin I to angiotensin II. As the virus binds to ACE 2, angiotensin I is not broken down. This angiotensin I is pro inflammatory and causes vasoconstriction.[4]

SARS-CoV-2 infection has been documented to cause a hyperinflammatory response. This in turn causes a hypercoagulable state.[5] Various studies have documented hypercoagulable states affecting different body regions like the heart, abdominal vessels, venous thromboembolism and acute cerebrovascular accident.[4,6] Cases of acute limb ischemia also been documented from various regions of the world[7,8] including both upper and lower limbs.[9]

The diagnostic modalities to determine the location of the thrombus in acute limb ischemia are the non-invasive Doppler ultrasonography and the invasive CT angiography.

Prophylactic anticoagulation in SARS-CoV-2 infection is being widely used to prevent the prothrombotic state and its complications. Inspite of its use, thrombosis of the upper and lower limb vessels have been documented to occur.[10] Thrombosis of the vessels and its management varies as per the location and the extent involved. For acute distal thrombosis minimally invasive interventions like intra-arterial thrombolysis is advisable. Medium and large artery thrombosis needs intra-arterial thrombolysis or thrombectomy followed by anticoagulation. Early identification and treatment is the mainstay to avoid complications.

Both our patients had palpable peripheral pulsations above the level of the gangrene. One of our patients was too sick to be shifted for a CT angiography. The patient with upper limb ischemia and digital gangrene underwent a Doppler ultrasonography which revealed a normal triphasic flow in all the peripheral arteries. CT angiography was not done and may be considered a limitation of the study in documenting the level of the arterial blockage. But the management of the patients was not dependent on the CT angiography. The patients also were not candidates for intra-arterial thrombolysis. One of them was managed conservatively and the second patient required surgical intervention. These two

cases highlight the peripheral vascular complications which needs to be considered during the care of the SARS-CoV-2 patients with moderate to severe pneumonia. These patients survived the infection but have to live with the residual non-pulmonary morbidity.

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WHAT MONEY CAN'T BUY

COVID 19 is not on illness but a test.

For country heads who took off money and efforts

from the bio-science and research;

Those businessmen who thought

With Advertising they will, amass the wealth;

For those parents who thought

costly play stations will make their children safe;

Deaths are happening people falling ill,

can, you see it, not Geeta colony or Dharavi

but it's the Bollywood, politicians' homes, Bandra and pal, hill!

Who knew that money con decay in artery and veins?

Bringing diabetes hypertension and clot in brain!

A poor man on rood seems be healthier

than the rich mon in confines of cosy home.

It, Tsunami of different kind and different time,

When wealthy are chosen one and poor are left out!

O Man, don, you see,

It, a mirror. show you what is wrong and what is right!

Fresh breeze and shining sun are the

What money can't buy they are

The anchor of new world and new life!

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One Lung Ventilation for Minimally Invasive Cardiac Surgery in COVID-19 Era

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INTRODUCTION:

One-lung ventilation (OLV) during Coronavirus pandemic (COVID-19) constitutes a very high risk procedure for aerosol generation. The reasons include repeated use of flexible fiberoptic bronchoscopy for confirmation of lung isolation, troubleshooting perioperative hypoxaemia and bronchial suctioning. These have serious implications for healthcare professionals and providers.

Although recommendations exist for airway management in COVID-19 patients, no such guidelines have been formulated for prevention of aerosol generation during bronchoscopy and OLV.[1,2] Case reports suggest the use of high-efficiency particulate filters during OLV, but these reports avoided the use of bronchoscopy for fear of aerosol generation.[3] We describe a simple closed-loop method for prevention of aerosol generation during bronchoscopy for OLV.

METHODOLOGY:

We use a sterile, non-allergenic, single-use plastic laparoscopic camera port cord cover as a barrier against aerosol generation for bronchoscopy during OLV. The cover is open at both the ends and is cut according to the length of the bronchoscope, leaving sufficient length for taping at the proximal and distal ends. The proximal end of the cover is taped at the bronchoscope handle, and the distal end is taped to the single lumen tube proximal to the cuff inflation line, with the bronchial blocker in situ. The distal end also incorporates the connector and a small slit is made in the cover to allow connection with the ventilator circuit. The bronchial blocker is also included in the cover and is to be moved independently. Once the endotracheal tube is in position, the ventilation is stopped and the blocker is introduced up to 35-40 cm mark inside the tube. Then the bronchoscope is to be introduced with the cover. The distal end of the cover is securely taped, the protective cap at the proximal ventilating port is opened to introduce the bronchoscope in to the lumen of the endotracheal tube. The bronchoscope can then be negotiated within the lumen for confirming the position of the blocker and the blocker can be adjusted accordingly. Once the blocker has been placed in the desired position, it is secured to prevent any dislodgement. **(Fig.1)** The pilot balloon and the suction port of the blocker are then brought to the exterior through a small cut in the cover and taped securely. **(Fig.2)**

It is better to leave the bronchoscope in situ throughout the procedure to prevent environmental contamination. Therefore, the scope can be hung easily on a stand next to the patients head. **(Fig.3)** In order to accomplish this, the length of the cover must be at least 45-48 inches or roughly 4 feet. To re-introduce the bronchoscope, the proximal end is opened and the scope is introduced.

Fig. 1
Bronchial blocker inside the endotracheal tube along with the protective cover

Fig. 2
The pilot balloon & suction port of blocker are brought to the exterior & tightly secured.

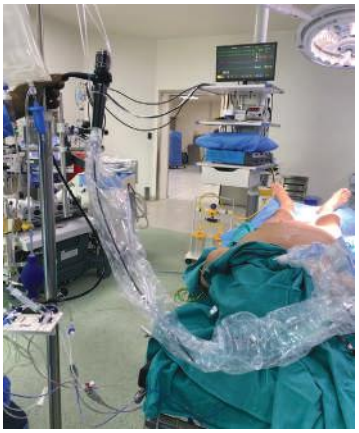

Fig. 3
The closed loop system is to be hung vertically on the stand.

SUMMARY AND CONCLUSION:

We have since use the closed-loop sheath in 6 patients who were non-COVID undergoing minimally invasive cardiac surgery. The ease of negotiating the scope through the sheath cover and the endotracheal tube was graded on a 3-point Likert scale of 1 to 3 as follows: 1 – scope negotiated easily without any difficulty; 2 – moderate difficulty in negotiating the scope; and 3 – scope negotiation very difficult. In all patients, the score was 1, with scope negotiation performed easily because the width of the cover is 18.5 cm, which allows for flexibility to manoeuvre the scope even after taping it at the respective ends. The covers are inexpensive and commercially available. Similar protective barriers have been reported recently for use with trans-oesophageal echocardiography probes and in double lumen tubes.[4,5] Considering the fact that 41.3% of COVID-19 cases were hospital acquired, of which >70% of infected cases were healthcare professionals,[6] we suggest use of these closed-loop barriers as an additional protection against aerosol contamination in all patients undergoing one-lung anaesthesia and ventilation for minimally invasive cardiac surgery. This will further help to save use of scarce personal protective equipment.

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Hybrid Endovascular Management of Radiation Necrosis induced ECA Pseudoaneurysm in Head and Neck Tumour: Case Report

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ABSTRACT:

A 45 year-old man with a history of surgery and radiotherapy (RT) of carcinoma in oral cavity 2 years back presented with recurrent bouts of per oral massive bleeding despite ipsilateral external carotid ligation. A huge External Carotid Artery (ECA) pseudoaneurysm (pseudoAN) was detected at the origin of internal maxillary artery on CT angiography. Hybrid management of this complicated aneurysm (surgical exploration and opening of ligation followed by endovascular Glue embolization of the aneurysmal sac was done. Clinicians must be aware that the ligation of ECA alone after Post RT bleed in head neck tumours is not always effective and can turn out to be troublesome.

Keywords: Radiation-induced, Pseudoaneurysm, Glue embolization, External carotid artery, Surgical exploration

INTRODUCTION:

Radiotherapy (RT), which is often indicated for the cancer of the head and neck region, can often cause acute or chronic injuries around the radiation site. It is a known characteristic of radiation to cause long-term effects progressing in stages after RT.[1] Scarring, ulceration and the mucosal fibrosis of the skin, pharynx, and esophagus are well known as late radiation injuries.[2] Additionally, sclerotic change of the arterial walls with a reported severity of 20–40% occurs after radiation and gradually worsens.[3,4] Meanwhile, pseudoaneurysms (pseudoANs) occurring after RT for head and neck cancer are rarely observed in the external carotid artery (ECA). The morbidity and mortality rates of ECA aneurysms (ECAAs) are high if the condition remains untreated. Vascular surgical intervention is frequently considered essential to relieve local symptoms and decrease the risk of stroke and aneurysm rupture. Both surgical and endovascular treatments have been used in the past decades.

Lack of endovascular inaccessibility of the carotid artery due to surgical ligation and technical difficulty involved in direct surgical exploration of aneurysm, the selection of treatment for ECA Aneurysm is challenging in our case.

CASE REPORT

A 45 year-old man had recurrent episodes of per oral bleeding after radiotherapeutic treatment of recurrent left retromolar trigone malignant mass. He had history of radical surgery and complete radiotherapy (a total dose of 64Gy) 2 years back. In the periphery due to unavailability of Interventional Radiologist or Onco-surgeon, ipsilateral ECA ligation was done in emergency without any prior imaging. However inspite of this, episodes of massive oral bleeding continued, so he was referred to our hospital for further evaluation and treatment. On clinical examination, multiple oro-cutaneous fistulous tracts in neck and cheek region were observed. The patient was alert with no Neurological deficits however unable to open the mouth. CT angiography of neck revealed, huge broad neck ECA aneurysm (~13x11mm) in the left side of oral cavity beneath the angle of the mandible with focal cut off of ECA at its origin (Due to ligation).

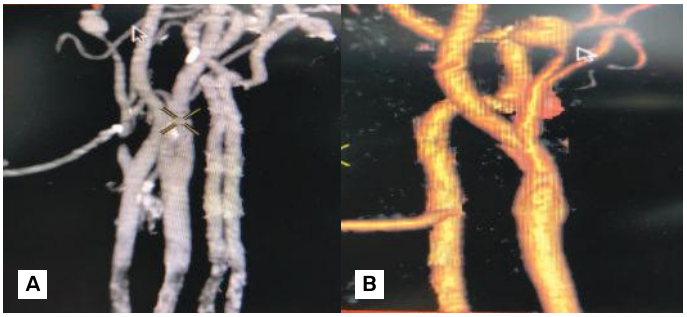

Fig. 1 A. Maximum Intensity projection (MIP) B. Surface shaded Volume Rendered Technique images showing large ECA Aneurysm (black arrow) at origin of Internal Maxillary artery with focal cut off of ECA near its origin (white arrow)

From his medical history and the radiological imaging findings, the diagnosis of radiation-induced pseudoaneurysm was made. We recognized that urgent therapeutic intervention was needed to prevent aneurysmal re-rupture. At presentation, the patient was taking no medication for hypertension, ischemic coronary disease, diabetes mellitus or dyslipidemia.

Considering his general condition, single surgical or endovascular treatment was not possible. Open surgery i.e. surgical repair of end-to-end anastomosis under direct observation of both proximal and distal ends of aneurysm, was not possible in our case due to

extensive radiation fibrosis, complex anatomical site of aneurysm and inability of patient to open the mouth due to submucosal fibrosis. Endovascular management was also not possible due to inaccessibility to aneurysm as parent vessel was already ligated so rapid decision was taken for Hybrid management.

Under General anesthesia, DSA angiography of left Common Carotid Artery (CCA) revealed complete cut off of ECA near its origin with normal opacification of Internal Carotid Artery (ICA). Left vertebral angiogram revealed filling of distal ECA and aneurysm by collateral from vertebral artery via occipital artery. However, due to acute angle and narrow calibre of the collateral, superselective catheterization with microcatheter could not be done.

Then the surgeon explored the neck to open the ligation thread of ipsilateral ECA which was technically challenging and quite difficult due to post radiation extensive fibrosis and feeble palpation of pulse at CCA and ICA. After herculean efforts, the tiny thread was identified and cut safely. Post-surgical intervention, CCA angiogram revealed complete opacification of ECA and pseudo aneurysm however distal trapping of aneurysm could not still become possible even with microcatheter inspite of multiple attempts. So controlled endovascular glue embolization of pseudoaneurysm with lipiodol (in 1:1 ratio) was done successfully with no post procedure focal neurological deficit.

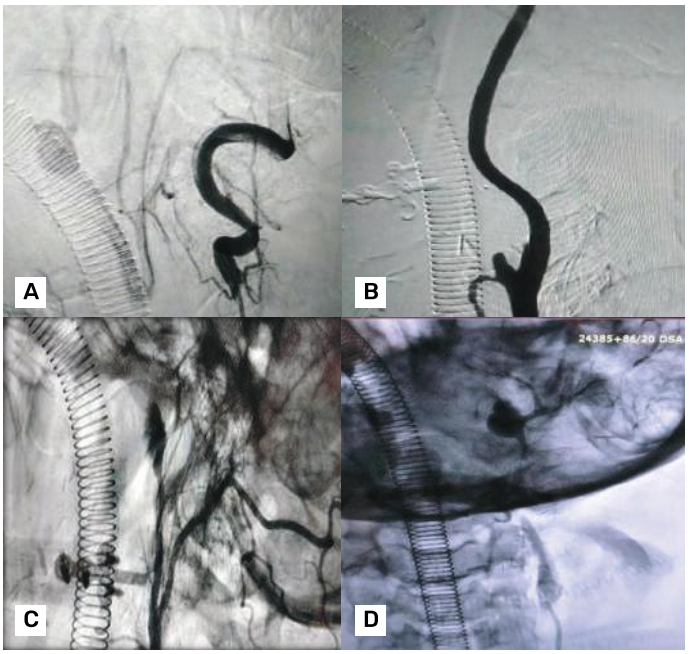

Fig. 2 A. Digital Subtraction left vertebral Angiogram image showing ECA Pseudoaneurysm (black arrow) filling from vertebral artery via occipital artery (white arrow) B. Left Common carotid angiogram shows focal cut off of Left ECA just after origin of superior thyroid artery (Post ligation status) C. Left ECA angiogram shows opacification of aneurysm after opening of surgical ligation thread at origin of ECA D. Post embolisation glue cast in Aneurysmal sac

DISCUSSION:

The course of our case suggests two important clinical issues. First, it serves to remind us that ligated carotid arteries due to chronic post-irradiation injury in head and neck tumours can progress to a pseudo aneurysm over time (though this is a rare event) by collateral supply from vertebral or other neck vessels. We speculate that prolonged hemodynamic stress might have accelerated the necrosis of the vessel wall over a long period of time, resulting in an aneurysmal change under the subsequent damage to the vascular endothelial cells by the RT. The location, etiology, and features of the aneurysm in combination with previous experience are important factors that determine the selection of the optimal intervention strategy.

Second, endovascular intervention is worth considering not only as an urgent or palliative procedure but also as an effective treatment indicated for remission in cases of post-irradiated cervical ECA and ICA pseudoaneurysm.

Endovascular treatment compromises the use of pushable and detachable micro Coils, Polyvinyl Alcohol particles, Gelfoam, Stent Graft depending upon the location, anatomy, etiology of bleeding in head and neck tumours.

Hybrid techniques have further been described in cases of ligated ECA and high ICA aneurysms with a proximal ICA kink and/or loop. Open surgery can expose the carotid artery and the anatomic variation can be removed before or after endovascular repair. Consequently, a hybrid operation is an available choice of treatment for complicated cases.

Nevertheless, there are still many unclear points regarding the treatment strategy for this pathology. The follow-up periods in the available studies have varied widely in length because of the difficulty of managing disease progression in the advanced stages. Therefore, we cannot clarify the radicality of endovascular approach. Further, several major technical complications have recently been reported, including re-bleeding, exposure of the devices due to ulcerated skin associated with infection or tumor necrosis, and acute embolism or delayed cerebral ischemia associated with in-stent thrombosis. As an alternative, surgical resection of the aneurysm and graft bypass operation is often chosen as a radical course of treatment, though this approach also has potential complications including infection and anastomotic leak caused by weakness in the vessel walls and thinning of the skin.

CONCLUSION:

We suggest performing endovascular intervention in patients with post-irradiated pseudoaneurysm as a minimally-invasive procedure for this advanced clinical disease. Endovascular And /Or Surgical treatment yields a relatively satisfactory outcome in patients with ECA Aneurysms.

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Extensor Hallucis Longus Tendon Injury at the Level of Ankle: A Case Report

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ABSTRACT:

Extensor hallucis longus (EHL) tendon injuries mostly occur with lacerations sustained over the dorsum of the foot and lead to hallux dysfunction. We present a case of isolated extensor hallucis longus tendon injury which occurred as a result of laceration over the anterior aspect of ankle. To our knowledge, there are no case report regarding injuries to the extensor hallucis longus tendon at the level of ankle joint. Tendon was repaired end to end using Modified Kesseler suture. Below knee cast was applied supporting the repair by holding the great toe in extension. The functional outcome of the patient was assessed using Hallux Metatarsophalangeal – Interphalangeal scale. The score at 3 months follow up was 97. Hence we concluded that primary end to end repair of extensor hallucis longus tendon lacerations at the level of ankle is a reliable procedure that restores hallux alignment and function.

INTRODUCTION:

The extensor hallucis longus (EHL) is a muscle situated between the tibialis anterior and the extensor digitorum longus (EDL). The EHL arises from the middle half of the fibula and from the interosseous membrane, medial to the origin of the EDL. The muscle belly becomes a long tendon, passes behind the superior and inferior extensor retinaculum, crosses the anterior tibial artery and vein from the lateral to the medial side near the ankle, and finally inserts on the dorsal aspect of the base of the distal phalanx of the big toe.[1] The function of the EHL is to extend the big toe, dorsiflex the foot, adjunct foot eversion and inversion and stretch the plantar aponeurosis.[2]

Isolated laceration of the EHL tendon at ankle is not uncommon but is rarely reported in the literature.[3] The literature is also inconsistent concerning surgical repair of the EHL.[4] Extensor hallucis longus tendon injury and surgical treatment recommendations are infrequently reported. In contrast to long extensor tendon injuries to the foot, flexor and extensor tendon injuries of the hand have been extensively studied and surgical treatment protocols have been delineated.[5]

Extensor hallucis longus (EHL) tendon injuries mostly occur with lacerations sustained over the dorsum of the foot and lead to hallux dysfunction.[6] We present a case of isolated extensor hallucis longus tendon injury which occurred as a result of laceration over the anterior aspect of ankle.

CASE REPORT:

A 31 year old male patient presented to the outpatient department with history of glass injury to the dorsal aspect of the left ankle two weeks back. The chief complaint of the patient was inability to extend his great toe since the time of injury. On examination of left ankle and foot, there was no bony tenderness or crepitus. Healed scar mark was present over the dorsum of ankle. Passive extension of the great toe was possible but active extension was lacking. **(Fig. 1)** There was no neurovascular deficit. A diagnosis of traumatic extensor hallucis longus tendon injury was made and it was supported by ultrasonography findings. The patient was prepared for surgery after all routine investigations were normal and pre anaesthetic evaluation was completed.

Fig. 1.
Great Toe in Planter flexion

SURGICAL TECHNIQUE:

Structures were identified and skin markings were done. **(Fig. 2)** Skin incision was taken and soft tissue was separated till the level of extensor tendons. Neurovascular bundle was identified and protected. Distal stump of extensor hallucis longus tendon was delivered into the wound and tagged. Dissection carried out proximally under the extensor retinaculum. Tibialis anterior tendon was identified. Proximal stump of the extensor hallucis longus tendon was identified and delivered into the wound. **(Fig. 3)** Tendon was repaired end to end using Modified Kesseler suture with 3-0 prolene. **(Fig. 4)** The tendon sheath repaired with 5-0 prolene. Wound was closed in layers after washing. **(Fig. 5)** Below knee cast was applied supporting the repair by holding the great toe in extension.

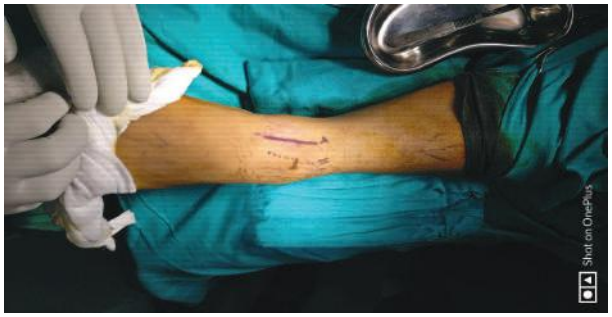

Fig. 2
Surface Marking

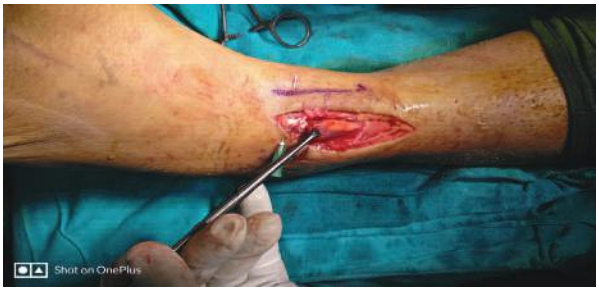

Fig. 3
Proximal and distal cut ends of the tendon

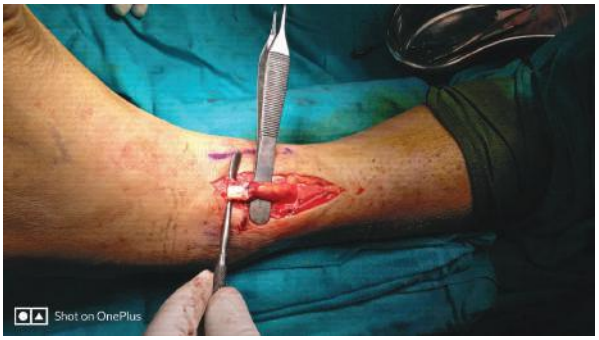

Fig. 4
Proximal and distal cut ends of the tendon

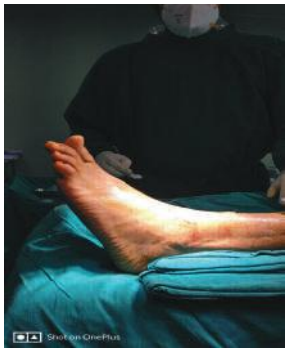

Fig. 5
Posture after closure.

POST-OPERATIVE PERIOD:

The patient was given adequate post-operative antibiotic cover and physiotherapy with the goal to prevent secondary complication and to mobilise the patient out of bed. The patient was started with non-weight bearing ambulation with walker on the first post-operative day. The sutures were removed at 2 weeks post-surgery. The functional outcome of the patient was assessed using Hallux Metatarsophalangeal – Interphalangeal scale **(Fig. 6)**.[7]

Hallux Metatarsophalangeal-Interphalangeal Scale

Pain (40 points)	
None	40
Mild, occasional	30
Moderate, daily	20
Severe, almost always present	0
Function (45 points)	
Activity limitations	
No limitations	10
No limitation of daily activities, such as employment	7
Limited daily and recreational activities	4
Severe limitation of daily and recreational activities	0
Footwear requirements	
Fashionable, conventional shoes, no insert required	5
Comfort footwear, shoe insert	3
Modified shoes or brace	0
MTP joint motion (dorsiflexion plus plantarflexion)	
Normal or mild restriction (75° or more)	10
Moderate restriction (30°-74°)	5
Severe restriction (less than 30°)	0
IP joint motion (plantarflexion)	
No restriction	5
Severe restriction (less than 10°)	0
MTP-IP stability (all direstions)	
Stable	5
Definitely unstable or able to dislocate	0
Callus related to hallux MTP-IP	
No callus or asymptomatic callus	5
Callus, symptomatic	0
Alignment (15 points)	
Good, hallux well aligned	15
Fair, some degree of hallux malalignment observed, no symptoms	8
Poor, obvious symptomatic malalignment	0
Total=	100

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From: http://www.aofas.org/i4a/pages/index.cfm?pageid=3494

Fig. 6.
Scoring System for outcome

The cast was removed at 6 weeks post-op and the patient was started on physiotherapy and weight bearing was allowed. The score at 3 months follow up was 97.

DISCUSSION:

In acute extensor hallucis tendon injuries, treatment options are direct primary repair or tendon reconstruction.[6] In the literature, injuries of the extensor hallucis longus tendon have been reported at the dorsum of foot. To our knowledge, there are no case reports regarding injuries to the extensor hallucis longus tendon at the level of ankle joint. The injury of extensor hallucis longus at this site occurs at the level of musculotendinous junction. We used similar method as used for distal injuries of the tendon and achieved good functional outcome.

CONCLUSION:

Primary end to end repair of extensor hallucis longus tendon lacerations at the level of ankle is a reliable procedure that restores hallux alignment and function.

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Transcatheter Aortic Valve Replacement (TAVR) in very high risk patients for surgical valve replacement – Our Experience

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ABSTRACT:

Introduction: Transcatheter aortic valve replacement (TAVR) is widely applied for the treatment of high risk severe aortic stenosis (AS) with multiple co-morbidities in developed countries but in our country, it is still being done only at few select centers with multidisciplinary team facility. Here we present our experience with Transcatheter aortic valve replacement (TAVR) in very high risk surgical patients in our hospital.

Methods: We have done three transcatheter aortic valve replacements (TAVR) since we started. One patient had balloon expandable valve and two patients had self-expandable valve. All the patients had multiple co-morbidities making them very high risk for the surgical aortic valve replacement. The valve and heart functions of all patients before and after the TAVR procedure were compared. TAVR endpoints, device success, and adverse events were assessed during hospital stay and follow-up visits.

Results: Mean age of the patients was 74.6 years with oldest patient being 79 years. All three patients were male. All the procedures were done by trans-femoral route. Two procedures were done under conscious sedation and one was done under general anesthesia because of severe interstitial lung disease. One patient had additional PCI and stent to LAD at the time of TAVR. The recovery was uneventful in all three cases and have been doing well in follow up period.

Conclusion: TAVR technology is safe and effective and can be used for patients with severe AS who are at high risk for surgical aortic valve replacement. At our center we are doing it ourselves and using a heart team approach comprising of cardiac surgeon, cardiologist and cardiac anesthetist with team being led by cardiac surgeon to give optimal result to the patients.

Key words: Aortic stenosis, TAVR, Trans-femoral, Heart team, cardiac surgeon

INTRODUCTION:

Aortic stenosis (AS) is the second-most frequent cardiovascular disease after coronary artery disease and systemic arterial hypertension with a prevalence of 0.4% in the general population and 1.7% in the population >65 years old.[1] Congenital abnormality (bicuspid valve) and older age are powerful risk factors for calcific AS. Metabolic syndrome and an elevated plasma level of lipoprotein (a) have also been associated with increased risk of calcific AS. Congenital AS is mainly caused by bicuspid aortic valve. Acquired AS is often termed "senile" or "calcific valvular" AS, which is considered a degenerative process. The mortality rate of AS patients older than 75 years is as high as 2.8%.[2] Although performing surgical aortic valve replacement (SAVR) under extracorporeal circulation is still the gold standard treatment for AS with good outcomes, it can also lead to significant patient trauma, inflammatory stress, and other potential risks specially in high risk patients with multiple co-morbidities as calculated by Society of Thoracic Surgeons (STS) score. This is especially true for the frail elderly population with severe circulatory, respiratory, or urinary system disease, which greatly increases the surgical risk.

At the beginning of this century, transcatheter aortic valve replacement (TAVR) heralded a new era of minimally invasive non-surgical replacement of aortic valve. In 2002, Cribier and colleagues accomplished the first TAVR in humans. TAVR has been proven to be an effective and safe treatment and is being carried out in developed countries for patients considered high risk for SAVR routinely.[3,4] However, in a developing country like ours, the technique is relatively new and is being done only at few select centers. Here we present initial experience with TAVR at our upcoming center, bringing us in the league of few select and well established centers in the country doing this procedure successfully.

PATIENTS AND METHODS:

Three very high risk patients of severe calcific aortic stenosis presented to us for surgical valve replacement and were evaluated for TAVR. All three patients were evaluated preoperatively using clinical evaluation, transthoracic echocardiography (TTE), coronary angiography (CAG), computed tomographic angiography (CTA) to see for aortic annulus, sinus height, distance from coronary ostia, aortic angulation, peripheral vessels and pulmonary function tests to assess the cardiac structure and function, systemic

vascular conditions, and other co-morbidities. The routine hematologic investigations were done including kidney and liver function tests. Any H/o previous surgery or any other associated pre-existing illness like thyroid dysfunction were noted.

A heart team comprising of cardiac surgeon, cardiologist, cardiac anesthesiologist and radiologist was used in all cases to evaluate the patient comprehensively. The patients were deemed to be very high risk for surgical aortic valve replacement due to associated co-morbidities. Since TAVR was considered to be safer and better option for such patients, they were planned for TAVR after discussing all the risks and benefits of both procedures in detail with patients and their families. All the three patients were male. The mean age of patients was 74.6 years with oldest patient being 79 years.

CASE 1:

Our first patient was 75 years old male, who presented with H/o dyspnea on exertion (NYHA-IV) along with H/o syncope. The patient had H/o coronary artery bypass grafting in 2005. Echocardiography revealed severe degenerative calcified aortic valve stenosis with valve gradient of 126/89 mm Hg, valve area of 0.6 cm^2, mild aortic regurgitation, left ventricular ejection fraction (LVEF) of 35-40% and mild mitral regurgitation. Patient was in pre-operative heart failure. His serum creatinine was 1.8 mg% with moderate renal dysfunction. He was diabetic and hypothyroid on treatment. Coronary angiography was done which showed patent graft to LAD and OM. Patient was admitted in ICU, electively intubated in view of heart failure and started on medical management and diuresis. The heart team was involved and after detailed evaluation and discussion with family, patient was planned for TAVR. His pre-operative STS score was 11.7%. CT study of the aorta revealed calcified aorta. Detailed evaluation of aorta and peripheral vessels was done. Patient was extubated in ICU after stabilization and the procedure was done under conscious sedation with MYVAL valve 24.5 mm balloon expandable valve. Patient had an uneventful recovery post procedure. Post procedure ECHO showed a valve gradient of 28/8 mm Hg and LVEF of 45%. He was discharged on day 3 of procedure. At 3 months follow up patient was asymptomatic with normal hematological parameters, ECHO showed LVEF 45%, normal function prosthetic valve and no valvular or para-valvular leak.

CASE 2:

Our second case was a 70 years old male, Sudanese national, who had been evaluated in his native country for recurrent syncopal episodes and dyspnea on exertion (NYHA-III) and found to have severe degenerative calcific aortic stenosis with aortic valve gradient of 134/83 mm Hg (peak and mean gradient respectively). Chest X- ray revealed calcified ascending aorta. Patient was a known case of interstitial lung disease. He refused any intervention in his native country and was referred to us for further management. The patient was evaluated in detail with echocardiography, hematological investigations and CT study of aorta along with HRCT chest. In view of his significant interstitial lung disease and calcified ascending aorta along with symptoms, patient was deemed to be very high risk for surgery. After discussing with the family, patient was planned for TAVR. TAVR was done under general anesthesia as patient was unable to hold breath due to interstitial lung disease. The procedure was uneventful and valve was replaced with 34 mm Evolute-R self-expanding valve. The patient was extubated in the ICU after 2 hours. Post-operative ECHO revealed no para-valvular leak with a peak and mean gradient of 25/7 mm Hg respectively. Patient was shifted out of ICU on day 2 of procedure and was discharged on day 3. He followed up after 3 months and was completely asymptomatic. **(Fig. 1-2).**

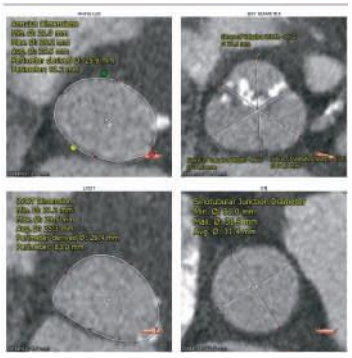

Fig 1: Aortic Assessment

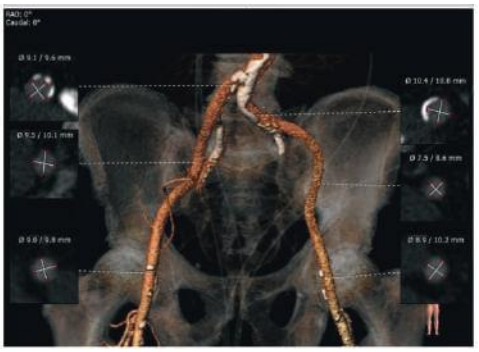

Fig 2: Assessment of Femoral Vessels on CT Study of Aorta

CASE 3:

Our third case was a 79 yrs old male patient, who presented to us in NYHA class IV. Echocardiography showed severe degenerative calcific aortic stenosis with a peak and mean gradient of 143/97 mm Hg, valve area of 0.7 cm^2 and LVEF of 35%. There was mild to moderate mitral stenosis with a gradient of 15/8 mm Hg, severe pulmonary artery hypertension, preoperative atrial fibrillation and left bundle branch block (LBBB). His serum creatinine was 1.8 mg% and coronary angiography showed significant proximal LAD disease. The pre-operative STS score was 8.97% with a 30.78% risk of morbidity or mortality. So he was planned for TAVR with PCI and stent to LAD. CT study of the aorta was done to evaluate the same and procedure was completed uneventfully under conscious sedation. On table check angiography showed 90% proximal LAD stenosis so stent to LAD was put and TAVR was done with 29 mm Evolute-R self-expanding valve. The patient was shifted back to ICU uneventfully. He

continued to be in AF in post-operative period with LBBB and was monitored and discharged uneventfully on day 3 of procedure. Post-operative ECHO showed a valve gradient of 26/7 mm HG with no regional wall motion abnormality and LVEF of 50%. **(Fig. 3-6)**

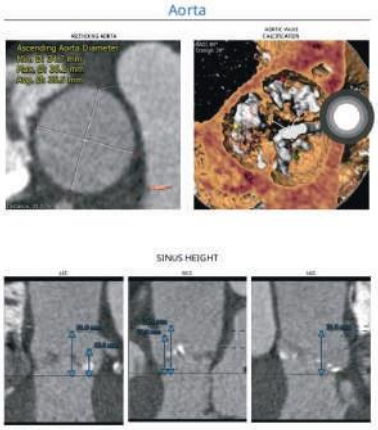

Fig 3: Assessment of the Aortic Valve & Ascending Aorta

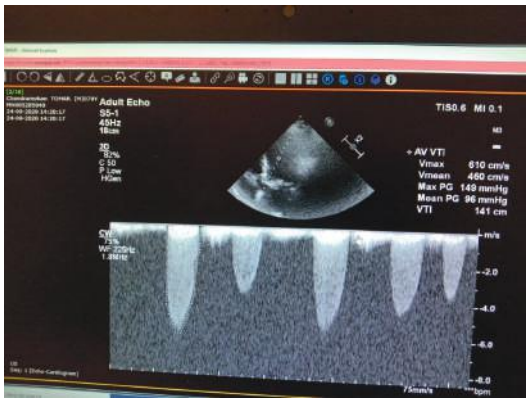

Fig 4: Preoperative ECHO showing gradient across the Aortic Valve

Fig 5: PTCA & Stent to LAD for Tight Ostial LAD Disease

Fig 6: The Team led by Dr. YK Mishra performing the procedure

DISCUSSION:

Degenerative calcific aortic stenosis also called as senile calcific AS is a significant problem that is directly correlated with advanced age. Medical management has a limited role only in very high risk surgical patients or patients with mild to moderate aortic stenosis and the treatment of degenerative severe calcific AS has primarily been Surgical Aortic Valve Replacement (SAVR). SAVR is one of the most frequently performed adult cardiac surgical procedures. Multiple studies have demonstrated that well over 30% of patients with severe aortic stenosis are denied AVR due to a high risk of surgical complications. These numbers do not include patients who are never referred for surgery, either because they are too high-risk or because the patients themselves are not willing to undergo open heart surgery. In the past decade, the emergence of TAVR has offered a less invasive approach for the treatment of high risk patients with severe AS. In this vein, TAVR is a transformative procedure, opening the door to many patients who would otherwise not be treated.

Table 1
Benefits of Transfemoral TAVR over SAVR: The Patient's Perspective

Procedure	Risks	Early Outcomes	Long-Term Follow-Up
• Less invasive • No cardiopulmonary bypass • No orotracheal intubation • No intensive care unit	• Lower risk of new-onset atrial fibrillation, bleeding events, and kidney injury • Major benefit in female patients	• Shorter hospitalization • Faster return to normal life • Faster regain of quality of life	• Assess the need for reintervention • Long-term anticoagulant therapy

Abbreviations: SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

Transcatheter aortic valve replacement (TAVR) is a less invasive, percutaneous method developed for replacing the aortic valve in patients with severe calcific aortic stenosis and has unique benefits **(Table 1)**. Randomized data support TAVR as an option for patients at high and intermediate surgical risk [5,6,7,8] The first TAVR valve was implanted in 2002, CE Mark approval was granted in 2007, and FDA approval was not obtained until 2011. Initial experience was largely with inoperable and high-surgical-risk patients, and owing to the limited life expectancy of these cohorts, robust longer-term durability data was not available. The procedure has been around for more than a decade now and there is enough clinical and long term follow-up data from high

risk patients to support the efficacy of this procedure. The indications for TAVR are now expanding to include some intermediate risk patients based upon their STS score. Initially the procedure was limited to only degenerative calcific aortic stenosis but now studies are also ongoing to include some rheumatic calcific aortic stenosis who are at high surgical risk.

The procedure is usually performed via trans-femoral or trans-apical route and can be done under general anesthesia or sedation, depending on patient's general condition and associated co-morbidities. The risk stratification is usually done on the basis of STS score of the patient. It is a scoring system to assess the risk of post-operative mortality and morbidity, and classifies the patients in low, intermediate, high and prohibitive risk of surgery. The scoring system takes into account the age and general condition of the patient, diabetic status, hematologic, renal, liver function parameters, echocardiographic findings, angiographic findings and whether it's a redo procedure or combined procedure. The values are filled in an online pre-formed proforma and the risk of mortality, morbidity, long hospital stay, and readmission is calculated by a web based software by statistical analysis. Based on the STS score, risk of surgery or intervention is stratified. If the value is 1-4%, it is low risk, 4-8% intermediate risk, 8-12% high risk and >12% very high risk/prohibitive.

In our patients, the STS score for all 3 patients was in high to very high risk category. Two patients had pre-operative renal dysfunction with moderate to severe left ventricular dysfunction and one patient had calcified porcelain aorta which in itself is a contraindication for any aortic intervention.

The main complications following TAVR include para-valvular leak, embolic stroke, annular rupture, coronary ostia occlusion, device embolization, pericardial tamponade, heart block and peripheral vascular complications. A careful pre-operative planning and assessment and multidisciplinary team helps in averting these complications.

CONCLUSION:

TAVR is safe and effective procedure for patients who needs aortic valve replacement but are at high risk for surgery due to either cardiac risk factors like porcelain aorta or due to associated co-morbidities. A careful pre-operative assessment and heart team (including cardiac surgeon, cardiac anesthetist, cardiologist and radiologist) is required to get optimal results in such patients. In our second patient with porcelain aorta and severe interstitial lung disease with symptomatic AS, such procedure is lifesaving. In our third patient with symptomatic severe calcific AS and pre-operative arrhythmia with moderate MS with severe PAH with severe left ventricular dysfunction open heart surgery would mean double valve replacement for which the patient had prohibitive risk of surgery. This procedures is ideal for such cases.

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Sciatic Notch Dumbbell Shaped Tumor – Combined Antero-Posterior Approach for En-Bloc Dissection

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BACKGROUND:

Soft tissue sarcomas (STS) are malignant neoplasms of mesenchymal origin[1]. Their heterogeneity and varied presentations have made it difficult to establish a consensus guideline for their management. Though they are treated with multimodal therapies, surgical intervention in form of monobloc resection with negative margins remains the standard of care[2].

Sciatic notch dumbbell shaped tumors (SNDT) pose a unique surgical challenge because of complex regional anatomy. Due to their rarity, descriptions of surgical techniques employed to resect SNDT are scarce. These tumors have poor prognosis because of high rates of local recurrence and surgical morbidity[3]. Here we describe the operative technique of resecting SNDT.

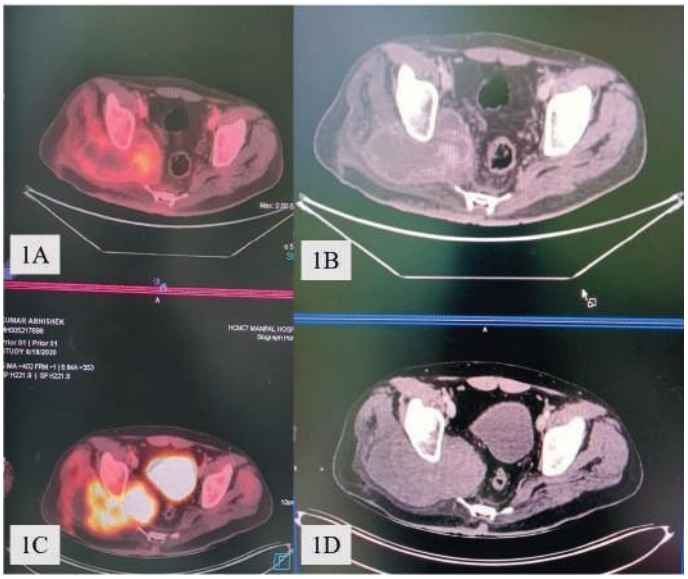
CASE PRESENTATION:

Our patient was a 34 years old male who presented with pain in right knee and right foot drop. Clinical examination revealed an immobile mass in right gluteal region with right peroneal nerve palsy. He also had multiple neurofibromas present all over the body and their number had increased in last 4 years.

MRI revealed 13.4 x 7.9 x 5.8 cm mass in right piriformis muscle encasing right sciatic nerve, medially bulging into the pelvis and laterally crossing greater sciatic notch into gluteal area posterolateral to ilium and just superior to ischial spine. It was pushing the right internal iliac artery medially but not encasing or engulfing. It was starting just below the bifurcation of common iliac veins with internal iliac vein splayed over its anterior surface

Image guided transgluteal core biopsy and further immunohistochemistry revealed large epithelioid/ spindle tumor cells with complete loss of H3K27me3 expression, favouring diagnosis of malignant peripheral nerve sheath tumor (MPNST).

PET-CT done for staging confirmed it as localised disease. On the recommendation of institutional tumor board, patient was given 4 cycles of neoadjuvant chemotherapy and reassessed for surgery. Post chemotherapy, both MRI scan and PET-CT showed slight decrease in size with increase in necrotic component and significant decrease in metabolic activity on PET-CT. **(Figs 1 A-D)**



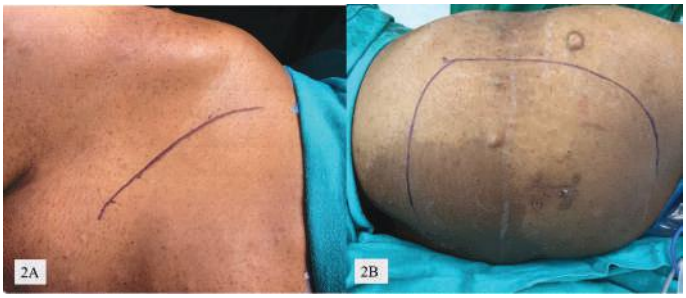
Figures 1 A-D
Pre-chemo (Fig 1 C & D) and Post-chemo (Fig 1 A & B) PETCT images showing significant post chemo tumor necrosis (seen on CT images) and significant reduction in metabolic activity (fused PET-CT images)

SURGICAL TECHNIQUE:

The main goal of surgery in STS resection is to achieve en-bloc resection with clear margins. Tumor capsule breach or piece meal resection leads to local contamination and increases the chances of local recurrence which is usually multi-centric and not amenable to curative resection[4]. As the tumor was encasing the sciatic nerve which was non-functional and infiltrating the gluteus maximus muscle on imaging, decision was made to sacrifice the nerve and completely excise the muscle to achieve optimal oncologic clearance.

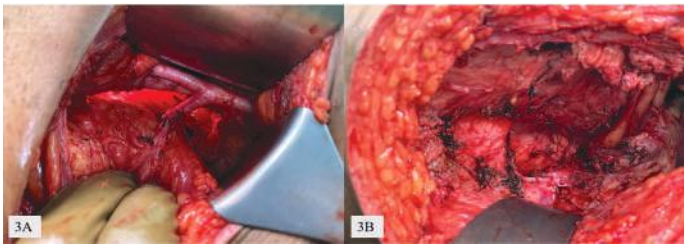
We resected the tumor in one stage by using a combined anterior and posterior approach with patient in lateral decubitus position. We started with anterior approach by giving incision parallel to and above the inguinal ligament **(Fig. 2A)** entering the pelvic space retroperitoneally by pushing the peritoneum supero-medially. The ureter and gonadal vessels were retracted medially. The internal iliac artery was exposed and lateral sacral, superior and inferior gluteal arteries ligated which significantly reduced the tumor blood supply. Internal iliac vein, which was splayed over the mass, was ligated just distal to its junction with external iliac vein. The obturator nerve was found stretched over the

anterior surface of tumor and was dissected free and retracted. The tumor then was freed circumferentially, completely separating it from its pelvic attachments.



Figures 2A & B
Incision markings. A – Anterior incision parallel to & above inguinal ligament (Head end is to the right of picture); B – Posterior incision (Gluteal area; head end is to the left of picture)

For the posterior approach, incision was made beginning at the posterior aspect of the crest of the ilium, curving distally following the gluteus maximus muscle along the iliotibial band, passing over the greater trochanter. **(Fig 2B)** A fascio-cutaneous flap was raised to expose the entire gluteus maximus muscle which was then released from iliotibial band up to the iliac crest. Sciatic nerve identified at lower border of gluteus maximus muscle and divided. After the initial release from its insertion, muscle was then released from its origin along the para-sacral region from the coccyx to postero-inferior sacroiliac joint (PISIJ). Both the superior and inferior gluteal vessels are encountered in this part of dissection, however, their ligation at origin from internal iliac artery done during anterior approach makes their dissection easier and limits the blood loss[5]. **(Figs 3A & B)**. The resected gluteus maximus muscle along with its contained tumor was then circumferentially freed from surrounding attachments. The specimen got delivered through the posterior incision by working through both anterior and posterior approach. **(Fig 4)** Suction drain was inserted and wounds were closed in layers.



Figures 3A & B
Post excision operative field. A – Anterior view showing Bifurcation of common iliac artery & preserved internal iliac artery. The light is coming through sciatic notch. B – Posterior view

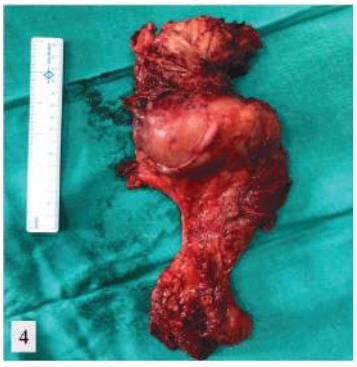


Figure 4
Specimen showing the dumbbell shaped tumor – upper part showing intrapelvic part and attached gluteal muscles in the lower part.

Postoperatively patient had an unremarkable recovery. He was discharged on post-op day 7. Limb function was preserved except the foot drop which he was having preoperatively also due to involvement of sciatic nerve. On final histopathology, it was reported to be a 10 x 5 x 3.5 cm poorly differentiated MPNST, grade II with clear margins. About 40% of viable tumor was present in specimen post chemotherapy. It was discussed in tumor board meeting and now he is planned for adjuvant chemotherapy followed by radiotherapy.

DISCUSSION:

SNDT have the capacity to grow large as the clinical symptoms produced are non-specific and patients present late[6]. Their relatively rare occurrence has made it difficult to perfect the surgical approach.

Surgical resection of SNDT requires a balance between adequate oncologic resection and preservation of function[7]. We performed a simultaneous anterior (retroperitoneal) and posterior approach, as described by Gaignard E et al, to limit inadvertent injury to surrounding organs as well as to have exposure from both sides[4]. Spinner RJ et al performed the dissection by transabdominal and transgluteal approach[3]. They went intraperitoneally first to complete intrapelvic dissection and then changed the position of patient for extra pelvic part. We went extraperitoneally in our anterior approach as it decreases the chances of intraperitoneal visceral injury and has early recovery of bowel function. Also our approach can be done in same lateral decubitus position saving the intraoperative time.

The role of good quality imaging is paramount in determining the pelvic arterial anastomotic networks and sciatic nerve in relation to the tumor. In our case, PET-CT showed the upper border of tumor a centimetre below the bifurcation of common iliac artery and abutting the bifurcation of common iliac vein. The sciatic nerve was completely encased in MRI scan. These anatomical relationships on multiple images allow surgeon to plan the course of surgery and in predicting outcomes. We ligated the lateral sacral, superior and inferior gluteal arteries first which helped in decreasing the tumor vascularity. This step done before mobilising the tumor decreases the blood loss. Though not in this case, sometimes ligation of internal iliac artery proper

is also done when necessary but it can cause buttock claudication. Thus we painstakingly dissected the main internal iliac artery away from tumor carefully ligating all its branches going towards the tumor. Since MRI showed gluteus maximus muscle infiltration and its excision has little impact on the normal gait and pelvic stability, we excised it completely to achieve oncologic clearance.

We removed the tumor as monobloc specimen which is necessary to avoid local seeding. Here sciatic notch osteotomy was not required as we could deliver the tumor in posterior field through sciatic notch. Spinner et al suggested that it was not necessary to expand the sciatic notch to remove benign tumors and in one case they removed multiple masses in piecemeal fashion from pelvis[3]. In case of malignant tumors, we discourage such approach as tumor fragmentation increases the risk of local recurrence and becomes an indication for adjuvant radiotherapy[8]. MRI imaging also helps in determining whether sciatic notch osteotomies are required or not[9]. The division of sacrospinous and sacrotuberous ligaments provide more space for manipulation. However, marginal osteotomies may be required to enlarge the sciatic foramen. Li et al described C – shaped osteotomy during posterior approach with bone cutter preventing damage to hip and sacroiliac joint[10].

CONCLUSION:

A combined anterior-posterior approach provides access to SNDTs from both sides and facilitates excision as single specimen. Thorough pre-operative work-up with adequate use of imaging guides in surgical planning. Retroperitoneal approach avoids disturbance from intraperitoneal organs and prevents any inadvertent injury to these organs also. Ligation of feeding vessels from internal iliac artery reduces intraoperative blood loss during posterior dissection. We also advocate expansion osteotomy if needed to deliver large mass through sciatic notch in one piece. The muscles infiltrated in gluteal region should be completely excised to ensure adequate margins and it appears to have little functional effect.

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Gigantic Uterine Mass in a Young Girl – Case Report

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ABSTRACT:

Although uterine leiomyomas are the most common neoplasms of the female genital tract, they are relatively uncommon in women under the age of 19. Only a few cases of uterus leiomyomas have been reported in this age group. Preoperative imaging evaluation is mandatory in adolescent women for the accurate detection, localization, and characterization of uterus leiomyomas.

We report a case of a 15-year-old girl admitted to our hospital for irregular menses, constipation, and abdominal distention. The patient underwent ultrasound and MR examination of the pelvis. Both imaging modalities revealed uterine enlargement and the presence of innumerable variably sized leiomyomas. The patient underwent open myomectomy, following MR examination of the pelvis. Histopathologic examination following exploratory laparotomy confirmed the presence of uterine leiomyoma.

INTRODUCTION:

Leiomyomas, also known as fibroids, fibromyomas or fibromas represent the most common uterine neoplasm of female genital tract, occurring in 20-30% of women between the ages of 35 and 50 years. The overall incidence is around 4% to 11%, it rises to 35% during the reproductive age and to 40% in women over 50 years old.

Many risk factors are associated with the development of leiomyomas, such as early menarche, obesity and nulliparity with exposure to sex steroid hormones, especially estrogen. However the benign tumors are extremely rare in women under the age of 19 years and the biological behaviour of such leiomyomas is unknown.

An accurate detection, characterization and localisation of uterine leiomyomas is important in these patients. MRI imaging is considered the examination of choice for detection and localisation of uterus fibroids. We present a case of 15 years old girl with fibromatous uterus, evaluated with MRI examination.

CASE REPORT:

A 15 years old female patient was seen in the outpatient department with complaints of irregular periods, spotting per vaginum, perception of development of gradual mass in the abdomen with easy satiety and constipation off and on for 5 months. Her family history, past medical and surgical history were unremarkable. Menarche occurred at 13 years of age. She had irregular and heavy menstrual periods, lasting upto 6 days without any dysmenorrhea. The patient had never used oral contraceptive pills or other hormonal therapies. Abdominal examination revealed a large mass, tense, with irregular margins arising from pelvis upto epigastric region. A vaginal examination was not performed because the patient was a virgin. Rectal examination confirmed the presence of a large, irregular mass with tense elastic consistency, which seemed to originate from anterior uterine wall.

Hematological and biochemical parameters were normal. There was no sign of systemic infection (Temperature 37ºC, TLC 6900; CRP & ESR negative). Tumor markers (Ca 19.9, b HCG, alpha fetoprotein, LDH were normal). Ca 125 was however raised – 146.60.

Abdominal ultrasound revealed a large solid mass extending upto epigastrium, size 285mm x 139mm x 221mm and 4.5 kg weight approximately, arising from the fundus of uterus with broad based pedicle (? Lipoleiomyosarcoma). MRI showed a large pedunculated fibroid from anterior uterine wall, filling entire pelvis and abdomen, reaching upto inferior surface of liver, 2 other solid enhancing lesions seen in lower abdomen anterior to uterus, inferior to above mentioned larger mass (possibility of leiomyosarcoma could not be excluded).

On the basis of the imaging findings, patient was advised surgery. Patient was admitted and taken up for surgery after the required clearances. A midline incision was given from suprapubic region to epigastric region. The uterus had increased volume because of the presence of large mass in the anterior fundal wall, approximate size of 30 x 18 cms, enveloped by omental adhesions. Adhesions were present between omentum and colon on the upper margin and fundus of uterus in the lower margin. Increased vascularity and blood vessels stretched over the mass were seen. Mass was excised in toto after ligating feeder blood vessels. Vasopressin was instilled on the peduncle over fundus of uterus, careful dissection and excision of mass was done. Fundus musculature and capsule refashioned with no 1 vicryl, interrupted and baseball sutures taken to secure haemostasis. The post-operative period was uneventful.

On histopathological examination, the mass appeared as a typical myoma. It weighed 4 kg and was covered by fibrous pseudo capsule below which thin venous net was present. On cut section, the mass had a fasciculated

appearance with red colour and soft consistency. There were hemorrhagic and necrotic areas. Microscopic examination revealed a leiomyoma.

On follow up, the patient reported heavy vaginal bleeding at the first menstrual period after surgery followed by irregular menses in the next cycle. Further cycles were regular and painless. Ultrasound was performed after 3 months of surgery which demonstrated an average size uterus with no recurrence of myomas. Stitch line was healthy and patient was symptomatically better.

Fig.1
Large Intra-abdominal Mass (Pre-operative)

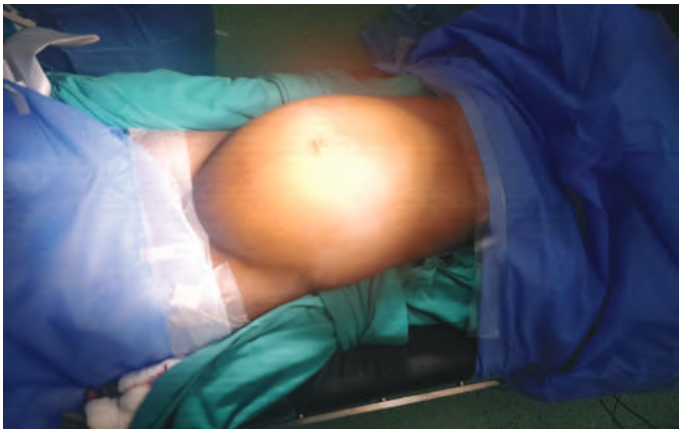

Fig. 2
Midline Incision given

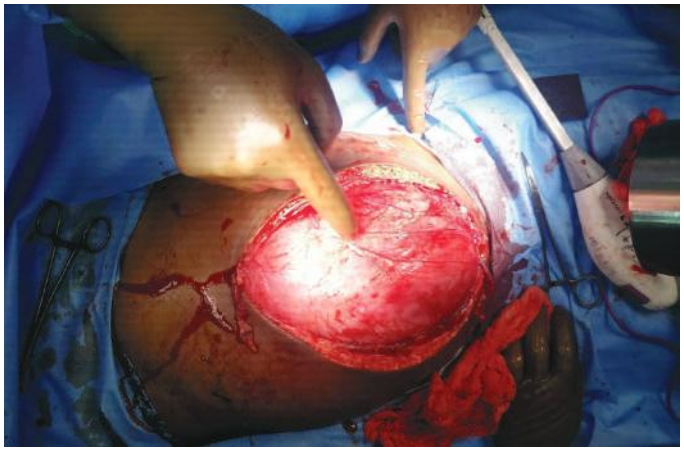

Fig. 3
Large mass extruding from incision

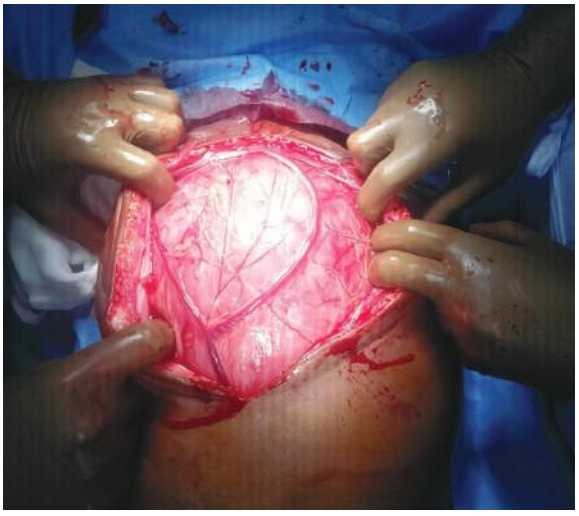

Fig. 4
Dissection of mass from adhesions to the parieties

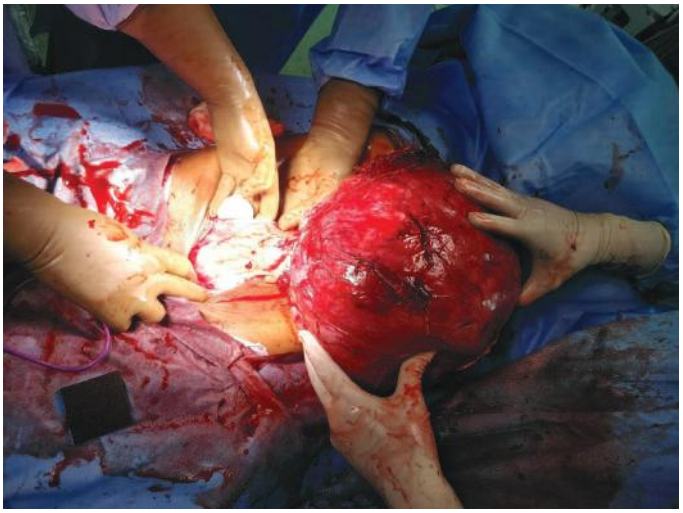

Fig. 5
Excised Mass (Weight 4 kg)

DISCUSSION:

Leiomyomas of the uterus in women under 20 years of age are rare and occur much less often than adnexal lesions. Although ultrasound studies are usually sufficient to make the distinction between the two, MRI generally is superior to sonography in this regard. In this young population, myomectomy is the surgical procedure of choice to preserve fertility.

At presentation, uterine myomas may be asymptomatic (30%–80% of cases), but abdominal and back pain, compression symptoms, and vaginal bleeding with anemia are frequently present at diagnosis. Fields and Neinstein compared the first clinical presentation of uterine myomas in adolescents with the presenting symptoms in the adults. They observed that, in adolescents, 30% of myomas are asymptomatic (50%–80% in the adults), 50% cause menstrual abnormalities (30% in adults), and urinary abnormality is less frequent

than in adults (5% in adolescents versus 20% in adults). In their series of 10 patients younger than 21 years of age, 40% of the patients also had symptom of compression and 20% had back pain.

The patient in the current report required surgery because of irregular menstrual cycles, increasing abdominal size and constipation. Other conditions that may cause these symptoms include hemorrhagic corpus luteum, adnexal torsion, and ectopic pregnancy. However, our patient was a virgin and previous radiological imaging suggested the diagnosis of uterine myoma. The preoperative workup is particularly relevant in adolescents because fertility sparing and low surgical injury are mandatory in this population. Clinical examination, abdomino-pelvic ultrasound, computed tomography (CT), and MRI are commonly used in the differential diagnosis of pelvic masses and uterine myomas. Ultrasound is the first-line imaging technique used to evaluate a pelvic mass because of its easy availability and safety. The second-line imaging techniques are CT and MRI, the latter being the most effective technique to evaluate uterine myomas.

Leiomyomas in young population often show histologic features favouring the diagnosis of malignancy. Half of the reported cases demonstrated increased cellularity, mitotic activity, and cellular atypia. These pathologic characteristics were not met in our patient.

Uterine leiomyomas, although rare, should be considered in adolescent women presenting with a pelvic mass and abdominal pain, or menstrual disorders and abnormal uterine bleeding, as in our case. The management of leiomyomas in this age should be conservative for the preservation of fertility. Therefore, the preoperative characterization of the nature of these tumors is extremely important. The diagnosis should be based on imaging findings, that is, sonographic and magnetic resonance imaging features.

When myomas are typical with no sign of degeneration, they appear at MRI as homogeneous and have hypointense signal. However, myomas may have a variety of degenerations (myxoid, hyaline, hemorrhagic, cystic, fatty, and calcified) and degenerated myomas have heterogeneous signal intensity on MRI. In the presence of rapid growth of the mass, signs of degeneration on MRI, free fluid in the pouch of Douglas or ascites, a differential diagnosis with malignancies (such as leiomyosarcoma) should not be neglected. MRI has a specificity, sensitivity, positive predictive value, negative predictive value, and diagnostic accuracy of 93.1%, 100%, 52.6%, 100%, and 93.1%, respectively, in differentiating benign myomas from uterine sarcomas. These values increase to 93.8%, 100%, 83.3%, 100%, and 95.2% with dynamic MRI alone, and 100%, 100%, 100%, 100% and 100% with combined use of LDH and MRI. Another study suggested that the combined use of T2-weighted and diffusion-weighted MRI for the differentiation of uterine sarcomas and benign myomas allows a specificity and sensitivity of 100% to be obtained. In our patient, MRI demonstrated a homogeneous mass without signs of degeneration, confirming the suspicion of benign uterine myoma, and it was decided that more advanced imaging techniques were not required. The myomectomy was performed by laparotomy because of the mass size. In addition, our patient was a virgin, thus preventing the use of a uterine manipulator during laparoscopic myomectomy.

Only an accurate pathological examination of the mass, including immunohistochemistry, allows a differential diagnosis between benign myomas and low-grade sarcomas. Increased cellularity, nuclear atypia, and increased mitotic activity are features that can be found in an adolescent population and suggest the need to carefully evaluate the tumor to exclude malignancy or malignant transformation. Other common features that should be carefully examined are tumor cell necrosis, atypical mitotic figures, infiltrative borders and, in a minority of cases, vascular invasion. Immunohistochemistry (positivity for smooth-muscle markers such as desmin and h-caldesmon) may facilitate the diagnosis of poorly differentiated tumors. The rapid growth and uncommon large size of uterine myomas, as in this report, may also be associated with malignant transformation. However, till now, no case of uterine leiomyosarcoma has been reported in adolescents and they are very rare under the age of 19 years.

The management of myomas can be conservative, medical or surgical. If myomas are small and asymptomatic or well controlled with hormone therapy, observation can be enough. Surgical treatment is necessary if symptoms are present and evolve or if the mass has a rapid growth. Myomectomy must be the first choice because preservation of fertility is the main factor for the adolescent population.

The follow-up of these young patients is another important element that should be carefully considered. In our case, at 3 months follow-up no recurrence was found. A recent report demonstrates that, even though extremely rare, recurrence after surgery is possible and should not be ignored.

CONCLUSION:

Uterine leiomyomas should be considered in adolescent women presenting with a pelvic mass and abdominal pain. The management of the leiomyomas in this age group should be conservative, with the goal of preserving fertility. Accurate evaluation of etiology of these tumors is important for further counselling.

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Optical Coherence Tomography (OCT) and its Uses

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INTRODUCTION:

Optical Coherence Tomography (OCT) is a non-invasive, non-contact imaging system providing high resolution cross-sectional images of the posterior segment of the eye. Anterior Segment OCT (AS-OCT) is also now available and is finding applications in various diseases of the anterior segment of the eye. OCT uses near-infrared light interferometry, and images are created by the analysis of interference between reflected reference waves and those reflected by tissue.[1]

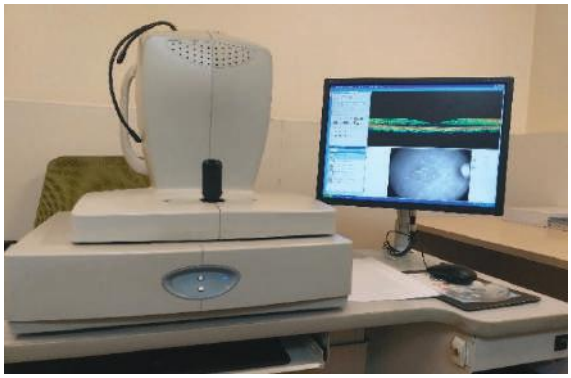

Fig. 1
RT-Vue Optical Coherence Tomography

Fig. 2
Procedure of OCT

Most instruments in current use, including the RT-Vue OCT machine in Department of Ophthalmology at Manipal Hospital, Dwarka, employ spectral/ Fourier domain technology in which information for each point on the A-scan is collected simultaneously, speeding data collection and improving resolution.

APPLICATIONS OF OCT:

The availability of OCT has revolutionized the practice and management of retinal diseases in the field of Ophthalmology. The ability to view retinal microstructure with resolution of a few microns immensely increases our understanding of the ongoing disease process, helps formulate management protocol and provides a quick and non-invasive tool for repeated assessments during follow-ups to guide further treatment.

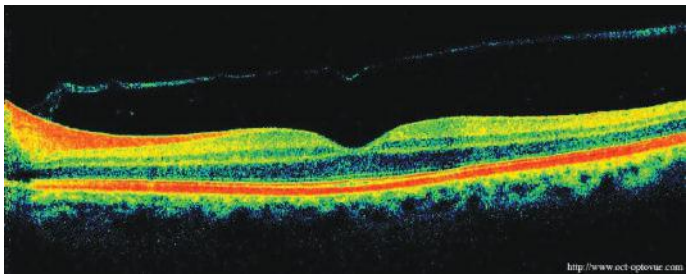

Fig. 3
Normal OCT

The common applications of OCT in current practice include:

RETINAL DISEASES:

1. Diabetic Retinopathy-

OCT Macula is an indispensable tool for the assessment of Diabetic Macula Edema.[2] It tells us about the kind of edema present, the foveal thickness (magnitude of the edema), helps us to plan treatment and serves as a guide to monitor treatment response during future follow-ups.

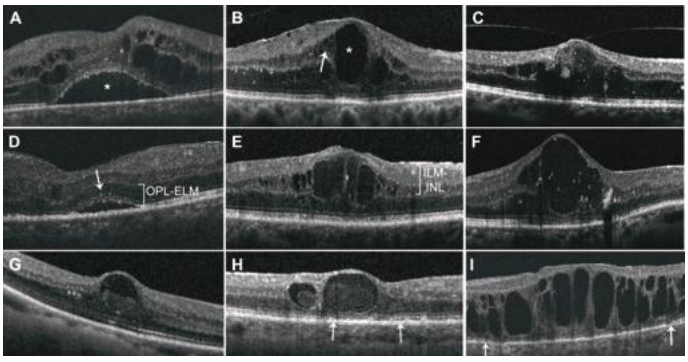

Fig. 4
Types of diabetic macular edema on OCT

2. Retinal Vascular Occlusions-

OCT Macula helps in assessment of macular edema associated with retinal vascular occlusions- Branch Retinal Vein Occlusion (BRVO), Central Retinal Vein Occlusion (CRVO), Tributary Retina Vein Occlusion (TRVO) and Hemi-Retinal Vein Occlusion. It helps to guide treatment and assess treatment response.

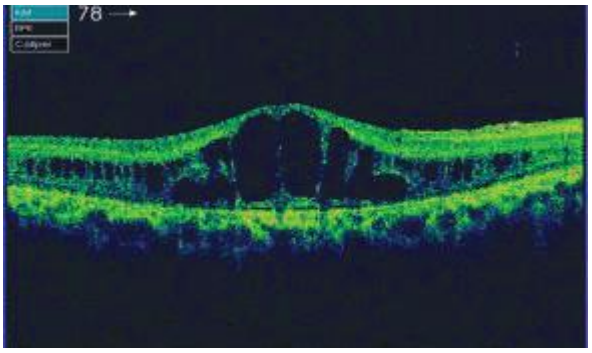

Fig. 5
Cystoid macular edema on OCT

3. HCQS Maculopathy-

SD-OCT is an important tool for early diagnosis of macular toxicity due to Hydroxychloroquine and can identify very early cases of toxicity.[3] The early detection can help limit the vision loss by early cessation of the drug.

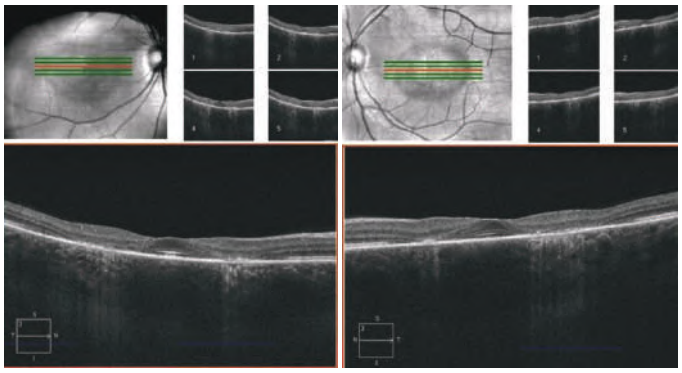

Fig. 6
Spectral-domain optical coherence tomography: Bilateral parafoveal outer retinal and retinal pigment epithelium atrophy with central sparing ("flying saucer sign")

4. Age-Related Macular Degeneration and other Macular Diseases-

OCT is an indispensable tool for the diagnosis and management of Age-Related Macular Degeneration (ARMD) and other macular diseases like Central Serous Retinopathy, Traumatic Berlin's Edema, Cystoid Macula Edema, to name a few.

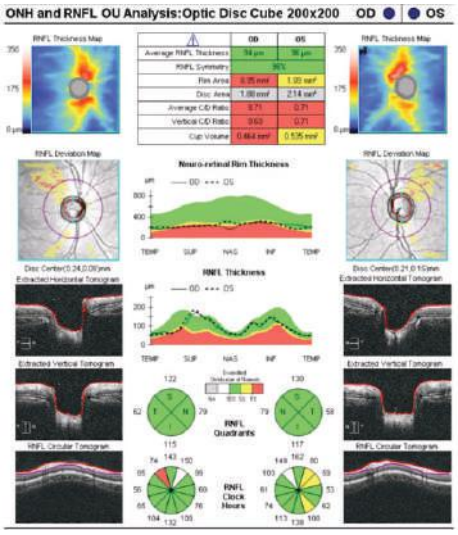

Fig. 7
OCT in Glaucoma

OPTIC NEUROPATHIES:

1. Glaucoma

OCT RNFL (Retinal Nerve Fibre Layer) and ONH (Optic Nerve Head) are important tools for early diagnosis and follow-up for disease progression.[4] Being an irreversible disease, early diagnosis of Glaucoma is of utmost importance to limit visual loss from the dreaded disease.

2. Papilledema

Edema of optic nerves resulting from raised intracranial pressure can be easily documented and monitored with the help of OCT RNFL. The quantitative assessment lends reproducibility and ease of follow-up

3. Pseudopapilledema

The differentiation of papilledema from pseudopapilledema due to the presence of Optic Nerve Drusens can mostly be done with the help of OCT ONH.

4. Optic Neuritis

OCT RNFL serves as an important tool for measuring the extent of edema, and then nerve fibre layer atrophy, in cases of Optic Neuritis. OCT has also been used as a marker of axonal loss in cases of Multiple Sclerosis and neurodegenerative disorders.[5]

CONCLUSION:

Thus, to conclude, Optical Coherence Tomography is an indispensable tool in the armamentarium of any Ophthalmologist and enables one to diagnose, treat and follow up patients of varied retinal and optic nerve disorders with great precision and ease.

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Importance of Correct Doffing Technique of Personal Protective Equipment (PPE) during COVID-19 pandemic

Manisha

Infection Control Nurse, Manipal Hospital, Dwarka

Personal protective equipments (PPE) should be removed in sequence that decreases the potential for cross contamination. Correct PPE doffing (removal of PPE) technique during COVID-19 pandemic is just as important as other interventions for preventing the disease. Appropriate doffing technique protects healthcare workers (HCW's) from exposure to potential infectious material that may have settled on the PPE while attending the infected patients. During doffing of PPE, pathogens can be transferred from PPE to the bodies of HCWs, putting HCWs and patients at risk of exposure and infection.

In one of the study, 162 times doffing practices of healthcare workers were observed while treating the 52 patients infected with respiratory viral pathogens. Overall, 90% of observed doffing was incorrect, with respect to the doffing sequence, doffing technique, or use of appropriate PPE.[2]

Deviations from the recommended PPE doffing protocol can increase potential for contamination of the HCW's clothing or skin. If possible, the process should be supervised by a co-worker at a distance of 2 metres to reduce the risk of healthcare worker contaminating themselves while doffing. The PPE after doffing should be discarded in appropriate colour coded waste bins.

So, imparting appropriate training, displaying donning & doffing sequence posters & monitoring the doffing procedure regularly are ways to ensure the compliance & preventing further spread of infection.

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Repurposed drugs for the COVID 19: Physicians propose and WHO disposes!

Smita Mishra

Mr Horace Greeley said once, – "Common Sense is very uncommon!" This is all about the recently published interim report of extended solidarity trial published in NEJM on 2nd December 2020.1

The article "Repurposed Antiviral Drugs for Covid-19" reported that antiviral drugs (hydroxychloroquine, remdesivir, lopinavir, interferon) failed to win the race when compared to the placebo, in an assigned group of patients. WHO does not trust drugs like ivermectin, Doxy etc. Many senior microbiologists, intensivists would laugh it out arguing that these drugs would only help in controlling parasitic infestations. Harrington et al., therefore, appropriately chose a title ("A Large, Simple Trial Leading to Complex Questions")2 for their argumentative editorial. They wrote- "No intervention acts on two persons in an identical fashion: patients present with different risk factors, are treated in different health care settings, and begin treatment at different stages of illness. In particular, the effectiveness of an antiviral agent can depend on whether a patient presents early (during viral pathogenesis) or later (when immunopathologic conditions or other complications may be more important)." They also pointed out the usefulness of the result of the 'solidarity trial' in denying the role of antiviral agents in patients who have entered in the second phase of illness described as the cytokine storm. Rightly, they asked "what is a more effective timing for the use of remdesivir, and should it be used in combination with other agents? How is the course of hospitalization affected by the type and level of care delivered in particular settings?"

This is the question of common sense: why not to use an antiviral agent when the virus is replicating? What role can they play once the war for life has entered a phase where the virus itself has been cornered?

This is the argument extended in the recovery trial against early use of steroids, so that, not to time it with viral replication phase.3 The results of the Recovery trial, however, supports the use of the steroids in late 1st and 2nd week when evidence of lung involvement is evident by rising oxygen requirement and falling SPO2 <95%. In various articles, it has been shown that viral replication in the upper respiratory tract, to a larger extent, is immunologically inert. Once the virus climbs down to the pneumocyte type II cells, its pathological journey starts and gets reciprocated by the dysregulated immunological response sequentially leading to diffuse alveolar damage, inflammatory infiltrates, microvascular thrombosis resulting into a simulating picture of adult acute respiratory syndrome.4 No wonder, classical findings of rising levels of interleukins 10/6, TNF α, evidence of lymphocyte exhaustion and lymphopenia ,come almost hand in hand.

Drugs like Doxycycline and Ivermectin have been used rampantly in every nook and corners of northern-western India. Interestingly, ICMR is playing once bitten and twice shy. Because, India was the first country which boldly adopted HCQ prophylaxis and was thoroughly criticized by Americans. The criticism came in the wake of deaths reported in COVID patients receiving HCQ. Analysis says, HCQ and also azithromycin are the potential drugs which may adversely affect conduction system; atleast 60-70% patients with late phase COVID, may have myocardial edema, making them a substrate for arrhythmia. need cautious use. It is the CDC which allows almost no medicines in first week of illness. India has improved in its recovery rate, remarkably from 60% to 95%. How? I keep on talking to many of my friends who were partying hard, and one after another, the whole group became COVID positive. They consulted a local physician and got a prescription of Ivermectin 24 mg, Doxy 100 mg twice a day, Zn, vit D, vit C and even favipiravir, as soon as the report was received, and recovered completely. There are many patients who presented with anosmia. Those who were treated with the Ivermectin, recovered within 7-10 days. I came to know about this in March but experienced it now when I became COVID 19 positive. Globally, people are experiencing good results of ivermectin use.5

Therefore, there are evidence that many repurposed antivirals, antiprotozoal, anti-bacterial drugs have hidden talents to combat COVID 19 atleast partially. These drugs are less harmful when one compares them to the 5-10% chance of having serious lung, heart, kidney and brain complications. Probably they need cardiac care, LMWH or antiplatelets, statins for a longer period. In nutshell, patients who recover the second or third phase, are not the fittest to survive.

Jeon et al. wrote "Among the 48 drugs that were evaluated in our study, 24 drugs showed potential antiviral activities against SARS-CoV-2, with IC50 values in between 0.1 and 10 μM, few of them are as follows- tilorone, cyclosporine, chloroquine, mefloquine, amodiaquine, proscillaridin, salinomycin, ouabain, cepharanthine, ciclesonide, oxyclozanide, anidulafungin, gilteritinib, berbamine, ivacaftor, bazedoxifene, niclosamide, and eltrombopag."6

It is common sense that the first 5 days are of viral replication and subsequently 10% chance of having immunological vicious storm. Conversely, it is logical to use repurposed antiviral drugs when the virus is replicating and steroid only when the body is brewing cytokines, to bring a storm and lymphocytes in backfoot.

Vaccines are illusionary, in view of the fact, the duration of trials has been accelerated too fast. Tinkering with immune system is always a double-edged sword. Oral Polio was introduced in 70s and a fear was expressed about its association with autism. It took many years to declare that vaccine is safe. Till now flu vaccine is not considered as efficient vaccine for the various reasons. We must remember that natural infection has failed to ensure long lasting immunity. There are articles suggesting that virus may co-exist with IgG in patients asymptomatic or mildly symptomatic patients.

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IMAGE CORNER

Bariatric Balloon Placement in Liver Transplant Donor

Kunal Das
Consultant and Head, Dept of Gastrosciences, Manipal Hospital, Dwarka

Case Summary

AB, a 44 yr Iraqi gentleman was admitted with End Stage Liver Disease with decompensation in the form of ascites for Liver transplantation. The live donor, XY who was a 34 yr old female and a family member was found to have grade III Fatty liver and was overweight. She had a BMI of 38.2. The donor was advised dietary and life-style modifications. She was offered Bariatric Balloon placement for temporary and quick weight loss, which she accepted.

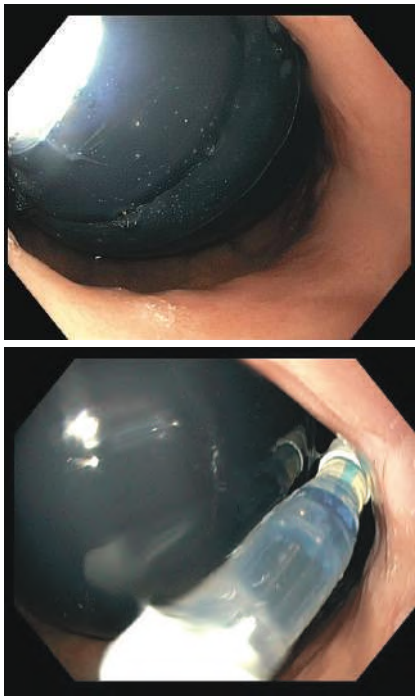


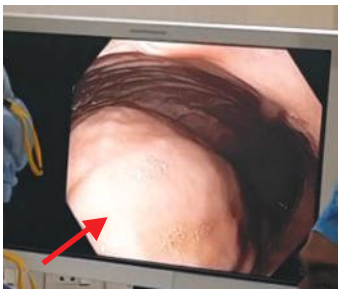
Fig 1. Bariatric Balloon (Spatz3)

Endoscopic Cystogastrostomy/ Stent Placement in a case of Pseudocyst Pancreas

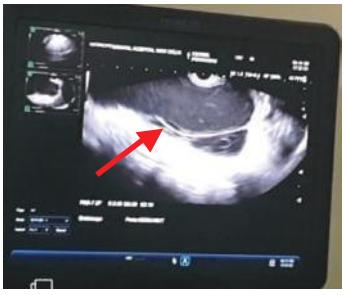
Lovkesh Anand[a], Vikram Gagneja[b], Vikas Taneja[b], Neeta Kejriwal[b], Himanshu Batra[b]
[a] Department of Gastroenterology & [b] Department of Pediatrics, Manipal Hospital, Dwarka

Case Summary

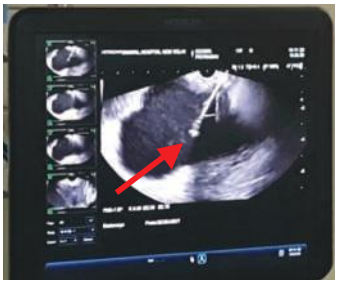
10 year old child was admitted with pain abdomen, recurrent vomitings and poor appetite for 1 week. H/o Pancreatitis 3 month back and was having recurrent pain abdomen since then. USG abdomen showed mass in the abdomen below the stomach. MRCP was done to confirm the pseudocyst pancreas. Endoscopic Ultrasound was done which confirmed the presence of large pseudocyst of size 13 x 11cm with homogenous echotexture. Cystogastrostomy was performed, after securing the airway, with a 15 mm × 10 mm cautery-enhanced lumen-apposing metal stent (Hot AXIOS stent). Immediately after stent deployment, a copious amount of dark fluid, approximately 700 ml, was drained from the cyst. Patient improved considerably and was discharged the very next day.



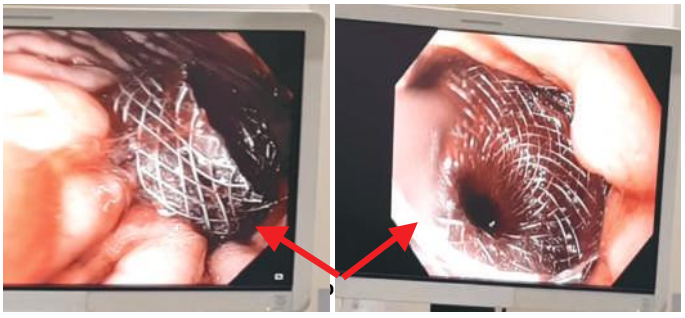
Extrinsic compression at the level of body of stomach on endoscopy



EUS showing large pseudocyst



EUS guided stent placement



JOURNAL SCAN

Dr Kunal Das
Consultant and Head, Dept of Gastrosciences, Manipal Hospital, Dwarka

1. Osimertinib in Resected EGFR-Mutated Non–Small-Cell Lung Cancer

N Engl J Med 2020; 383:1711-1723; DOI: 10.1056/NEJMoa2027071

Long Wu, Masahiro Tsuboi, Jie He, Thomas John, Christian Grohe, Margarita Majem, Jonathan W. Goldman, Konstantin Laktionov, Sang-We Kim, Terufumi Kato, Huu-Vinh Vu, Shun Lu, Kye-Young Lee, Charuwan Akewanlop, Chong-Jen Yu, Filippo de Marinis, Laura Bonanno, Manuel Domine, Frances A. Shepherd, Lingmin Zeng, Rachel Hodge, Ajlan Atasoy, Yuri Rukazenkov, Roy S. Herbst for the ADAURA Investigators

Abstract

Background: Osimertinib is standard-of-care therapy for previously untreated epidermal growth factor receptor (EGFR) mutation–positive advanced non–small-cell lung cancer (NSCLC). The efficacy and safety of osimertinib as adjuvant therapy are unknown.

Methods: In this double-blind, phase 3 trial, we randomly assigned patients with completely resected EGFR mutation–positive NSCLC in a 1:1 ratio to receive either osimertinib (80 mg once daily) or placebo for 3 years. The primary end point was disease-free survival among patients with stage II to IIIA disease (according to investigator assessment). The secondary end points included disease-free survival in the overall population of patients with stage IB to IIIA disease, overall survival, and safety.

Results: A total of 682 patients underwent randomization (339 to the osimertinib group and 343 to the placebo group). At 24 months, 90% of the patients with stage II to IIIA disease in the osimertinib group (95% confidence interval [CI], 84 to 93) and 44% of those in the placebo group (95% CI, 37 to 51) were alive and disease-free (overall hazard ratio for disease recurrence or death, 0.17; 99.06% CI, 0.11 to 0.26; P<0.001). In the overall population, 89% of the patients in the osimertinib group (95% CI, 85 to 92) and 52% of those in the placebo group (95% CI, 46 to 58) were alive and disease-free at 24 months (overall hazard ratio for disease recurrence or death, 0.20; 99.12% CI, 0.14 to 0.30; P<0.001). At 24 months, 98% of the patients in the osimertinib group (95% CI, 95 to 99) and 85% of those in the placebo group (95% CI, 80 to 89) were alive and did not have central nervous system disease (overall hazard ratio for disease recurrence or death, 0.18; 95% CI, 0.10 to 0.33). Overall survival data were immature; 29 patients died (9 in the osimertinib group and 20 in the placebo group). No new safety concerns were noted.

Conclusions: In patients with stage IB to IIIA EGFR mutation–positive NSCLC, disease-free survival was significantly longer among those who received osimertinib than among those who received placebo. (Funded by AstraZeneca; ADAURA ClinicalTrials.gov number, NCT02511106. opens in new tab.)

2. Neoadjuvant atezolizumab in combination with sequential nab-paclitaxel and anthracycline-based chemotherapy versus placebo and chemotherapy in patients with early-stage triple-negative breast cancer (IMpassion031): a randomized, double-blind, phase 3 trial

The Lancet. 2020; 396(10257): 1090-1100, DOI: 10.1016/S0140-6736(20)31953-X

Prof Elizabeth A Mittendorf, Prof Hong Zhang, Carlos H Barrios, Prof Shigehira Saji, Kyung Hae Jung, Roberto Hegg, et al.

Summary

Background: Preferred neoadjuvant regimens for early-stage triple-negative breast cancer (TNBC) include anthracycline-cyclophosphamide and taxane-based chemotherapy. IMpassion031 compared efficacy and safety of atezolizumab versus placebo combined with nab-paclitaxel followed by doxorubicin plus cyclophosphamide as neoadjuvant treatment for early-stage TNBC.

Methods: This double-blind, randomized, phase 3 study enrolled patients in 75 academic and community sites in 13 countries. Patients aged 18 years or older with previously untreated stage II–III histologically documented TNBC were randomly assigned (1:1) to receive chemotherapy plus intravenous atezolizumab at 840 mg or placebo every 2 weeks. Chemotherapy comprised of nab-paclitaxel at 125 mg/m 2 every week for 12 weeks followed by doxorubicin at 60 mg/m 2 and cyclophosphamide at 600 mg/m 2 every 2 weeks for 8 weeks, which was then followed by surgery. Stratification was by clinical breast cancer stage and programmed cell death ligand 1 (PD-L1) status. Co-primary endpoints were pathological complete response in all-randomized (i.e. all randomly assigned patients in the intention-to-treat population) and PD-L1-positive (i.e. patients with PD-L1-expressing tumour infiltrating immune cells covering ≥1% of tumour area) populations. This study is registered with ClinicalTrials.gov (NCT03197935), Eudra (CT2016-004734-22), and the Japan Pharmaceutical Information Center (JapicCTI-173630), and is ongoing.

Findings: Between July 7, 2017, and Sept 24, 2019, 455 patients were recruited and assessed for eligibility. Of the 333 eligible patients, 165 were randomly assigned to receive atezolizumab plus chemotherapy and 168 to placebo plus chemotherapy. At data cutoff (April 3, 2020), median follow-up was 20•6 months (IQR 8•7–24•9) in the atezolizumab plus chemotherapy group and 19•8 months (8•1–24•5) in the placebo plus chemotherapy group. Pathological complete response was documented in 95 (58%, 95% CI 50–65) patients in the atezolizumab plus chemotherapy group and 69 (41%, 34–49) patients in the placebo plus chemotherapy group (rate difference 17%, 95% CI 6–27; one-sided p=0•0044 [significance boundary 0•0184]). In the PD-L1-positive population, pathological complete response was documented in 53 (69%, 95% CI 57–79) of 77 patients in the atezolizumab plus chemotherapy group versus 37 (49%, 38–61) of 75 patients in the placebo plus

chemotherapy group (rate difference 20%, 95% CI 4–35; one-sided p=0•021 [significance boundary 0•0184]). In the neoadjuvant phase, grade 3–4 adverse events were balanced and treatment-related serious adverse events occurred in 37 (23%) and 26 (16%) patients, with one patient per group experiencing an unrelated grade 5 adverse event (traffic accident in the atezolizumab plus chemotherapy group and pneumonia in the placebo plus chemotherapy group).

Interpretation: In patients with early-stage TNBC, neoadjuvant treatment with atezolizumab in combination with nab-paclitaxel and anthracycline-based chemotherapy significantly improved pathological complete response rates with an acceptable safety profile.

3. What dose of aspirin should be used in the initial treatment of Kawasaki disease? A meta-analysis

Rheumatology. 2020; 59(8): 1826-1833, DOI: 10.1093/rheumatology/keaa050

Xinyi Jia, Xiao Du, Shuxian Bie, Xiaobing Li, Yunguang Bao, Mizu Jiang

Abstract:

Objective: The use of IVIG plus high- or low-dose aspirin for the initial treatment of Kawasaki disease remains controversial. The aim of this study was to evaluate the efficacy of IVIG plus high-dose aspirin compared with IVIG plus low-dose aspirin in the treatment of Kawasaki disease.

Methods: Studies related to aspirin therapy for Kawasaki disease were selected by searching the databases of Medline (PubMed), Embase and the Cochrane Library before March 2019. Statistical analyses were performed by using a Review Manager Software package and STATA v.15.1.

Results: Eight retrospective cohort studies, characterizing 12 176 patients, were analyzed. Overall, no significant difference was found in the incidence of coronary artery abnormalities between the high- and low-dose aspirin groups [relative risk (RR) 1.15; 95% CI: 0.93, 1.43; P = 0.19; random-effects model]. The patients treated with high-dose aspirin had slightly faster resolution of fever [mean difference (MD) −0.30; 95% CI: −0.58, −0.02; P = 0.04; random-effects model], but the rates of IVIG resistance (RR, 1.26; 95% CI: 0.55, 2.92; P = 0.59; random-effects model) and days in hospital (MD, 0.22; 95% CI: −0.93, 1.37; P = 0.71; random-effects model) were similar between the two groups.

Conclusion: Low-dose aspirin plus IVIG might be as effective as high-dose aspirin plus IVIG for the initial treatment of Kawasaki disease. Considering that high-dose aspirin may cause more adverse reactions than low-dose aspirin, low-dose aspirin plus IVIG should be recommended as the first-line therapy in the initial treatment of Kawasaki disease.

4. Life Expectancy after Bariatric Surgery in the Swedish Obese Subjects Study

N Engl J Med 2020; 383: 1535-1543. DOI: 10.1056/NEJMoa2002449

Lena M.S. Carlsson, Kajsa Sjöholm, Peter Jacobson, Johanna C. Andersson-Assarsson, Per-Arne Svensson, Magdalena Taube, Björn Carlsson, and Markku Peltonen

Abstract

Background: Obesity shortens life expectancy. Bariatric surgery is known to reduce the long-term relative risk of death, but its effect on life expectancy is unclear.

Methods: We used the Gompertz proportional hazards regression model to compare mortality and life expectancy among patients treated with either bariatric surgery (surgery group) or usual obesity care (control group) in the prospective, controlled Swedish Obese Subjects (SOS) study and participants in the SOS reference study (reference cohort), a random sample from the general population.

Results: In total, 2007 and 2040 patients were included in the surgery group and the control group, respectively, and 1135 participants were included in the reference cohort. At the time of the analysis (December 31, 2018), the median duration of follow-up for mortality was 24 years (interquartile range, 22 to 27) in the surgery group and 22 years (interquartile range, 21 to 27) in the control group; data on mortality were available for 99.9% of patients in the study. In the SOS reference cohort, the median duration of follow-up was 20 years (interquartile range, 19 to 21), and data on mortality were available for 100% of participants. In total, 457 patients (22.8%) in the surgery group and 539 patients (26.4%) in the control group died (hazard ratio, 0.77; 95% confidence interval [CI], 0.68 to 0.87; P<0.001). The corresponding hazard ratio was 0.70 (95% CI, 0.57 to 0.85) for death from cardiovascular disease and 0.77 (95% CI, 0.61 to 0.96) for death from cancer. The adjusted median life expectancy in the surgery group was 3.0 years (95% CI, 1.8 to 4.2) longer than in the control group but 5.5 years shorter than in the general population. The 90-day postoperative mortality was 0.2%, and 2.9% of the patients in the surgery group underwent repeat surgery.

Conclusions: Among patients with obesity, bariatric surgery was associated with longer life expectancy than usual obesity care. Mortality remained higher in both groups than in the general population.

(Funded by the Swedish Research Council and others; SOS ClinicalTrials.gov number, NCT01479452. opens in new tab.)

5. Safety and efficacy of galcanezumab in patients for whom previous migraine preventive medication from two to four categories had failed (CONQUER): a multicentre, randomized, double-blind, placebo-controlled, phase 3b trial

The Lancet Neurology. 2020; 19(10): 814-825. DOI: 10.1016/S1474-4422(20)30279-9

Prof Wim M Mulleners, Prof Byung-Kun Kim, Prof Miguel J A Láinez, Prof Michel Lanteri-Minet, Patricia Pozo-Rosich, Shufang Wang, Antje Tockhorn-Heidenreich, Sheena K Aurora, Russell M Nichols, Laura Yunes-Medina, Holland C Detke,

Summary

Background: Many patients who require migraine

preventive treatment have not been able to tolerate or have not responded to multiple previous preventive medications. We aimed to assess the safety and efficacy of galcanezumab, an antibody to calcitonin gene-related peptide, in patients with migraine who had not benefited from preventive medications from two to four categories.

Methods: CONQUER was a multicentre, randomized, double-blind, placebo-controlled, phase 3b trial done at 64 sites (hospitals, clinics, or research centres) in 12 countries (Belgium, Canada, Czech Republic, France, Germany, Hungary, Japan, the Netherlands, South Korea, Spain, the UK, and the USA). Patients were 18–75 years of age, with episodic or chronic migraine, with migraine onset before the age of 50 years, who had a documented failure of preventive medications from two to four drug categories in the past 10 years owing to lack of efficacy or tolerability, or both. Patients were randomized 1:1 to receive subcutaneous placebo or galcanezumab 120 mg per month (with a 240 mg loading dose administered as two 120 mg injections) for 3 months. For masking purposes, patients receiving placebo also received two injections during the first dosing visit. Randomization was done by a computer-generated random sequence by means of an interactive web-response system stratified by country and migraine frequency (low frequency episodic migraine, four to fewer than eight migraine days per month; high frequency episodic migraine, eight to 14 migraine headache days per month and fewer than 15 headache days per month; chronic migraine, at least eight migraine days per month and at least 15 headache days per month). The primary endpoint was the overall mean change from baseline in number of monthly migraine days during the 3-month treatment period in all patients who were randomly assigned and received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, NCT03559257, and is now completed.

Findings: Between Sept 10, 2018, and March 21, 2019, 462 participants with episodic (269 [58%]) or chronic (193 [42%]) migraine were randomly assigned and received at least one injection with placebo (n=230) or galcanezumab (n=232). Galcanezumab-treated patients had significantly greater reduction in migraine headache days versus placebo across months 1–3. The galcanezumab group had on average 4•1 fewer monthly migraine headache days compared with baseline (13•4), while the placebo group had on average 1•0 fewer than at baseline (13•0; between-group difference −3•1 [95% CI −3•9 to −2•3]; p<0•0001; effect size=0•72). Types and number of treatment-emergent adverse events were similar between galcanezumab and placebo. Treatment-emergent adverse events were reported in 122 (53%) of 230 patients in the placebo group and 119 (51%) of 232 patients in the galcanezumab group. There were four serious adverse events during the study, two (1%) reported in the placebo group and two (1%) reported in the galcanezumab group.

Interpretation: Galcanezumab was superior to placebo in the preventive treatment of migraine and was safe and well tolerated in patients for whom multiple previous standard-of-care preventive treatments had failed. Galcanezumab might represent an important treatment option for patients who have not benefited from or tolerated previous standard-of-care treatments.

Funding: Eli Lilly.

6. Gut metagenomics-derived genes as potential biomarkers of Parkinson's disease

Brain. 2020; 143(8): 2474-2489. DOI: 10.1093/brain/awaa201

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Abstract: Identification of the gut microbiome compositions associated with disease has become a research focus worldwide. Emerging evidence has revealed the presence of gut microbiota dysbiosis in Parkinson's disease. In this study, we aimed to identify the gut microbiome associated with Parkinson's disease and subsequently to screen and to validate potential diagnostic biomarkers of Parkinson's disease. This case-control study investigated gut microbial genes in faeces from 40 volunteer Chinese patients with Parkinson's disease and their healthy spouses using shotgun metagenomic sequencing. Furthermore, the identified specific gut microbial gene markers were validated with real-time PCR in an independent Chinese cohort of 78 Parkinson's disease patients, 75 control subjects, 40 patients with multiple system atrophy and 25 patients with Alzheimer's disease. We developed the first gut microbial gene catalogue associated with Parkinson's disease. Twenty-five gene markers were identified that distinguished Parkinson's disease patients from healthy control subjects, achieving an area under the receiver operating characteristic curve (AUC) of 0.896 (95% confidence interval: 83.1–96.1%). A highly accurate Parkinson's disease index, which was not influenced by disease severity or Parkinson's disease medications, was created. Testing these gene markers using quantitative PCR distinguished Parkinson's disease patients from healthy controls not only in the 40 couples (AUC = 0.922, 95% confidence interval: 86.4–98.0%), but also in an independent group of 78 patients with Parkinson's disease and 75 healthy control subjects (AUC = 0.905, 95% confidence interval: 86.0–95.1%). This classifier also performed a differential diagnosis power in discriminating these 78 patients with Parkinson's disease from a cohort of 40 patients with multiple system atrophy and 25 patients with Alzheimer's disease based on the panel of 25 biomarkers. Based on our results, the identified Parkinson's disease index based on the gene set from the gut microbiome may be a potential diagnostic biomarker of Parkinson's disease.

7. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

N Engl J Med 2020; 383: 1413-1424. DOI: 10.1056/NEJMoa2022190

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Abstract

Background: Sodium–glucose cotransporter 2 (SGLT2) inhibitors reduce the risk of hospitalization for heart failure in patients regardless of the presence or absence of diabetes. More evidence is needed regarding the effects of these drugs in patients across the broad spectrum of heart failure, including those with a markedly reduced ejection fraction.

Methods: In this double-blind trial, we randomly assigned 3730 patients with class II, III, or IV heart failure and an ejection fraction of 40% or less to receive empagliflozin (10 mg once daily) or placebo, in addition to recommended therapy. The primary outcome was a composite of cardiovascular death or hospitalization for worsening heart failure.

Results: During a median of 16 months, a primary outcome event occurred in 361 of 1863 patients (19.4%) in the empagliflozin group and in 462 of 1867 patients (24.7%) in the placebo group (hazard ratio for cardiovascular death or hospitalization for heart failure, 0.75; 95% confidence interval [CI], 0.65 to 0.86; P<0.001). The effect of empagliflozin on the primary outcome was consistent in patients regardless of the presence or absence of diabetes. The total number of hospitalizations for heart failure was lower in the empagliflozin group than in the placebo group (hazard ratio, 0.70; 95% CI, 0.58 to 0.85; P<0.001). The annual rate of decline in the estimated glomerular filtration rate was slower in the empagliflozin group than in the placebo group (−0.55 vs. −2.28 ml per minute per 1.73 m2 of body-surface area per year, P<0.001), and empagliflozin-treated patients had a lower risk of serious renal outcomes. Uncomplicated genital tract infection was reported more frequently with empagliflozin.

Conclusions: Among patients receiving recommended therapy for heart failure, those in the empagliflozin group had a lower risk of cardiovascular death or hospitalization for heart failure than those in the placebo group, regardless of the presence or absence of diabetes.

(Funded by Boehringer Ingelheim and Eli Lilly; EMPEROR-Reduced ClinicalTrials.gov number, NCT03057977. opens in new tab.)

8. Effect of Multilevel Upper Airway Surgery vs Medical Management on the Apnea-Hypopnea Index and Patient-Reported Daytime Sleepiness Among Patients With Moderate or Severe Obstructive Sleep Apnea

The SAMS Randomized Clinical Trial

JAMA. 2020; 324(12): 1168-1179. DOI:10.1001/jama.2020.14265

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Abstract

Importance: Many adults with obstructive sleep apnea (OSA) use device treatments inadequately and remain untreated.

Objective: To determine whether combined palatal and tongue surgery to enlarge or stabilize the upper airway is an effective treatment for patients with OSA when conventional device treatment failed.

Design, Setting, and Participants: Multicenter, parallel-group, open-label randomized clinical trial of upper airway surgery vs ongoing medical management. Adults with symptomatic moderate or severe OSA in whom conventional treatments had failed were enrolled between November 2014 and October 2017, with follow-up until August 2018.

Interventions: Multilevel surgery (modified uvulopalatopharyngoplasty and minimally invasive tongue volume reduction; n = 51) or ongoing medical management (e.g. advice on sleep positioning, weight loss; n = 51).

Main Outcomes and Measures: Primary outcome measures were the apnea-hypopnea index (AHI; i.e. the number of apnea and hypopnea events/h; 15-30 indicates moderate and >30 indicates severe OSA) and the Epworth Sleepiness Scale (ESS; range, 0-24; >10 indicates pathological sleepiness). Baseline-adjusted differences between groups at 6 months were assessed. Minimal clinically important differences are 15 events per hour for AHI and 2 units for ESS.

Results: Among 102 participants who were randomized (mean [SD] age, 44.6 [12.8] years; 18 [18%] women), 91 (89%) completed the trial. The mean AHI was 47.9 at baseline and 20.8 at 6 months for the surgery group and 45.3 at baseline and 34.5 at 6 months for the medical management group (mean baseline-adjusted between-group difference at 6 mo, −17.6 events/h [95% CI, −26.8 to −8.4]; P< .001). The mean ESS was 12.4 at baseline and 5.3 at 6 months in the surgery group and 11.1 at baseline and 10.5 at 6 months in the medical management group (mean baseline-adjusted between-group difference at 6 mo, −6.7 [95% CI, −8.2 to −5.2]; P< .001). Two participants (4%) in the surgery group had serious adverse events (1 had a myocardial infarction on postoperative day 5 and 1 was hospitalized for observation following hematemesis of old blood).

Conclusions and Relevance: In this preliminary study of adults with moderate or severe OSA in whom conventional therapy had failed, combined palatal and tongue surgery, compared with medical management, reduced the number of apnea and hypopnea events and patient-reported sleepiness at 6 months. Further

research is needed to confirm these findings in additional populations and to understand clinical utility, long-term efficacy, and safety of multilevel upper airway surgery for treatment of patients with OSA.

Trial Registration: Australian New Zealand Clinical Trials Registry: ACTRN12614000338662

9. BIVV001 Fusion Protein as Factor VIII Replacement Therapy for Hemophilia A

N Engl J Med 2020; 383:1018-1027. DOI: 10.1056/NEJMoa2002699

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Abstract

Background: Factor VIII replacement products have improved the care of patients with hemophilia A, but the short half-life of these products affects the patients' quality of life. The half-life of recombinant factor VIII ranges from 15 to 19 hours because of the von Willebrand factor chaperone effect. BIVV001 (rFVIIIFc-VWF-XTEN) is a novel fusion protein designed to overcome this half-life ceiling and maintain high sustained factor VIII activity levels. Data are lacking on the safety and pharmacokinetics of single-dose BIVV001.

Methods: In this phase 1–2a open-label trial, we consecutively assigned 16 previously treated men (18 to 65 years of age) with severe hemophilia A (factor VIII activity, <1%) to receive a single intravenous injection of recombinant factor VIII at a dose of 25 IU per kilogram of body weight (lower-dose group) or 65 IU per kilogram (higher-dose group). This injection was followed by a washout period of at least 3 days. The patients then received a single intravenous injection of BIVV001 at the same corresponding dose of either 25 IU or 65 IU per kilogram. Adverse events and pharmacokinetic measurements were assessed.

Results: No inhibitors to factor VIII were detected and no hypersensitivity or anaphylaxis events were reported up to 28 days after the injection of single-dose BIVV001. The geometric mean half-life of BIVV001 was three to four times as long as that of recombinant factor VIII (37.6 hours vs. 9.1 hours in the lower-dose group and 42.5 vs. 13.2 hours in the higher-dose group); the area under the curve (AUC) for product exposure was six to seven times as great in the two dose groups (4470 hours vs. 638 hours × IU per deciliter in the lower-dose group and 12,800 hours vs. 1960 hours × IU per deciliter in the higher-dose group). After the injection of BIVV001 in the higher-dose group, the mean factor VIII level was in the normal range (≥51%) for 4 days and 17% at day 7, which suggested the possibility of a weekly interval between treatments.

Conclusions: In a small, early-phase study involving men with severe hemophilia A, a single intravenous injection of BIVV001 resulted in high sustained factor VIII activity levels, with a half-life that was up to four times the half-life associated with recombinant factor VIII, an increase that could signal a new class of factor VIII replacement therapy with a weekly treatment interval. No safety concerns were reported during the 28-day period after administration.

(Funded by Sanofi and Sobi; ClinicalTrials.gov number, NCT03205163. opens in new tab.)

10. SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials

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Summary

Background: Both DAPA-HF (assessing dapagliflozin) and EMPEROR-Reduced (assessing empagliflozin) trials showed that sodium-glucose co-transporter-2 (SGLT2) inhibition reduced the combined risk of cardiovascular death or hospitalization for heart failure in patients with heart failure with reduced ejection fraction (HFrEF) with or without diabetes. However, neither trial was powered to assess effects on cardiovascular death or all-cause death or to characterize effects in clinically important subgroups. Using study-level published data from DAPA-HF and patient-level data from EMPEROR-Reduced, we aimed to estimate the effect of SGLT2 inhibition on fatal and non-fatal heart failure events and renal outcomes in all randomly assigned patients with HFrEF and in relevant subgroups from DAPA-HF and EMPEROR-Reduced trials.

Methods: We did a pre-specified meta-analysis of the two single large-scale trials assessing the effects of SGLT2 inhibitors on cardiovascular outcomes in patients with HFrEF with or without diabetes: DAPA-HF (assessing dapagliflozin) and EMPEROR-Reduced (assessing empagliflozin). The primary endpoint was time to all-cause death. Additionally, we assessed the effects of treatment in pre-specified subgroups on the combined risk of cardiovascular death or hospitalization for heart failure. These subgroups were based on type 2 diabetes status, age, sex, angiotensin receptor neprilysin inhibitor (ARNI) treatment, New York Heart Association (NYHA) functional class, race, history of hospitalization for heart failure, estimated glomerular filtration rate (eGFR), body-mass index, and region (post-hoc). We used hazard ratios (HRs) derived from Cox proportional hazard models for time-to-first event endpoints and Cochran's Q test for treatment interactions; the analysis of recurrent events was based on rate ratios derived from the Lin-Wei-Yang-Ying model.

Findings: Among 8474 patients combined from both trials, the estimated treatment effect was a 13% reduction in all-cause death (pooled HR 0·87, 95% CI 0·77–0·98; p=0·018) and 14% reduction in cardiovascular death (0·86, 0·76–0·98; p=0·027). SGLT2 inhibition was accompanied by a 26% relative reduction in the combined risk of cardiovascular death or first hospitalization for heart failure (0·74, 0·68–0·82;

p<0•0001), and by a 25% decrease in the composite of recurrent hospitalizations for heart failure or cardiovascular death (0•75, 0•68–0•84; p<0•0001). The risk of the composite renal endpoint was also reduced (0•62, 0•43–0•90; p=0•013). All tests for heterogeneity of effect size between trials were not significant. The pooled treatment effects showed consistent benefits for subgroups based on age, sex, diabetes, treatment with an ARNI and baseline eGFR, but suggested treatment-by-subgroup interactions for subgroups based on NYHA functional class and race.

Interpretation: The effects of empagliflozin and dapagliflozin on hospitalizations for heart failure were consistent in the two independent trials and suggest that these agents also improve renal outcomes and reduce all-cause and cardiovascular death in patients with HFrEF.

Funding: Boehringer Ingelheim.

11. Phase 3 Trial of RNAi Therapeutic Givosiran for Acute Intermittent Porphyria

N Engl J Med 2020; 382:2289-2301. DOI: 10.1056/NEJMoa1913147

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Abstract

Background: Up-regulation of hepatic delta-aminolevulinic acid synthase 1 (ALAS1), with resultant accumulation of delta-aminolevulinic acid (ALA) and porphobilinogen, is central to the pathogenesis of acute attacks and chronic symptoms in acute hepatic porphyria. Givosiran, an RNA interference therapy, inhibits ALAS1 expression.

Methods: In this double-blind, placebo-controlled, phase 3 trial, we randomly assigned symptomatic patients with acute hepatic porphyria to receive either subcutaneous givosiran (2.5 mg per kilogram of body weight) or placebo monthly for 6 months. The primary end point was the annualized rate of composite porphyria attacks among patients with acute intermittent porphyria, the most common subtype of acute hepatic porphyria. (Composite porphyria attacks resulted in hospitalization, an urgent health care visit, or intravenous administration of hemin at home.) Key secondary end points were levels of ALA and porphobilinogen and the annualized attack rate among patients with acute hepatic porphyria, along with hemin use and daily worst pain scores in patients with acute intermittent porphyria.

Results: A total of 94 patients underwent randomization (48 in the givosiran group and 46 in the placebo group). Among the 89 patients with acute intermittent porphyria, the mean annualized attack rate was 3.2 in the givosiran group and 12.5 in the placebo group, representing a 74% lower rate in the givosiran group (P<0.001); the results were similar among the 94 patients with acute hepatic porphyria. Among the patients with acute intermittent porphyria, givosiran led to lower levels of urinary ALA and porphobilinogen, fewer days of hemin use, and better daily scores for pain than placebo. Key adverse events that were observed more frequently in the givosiran group were elevations in serum aminotransferase levels, changes in serum creatinine levels and the estimated glomerular filtration rate, and injection-site reactions.

Conclusions: Among patients with acute intermittent porphyria, those who received givosiran had a significantly lower rate of porphyria attacks and better results for multiple other disease manifestations than those who received placebo. The increased efficacy was accompanied by a higher frequency of hepatic and renal adverse events.

(Funded by Alnylam Pharmaceuticals; ENVISION ClinicalTrials.gov number, NCT03338816. opens in new tab.)

CROSSWORD ANSWERS

Across

1. tocilizumab, 2. oxford, 3. covaxin

Down

1. corona, 2. moderna, 3. mrna, 4. two, 5. sputnik