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# MANIPAL MEDICAL JOURNAL

SHARING KNOWLEDGE EMPOWERING CARE

A QUARTERLY PUBLICATION OF
HCMCT MANIPAL HOSPITALS DWARKA, NEW DELHI

# EDITORIAL TEAM

# FROM THE EDITOR-IN-CHIEF'S DESK

It is with great sense of satisfaction that I present the third issue of MMJ. Our schedule and the consequent delay was due to the second wave of the surging pandemic and the professional & personal commitment of my fellow colleagues.

In this issue apart from interesting articles & case reports, we have started a Human Interest Story called " The turning point of my life". Four of our senior doctors have given their inputs in this issue. Our Department of Academics and Research as also MMJ turned 1 yr old on 22nd May 2021 and we are grateful for the continued support of everyone on the Editorial team. This issue also has an article by Ms Vasanthi, a journalist very closely associated with the Manipal group, highlighting the superb role our nurses have played in the pandemic. The pandemic had doctors and their families getting affected and apart from other things came a realisation that financial security was very important. An article on how wisely doctors should save has been brought out by a well known financial counsellor.I am sure it will help us all to plan for the future.

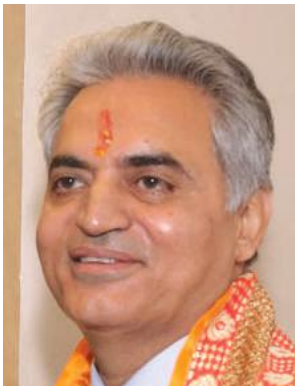
We are happy to share a message sent by the President IMA Dwarka, Dr Mukesh Verma lauding the efforts of Manipal Hospital Dwarka in handling the pandemic & bed crisis so efficiently as also the efforts of IMA Dwarka.

Our slogan "Sharing Knowledge, Empowering care" assumes great importance in our understanding of the second wave of the pandemic and we resolve to have timely issues of MMJ published in this year. My sincere thanks to all in our management for supporting us in our journey.

**Happy reading!!**

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

# MESSAGE



Manipal Hospital has established itself as a leading provider of high-quality health care in India during the past six decades. With a reputation for ethics and compassion, our hospital has dedicated itself to serving the nation. We stand out as a renowned hospital for all patients who walk through our doors because of our medical excellence, implementation of cutting-edge technology, and skilled people with a kind touch. We can completely showcase our centre of excellence, path breaking surgeries, treatment and how our medical staff goes above and beyond the call of duty because they feel every single life is priceless, through this exclusive concept of our medical journal.

Despite so many challenges, we have encountered many unsung heroes at our hospitals, and it gives me great pleasure to say that during such a difficult time, all of our staffs came together to fight the coronavirus by dedicating themselves day and night to provide the best medical care to the patients.

It is an honour and a pleasure for me to serve as President of the Human Care Medical Charitable, Delhi. I'd want to use this occasion to express my gratitude to the entire management team, led by our exceptional COO, Mr Pramod Alagharu. I'd also like to express my gratitude to all of the doctors, medical personnel, and complete team who collaborate with us as one huge HCMCT Manipal family to better the lives of our patients.

Congratulations and all the very best on this endeavour to bring out this medical journal, which will showcase the extraordinary clinical work of our eminent doctors.

Mr Sanjay Khurana,
President, Human Care Medical Charitable Trust

# MESSAGE

Dear Friends

Greetings from the Office of Indian Medical Association Dwarka

It's my pleasure to address you all through Manipal Hospital's academic journal. I am happy that Manipal Hospital is taking a quantum leap in field of medical academics and patient care. I congratulate Manipal Hospital Dwarka, especially Dr Leena Sreedhar editor-in-chief for bringing out such a beautiful academic initiative which aims to weave knowledge with social fabric of fraternity & Nation. I also appreciate Manipal Hospital Dwarka for giving exceptional services during pandemic and standing for Nation in trying times despite constraints & challenges.

The second wave of Covid pandemic has hit us hard & has been tragic both for the medical fraternity & society. We lost more than 600 doctors in Second wave alone. The tsunami of Covid overwhelmed all our medical infrastructure & logistics. Distress calls from friends, neighbours, relatives & fraternity members for admission, oxygen, life-saving drugs & ICU beds gave us guilt feeling, as we were overwhelmed & helpless at a point of time.

During these tough times, we tried our best to be helping hands & constantly tried to coordinate between ailing patients & hospital administrations. Despite close bonded relationship between Associations, officials & various hospital administrations, we felt miserable. We felt all emotions from hope to disappointment, frustration, anger & to hope again. I wish we could manage resources & needs better with good planning & communication in future to avoid this guilt that we couldn't save someone because the system was overwhelmed & couldn't accommodate the needy patients.

IMA Dwarka Team started giving Physical & Virtual consultation for Covid Care Centers in & around Dwarka under district administration. We now need to work on better logistics & improvise these centers for a possible wave in future. We tried hard arranging for oxygen concentrators, appropriate Covid logistics & ventilators to help society and frontline workers. We succeed a bit too. Two ventilators were donated on our initiative to GTB Hospital Delhi. We also received a donation of 10 oxygen concentrators from Shivanjali Foundation Malaysia. Now these are appropriately being used for front-liners & our neighbourhood of Dwarka.

Medical profession has the ability to inspire people. When hopes are lost, the medical fraternity has the capacity to bring back normalcy & happiness in people's lives. Let's hope & pray that this sorrow & sadness around mankind vanishes & we are back with a healthy & happy tomorrow. Let's also pledge to stand by our Covid martyrs who laid down their lives in line of duty. Let's be united & let's stand for dignity & respect that medical fraternity deserves.

I wish Manipal Hospital Dwarka & its health-force lots of courage, power & compassion to help everyone around.

Best Wishes for Manipal Medical Journal.

Jai Hind & Healthy Regards

**Dr Mukesh Verma**
President 2020-22
Indian Medical Association, Dwarka

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# Turning Point of My Life

**Dr Yugal K Mishra**

Chief of Clinical Services, Head of Cardiac Sciences and Chief Cardio Vascular Surgeon Manipal Hospitals, Dwarka, New Delhi

In 1960s, an old man, with a degree in Ayurveda used to sit in a small village, listening to the villagers about their sickness, painstakingly, noting down everything and seeking their hands to feel the nadi (pulse), then dispensing a little packet of drugs or mixture! Never to lose his cool, this man slowly became the fascination for a 13 year old school going boy. He never asked for anything but people would get strange things, like milk, vegetables, fruits etc. in return for his services and used to bless and praise him. This small period of interaction was enough to rollout a future plan for the child - a turning point, who became resolute to adopt medicine as his own preferred field.

True, as a child, I got influenced by my uncle who was a famous and accomplished Ayurvedacharya. My childhood was spent in a small village, amidst nature's lap, far away from the hustle of a big township. Nurturing a dream of Medicine was no less than asking for moon! My late grandmother, adopted and secured my childhood with love and strict discipline, after my mother left for her heavenly abode at 6 months of my age. My father, now a centurion, within his limited means, did whatever he could to help me pursue my dream. The journey from a small village Jariyari, to a small city Rewa, in the state of Madhya Pradesh, was much of trial and tribulation, for a teen with dreamy eyes.

S. S. Medical College, Rewa, M.P. was my alma mater. All my professors were accomplished and distinguished teachers. As a first year student, when I held a dissected heart for the first time, it felt like destiny was in my hands. It was love at first sight and this led me to the second turning point in my life – to become a cardiac surgeon.

As luck would have it, my HOD during post-graduation in surgery, was a cardio-vascular thoracic surgeon. He strengthened my resolution to become a cardiac surgeon. I cleared the AIIMS M.Ch. entrance exam with highest rank, but could not get through the interview for lack of some documents. But as said, if you have a strong desire, the Universe conspires! Destiny took me to another part of the world so that I could realize my dream and become privy to the greatest political event in contemporary history - Gorbachev arrest, release, and subsequent disintegration of mighty USSR!

I did my Ph.D. in Cardiovascular Surgery from the Bakulev Scientific Center of Cardiovascular Surgery, Moscow, an institute par excellence, which has a record of completing hundred thousand open heart surgeries and is known for lot of pioneering work such as Dynamic Cardiomyoplasty for the failing heart.

With an extensive experience of 35 years in the field of cardiac surgery, I have had the privilege of being part of many firsts – the first premier standalone heart institute of the country – Escorts Heart Institute, the first MIDCAB program, the first Minimal Access and Beating Heart CABG program, the first use of voice controlled single arm Robot in Minimal Access Cardiac Surgery and the 'Da Vinci-Robotic-Surgical-System.

I would like to quote the famous Ethiopian athlete Haile Gebrselassie- "When you run the marathon, you run against the distance, not against the other runners and not against the time." I believe every cardiac surgeon needs to be a marathon runner spiritually, to empower him during tough times, only to imbibe the excellence. As a professional, each and every turn in my career has been an enriching experience and taught me to overcome every hurdle with patience and positive frame of mind.

**Dr. (Lt. Gen) CS Narayanan, VSM*****

Consultant & HOD, Department of Neurology
Manipal Hospital, Dwarka, New Delhi

The icy peaks encasing you in a desolate frozen valley was the new reality.

The mirth, the shenanigans, the buoyant joie de vivre that were the very essence of being in medical school appeared to be distant dream from the past.

Adorning the three stars of a young Captain and tasked with the onerous responsibility of being the sole custodian of soldiers manning some of remotest outposts of the nation was a totally different ballgame. To be sure this was not the first time that one was donning a uniform. The hallmark beige attire with a maroon tie was a badge of honour given on entering the hallowed portals of Armed Forces Medical College.

Welcome to the 'Chatni' Brigade. Legend has it that this was named thus for a particularly good reason. Kaiyan Bowl is a deep depression hugging the line of control at the north-western border of Indian-controlled Kashmir. This sliver of territory was re-captured by Indian troops in a hard-fought battle long after the ceasefire of the 1971 Indo-Pak War. Our friends across the border occupy all the heights surrounding the valley, staring down at us. Troops posted here are expected stay put and to deter the enemy to the last man in the eventuality of hostilities breaking out again.

Reaching this devil's own backyard was no mean task either. One had to march for eight hours in pitch darkness as part of a 'foot column'. You walk at night to avoid the avalanches that come crashing down the steep slopes by daylight. Donned in extreme climate clothing, a body of about hundred men snake through

snow-covered mountains in sub-zero temperatures. Once you cross Tutmari Gali, a treacherous icy pass, and a steep descent thereafter, you are swallowed by the bowl.

The emotions that engulf you when you reach there for the first time are beyond description. The raw, stunning beauty of the place leaves you spell-bound. Soon enough, though, the desolation seeps into you slowly but surely. This is not a walk in the park. You are there for the long haul. Years on end. As the clock ticks ever so slowly, news trickles that your buddies from college are moving on in life. Some have gone to green pastures abroad; some have been selected for higher studies in the best of institutions. You get a sinking feeling in the pit of your stomach of being left out.

While the mind of the young medical graduate is swirling with these thoughts, the awakening of the Regimental Medical Officer begins.

It begins to dawn on you that you are the ultimate hope for close to five thousand men deployed in far more difficult pickets than the medical outpost that you are ensconced in. For these soldiers, every step is a matter of life and death in the frozen trenches that they are manning day and night in groups of five to ten.

The pride and purpose returns when you begin to make a difference. The realization that you contributed in no small measure in saving many a life and limb is truly humbling. You bite the bullet and venture into performing medical and surgical procedures like a seasoned professional at the ripe old age of twenty-two. There is no option. An evacuation by chopper is at best a chancy affair. It could take days and sometimes weeks in bad weather.

The men you command slowly begin to repose immense trust in you and it shows. In the meanwhile, an intense exchange of fire prompts an order for the construction of an underground operation theatre. The enthusiasm with which your men get on with the task, digging day and night in the face of adversity teaches something that all the years in medical college did not.

You soon start realizing that there is a larger scheme of things, way beyond your personal comfort and aspirations. The unbound happiness and gratitude with which our men in arms respond when you step out of the confines of the medical aid post to the far reaches of the mountains where they are soldiering leaves an indelible imprint in the memory.

That then, my dear friends, is the turning point in my life – My posting to Kaiyan Bowl at the Line of Actual Control in the Kashmir Valley. The transformation from a young medical student to a full-fledged Medical Officer in the Indian Armed Forces.

I went on the serve close to forty years in the Army Medical Corps. The journey was full of trials and tribulations, but none as life changing as the one in Chatni Brigade.

**Dr. (Col) Moti Lal Bera**
Consultant & HOD, Department of Radiology
Manipal Hospital, Dwarka, New Delhi

On looking back, my entire journey looks like a fairy tale and every difficult moment that I have come across since my childhood till date appears to be a turning point.

I started my journey from a humble peasant family in a remote village far away from city life and devoid of basic amenities. However life was full of peace and tranquility. My Grandfather was an outstanding Ayurveda practitioner, a social worker and an **active member of freedom movement**, who used to tell us about the social atrocities during freedom movement. He was a great thinker, philosopher and a visionary, whom my father followed to provide quality education to his children. It was his vision that guided me to pursue medicine as a career. I am born athlete and actively participated in sports activities in school, college, university and state levels, which inspired me to join the Army.

While serving in the Army, I was applauded on every occasion, whether it was professional matter or sporting field. At one time I was adjudged best sportsman of an Infantry Division and still have the vivid memories of an event in 1979 Command Championship, where I was just a step behind the winner of the 200 meters sprint, who happened to represent India.

After completing MD Radiology in 1986, I was posted to a field medical unit in the western sector due to exigencies of service. I was excited to command a field medical unit in the remote areas of Rajasthan along Indo-Pak border during **"Operation Brasstacks"** with enriching experience , a moment of pride though my specialty work suffered. Soon I was called back to specialist cadre in 1987. The next 12 years, I was completely focused on my profession including Advanced Training in MRI & CT scan in 1992-93. I was posted to Army Hospital (R&R) at Delhi for almost five years after my training, where I was actively engaged in teaching for MD/DNB students and research activities besides my clinical work.

Very soon all my dreams to provide quality work vanished, when I was posted to a peripheral Hospital in North-Eastern Sector. I tried my best to pursue the appropriate authority to provide me a suitable hospital with advanced radiological setup where I can continue my professional expertise, but with unfavourable outcome.

Every organization has its drawbacks, but it affected my career the most, when I joined Military Hospital, Shillong equipped with only X-ray & ultrasound machines. After few months of my posting, I realized that my professional knowledge and expertise was getting wasted. Though Army was my dream organization to work with, I still decided to quit Army to progress on the professional front. Neither was it a simple task nor an easy process, but I was determined and finally hung my Olive Green Uniform almost after 24 years of service in 2001 seeking my fortune outside – ***"The Turning Point in my Life"***.

Moving out to the private sector had its own challenges but I was determined to succeed. I found professional ethics a great challenge and at times I was worried about my decision, but it did not affect my ethos and morale. It was a matter of time that my good work started getting acknowledged and I had job opportunities from the best of the hospitals in the city. **Since then there was no looking back and it's been 20 years since leaving the Army and leading a satisfying professional career.**

I consider my tenure at **Indraprastha Apollo Hospital,** where I worked for eight years, as most satisfying and had the opportunity to operate India's first 64-slice MDCT, requiring additional training within India & Abroad. I had the opportunity to work with best in class professionals consisting of Cardiologists, Cardio-thoracic surgeons, Endo-vascular Interventionists and Transplant Surgeons to assist them in early diagnosis as well as pre-surgical planning & pre-endovascular interventions to best of my ability. I had also the privilege to operate 256-slice MDCT at FMRI, Gurgaon with a spectrum of imaging protocols beyond imagination, whether it was cardiovascular imaging, transplant related imaging, pediatric imaging, pre-surgical planning or various image guided diagnostic/ therapeutic procedures. I was also actively involved in teaching and clinical research during those days.

Looking back, I consider myself fortunate to experience the best of both worlds – be it **"Armed Forces"** or **"Private Sector"**. It's your passion which drives you and your positive attitude & dedication that helps you to achieve your goal at every ***"Turning Point of life"***.

**Dr. Sanjay Gogoi**
Consultant & HOD, Department of Urology & Renal Transplantation
Manipal Hospital, Dwarka, New Delhi

Upcoming 1982 Asian Games in New Delhi, had kept all the kids in my neighbourhood, quite exited. Retired Doon School English tutor, Mr Sinha, whom we all fondly called 'english uncle', had promised to show us the Asian Games on a Colour TV. Doordarshan had started colour transmission in the summer of 1982 and for us, the excitement knew no bounds.

I was in class XI and had decided to pursue engineering. Apart from the coaching classes, I was busy reading 'Electronics For You' and fabricating different DIY gadgets. I used to order spares from Bhagirath place and make tape recorders, amplifiers, TV signal boosters etc. This was my entrepreneurial best and I used to earn quite handsomely.

TV signal quality in Dehradun used to be quite erratic. My skills as a budding mechanic, inspired 'english uncle' to entrust his roof top TV antenna under my care. By the time the Colour TV set was delivered, I had done my job well. A week before the games, on a cold Friday evening, we watched Chitrahaar in full colour! Subsequently, for the whole of November and December, entire neighbourhood watched the games in their living room, sipping adrak ki chai.

Just about a month later, when we all retired to our usual chores, disaster struck. 'English Uncle' suddenly fell sick. No sooner we were informed, we rushed him to the neighbourhood hospital. The doctor promptly diagnosed his condition as acute myocardial infarction. Despite the best efforts, Mr Sinha died within 24 hours of admission.

This was a "Turning point of my life". I surrendered my engineering dreams and decided to pursue medicine. I ended up being a doctor, yet the engineering flame still kindles on.

# MOMENTOUS MOMENTS IN MEDICINE

## CRISPER – Genetic scissors: a tool for rewriting the code of life

Kunal Das
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"CRISPR" (pronounced "crisper") stands for Clustered Regularly Interspaced Short Palindromic Repeats, is a family of DNA sequences found in the genomes of prokaryotic organisms such as bacteria and archaea. [1] These sequences are derived from DNA fragments of bacteriophages that had previously infected the prokaryote. They are used to detect and destroy DNA from similar bacteriophages during subsequent infections. Hence these sequences play a key role in the antiviral (i.e. anti-phage) defence system of prokaryotes and provide a form of acquired immunity.

Emmanuelle Charpentier and Jennifer A. Doudna received The Nobel Prize in Chemistry 2020 jointly "for the development of a method for genome editing" [2] They have discovered one of gene technology's sharpest tools: the CRISPR/Cas9 genetic scissors. Using them one can change the DNA of animals, plants and microorganisms with extreme accuracy. This technology has had a revolutionary impact on the life sciences, is contributing to new cancer therapies and may make the dream of curing inherited diseases come true. Researchers need to modify genes in cells if they are to find out about life's inner workings. This used to be time-consuming, difficult and sometimes impossible work. Using the CRISPR/Cas9 genetic scissors, it is now possible to change the code of life over the course of a few weeks. "There is enormous power in this genetic tool, which affects us all. It has not only revolutionized basic science, but also resulted in innovative crops and will lead to ground-breaking new medical treatments," says Claes Gustafsson, Chair of the Nobel Committee for Chemistry. [2]

As so often in science, the discovery of these genetic scissors was unexpected. During Charpentier's studies of Streptococcus pyogenes, one of the bacteria that cause the most harm to humanity, she discovered a previously unknown molecule, tracrRNA. Her work showed that tracrRNA is part of bacteria's ancient immune system, CRISPR/Cas9 that disarms viruses by cleaving their DNA. Charpentier published her discovery in 2011. The same year, she initiated a collaboration with Jennifer Doudna, an experienced biochemist with vast knowledge of RNA. Together, they succeeded in recreating the bacteria's genetic scissors in a test tube and simplifying the scissors' molecular components so they were easier to use.

Since Charpentier and Doudna discovered the CRISPR/Cas9 genetic scissors in 2012, their use has exploded. This tool has contributed to many important discoveries in basic research, and plant researchers have been able to develop crops that withstand mould, pests and drought. In medicine, clinical trials of new cancer therapies are planned, and the possibility of cure of inherited diseases is possible.

**Emmanuelle Charpentier**

**Emmanuelle Charpentier** is the founder, scientific and managing director of the Max Planck Unit for the Science of Pathogens, Berlin. Dr. Charpentier has won many other awards for her contributions to the genome engineering field. The Breakthrough Prize in Life Sciences award, the Harvey Prize, and the Gruber Prize in Genetics are a few of the awards she has received. She quotes: "I haven't changed, and I won't change. The scientist that I am got me here, and that is the scientist that I want to remain." She was born in 1968 in Juvisy-sur-Orge in France, Charpentier studied biochemistry, microbiology and genetics at the Pierre and Marie Curie University (today the Faculty of Science of Sorbonne University) in Paris. [3] She was a graduate student at the Institut Pasteur from 1992 to 1995, and was awarded a research doctorate. Charpentier's PhD project investigated molecular mechanisms involved in antibiotic resistance. Charpentier worked as a university teaching assistant at Pierre and Marie Curie University from 1993 to 1995 and as a postdoctoral fellow at the Institut Pasteur from 1995 to 1996. She moved to the US and worked as a postdoctoral fellow at the Rockefeller University in New York from 1996 to 1997. During this time, Charpentier worked in the lab of microbiologist Elaine Tuomanen. [4]

Tuomanen's lab investigated how the pathogen Streptococcus pneumoniae utilizes mobile genetic elements to alter its genome. Charpentier also helped demonstrate how S. pneumoniae develop vancomycin resistance. After five years in the United States, Charpentier returned to Europe and became lab head and a guest professor at the Institute of Microbiology and Genetics, University of Vienna, from 2002 to 2004.

In 2004, Charpentier published her discovery of an RNA molecule involved in the regulation of virulence-factor synthesis in Streptococcus pyogenes. [5] Charpentier moved to Sweden and became lab head and associate professor at the Laboratory for Molecular Infection Medicine Sweden (MIMS), at Umeå University and held the position as group leader from 2008 till 2013. In 2015 Charpentier accepted an offer from the German Max Planck Society to become a scientific member of the society and a director at the Max Planck Institute for Infection Biology in Berlin. Since 2016, she has been a Honorary Professor at Humboldt University in Berlin, and since 2018, she is the Founding and Acting Director of the Max Planck Unit for the Science of Pathogens. [3]

She has been awarded numerous international prizes, awards, and acknowledgements, including the Nobel Prize in Chemistry, the Breakthrough Prize in Life Sciences, the Louis-Jeantet Prize for Medicine, the Gruber Foundation International Prize in Genetics, the Leibniz Prize, Germany's most prestigious research prize, the Tang Prize, the Japan Prize, and the Kavli Prize in Nanoscience. These tools facilitate genome modification with an unprecedented degree of precision, and far more cheaply and straightforwardly than any previous method. Not unlike today's simple, intuitive word processing programs, CRISPR/Cas9 is able to "edit" the genome by "cutting and pasting" DNA sequences: a technology so efficient and powerful that it has spread like wildfire round the laboratories of the world, explains the jury, "as a tool to understand gene function and treat disease".

**Jennifer A Doudna**

Jennifer A Doudna is a professor at the University of California Berkeley and a faculty scientist at the Department of Energy's Lawrence Berkeley National Laboratory (Berkeley Lab). She was one of the first to suggest that the bacterial enzymes that control microbial immunity (CRISPR-Cas9) may be used for programmable editing of genomes. Dr. Doudna has been the recipient of many other prestigious awards such as the Breakthrough Prize in Life Sciences, the Wolf Prize in Medicine, and the NAS Award in Chemical Sciences among a plethora of other awards for her outstanding contributions to the life sciences field. She quotes: "Go for your biggest and most exciting ideas and don't let anyone tell you that it won't work'. [2]

Jennifer Doudna was born on February 19, 1964, in Washington, D.C., as the daughter of Dorothy Jane (Williams) and Martin Kirk Doudna. Her father received his Ph.D. in English literature from the University of Michigan, and her mother, a stay-at-home parent, held a master's degree in education. When Doudna was in the sixth grade, her father gave her a copy of James Watson's 1968 book on the discovery of the structure of DNA, The Double Helix, which was a major inspiration. Doudna also developed her interest in science and mathematics in school. She was an undergraduate student at Pomona College in Claremont, California, where she studied biochemistry. Chemistry professors Fred Grieman and Corwin Hansch at Pomona had a major impact on her. She chose Harvard Medical School for her doctoral study and earned a Ph.D. in Biological Chemistry and Molecular Pharmacology in 1989.

After her PhD, she held Research Fellowships in Molecular Biology at the Massachusetts General Hospital and in Genetics at Harvard Medical School. Early in her scientific career, Doudna worked to uncover the structure and biological function of RNA enzymes or ribozymes. Later, Doudna joined Yale's Department of Molecular Biophysics and Biochemistry as an assistant professor in 1994 and she worked on X-ray diffraction-based structure of active site of a ribozyme at Yale. She later moved to UC Berkeley in 2016. As of 2020, Doudna was located at the University of California, Berkeley, where she directs the Innovative Genomics Institute (a joint center of UC Berkeley and the University of California, San Francisco), holds the Li Ka Shing Chancellor's Professorship in Biomedicine and Health, and is the chair of the Chancellor's Advisor Committee on Biology. [6] Her lab now focuses on obtaining a mechanistic understanding of biological processes involving RNA. This work is divided into three major areas, the CRISPR system, RNA interference, and translational control via MicroRNAs. [6]

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# The World No Tobacco day: Saying No to the Smoke

Anusheel Munshi
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About 5.7 trillion (5,700,000,000,000) cigarettes were smoked worldwide in 2016. [1]. The number would probably be even higher today. Tobacco has been a major health problem for several decades now. It is estimated that around 100 million people died prematurely in entire 20th century because of smoking, mostly in rich countries. [2]. According to the Global Burden of Disease study more than 8 million people died prematurely as a result of smoking in 2017. [3,4] The health burden of smoking is now making a shift from high-income to low-to-middle income countries, some estimates have suggested that one billion people could die from tobacco over the 21st century. [3,4] **(Table 1)**

31st May marks the "World No Tobacco Day." This day is aimed to create awareness about the tobacco menace all across the globe. The day is aimed not only to achieve just a 24-hour abstinence from tobacco but to facilitate giving up tobacco, in all forms, for good. It is also purposed to draw attention to the widespread prevalence of tobacco use and to its plethora of negative health, social and economic effects.

There are various categories of smoke. **First hand smoke** denotes the smoke directly inhaled by the smoker. **Second hand smoke** means the smoke emitted from burning tobacco and also the smoke breathed out by the smoker, which is then inadvertently inhaled by those present around. **Third hand smoke** means the smoke absorbed by the objects such as sofa, pillows and bed, which can be then emitted and inhaled by those around.

**Table 1: Tobacco Fact sheet [5,6]**

| | |
|---|---|
| 1 | Tobacco eventually kills half of its users |
| 2 | Tobacco alone is responsible for claiming more than 8 million deaths each year worldwide. |
| 3 | Out of 7.5 billion people living on earth, 1.3 billion (20%) use tobacco. |
| 4 | 80% of the tobacco users live in low/middle income countries |
| 5 | 14% of Indian adults use tobacco (24% males, 3% females) |
| 6 | Among tobacco users, in India, 60% consume tobacco within one hour of getting up |
| 7 | Nearly 1 million die in India every year due to tobacco use |

Tobacco is a known risk factor for several cancers such as those of the mouth, tongue, throat, lung, esophagus, urinary bladder to name a few. Even if one is lucky not to have these diseases, tobacco smoke can affect the lungs function causing respiratory disease such as asthma, chronic obstructive airway disease and others. Smokers have a manifold higher chance of developing cardiac problems such as high blood pressure and heart attacks.

Tobacco and smoking have been much integrated into the lifestyle of the common man. Sharing a cigarette or hookah is often considered an act of brotherhood and love in most regions of globe. Tobacco comes back in many avatars, including flavoured tobacco, smoking pipes of hookahs and many more. All are equally harmful and dangerous. Sadly, many amongst teenagers and younger generation are falling prey to this malady.

Smokers harm themselves, and through secondary smoke and tertiary smoke affect the lives of their near and dear ones. The financial burden of smoking may appear small on a day to day basis, but the cumulative spending over smoking for a lifetime would reveal a big financial loss.

There is some good news, though. Even for people who have been smokers for long, the risk of developing cancer and other allied diseases drops as soon as they stop smoking for good and continues to decline for a long time. The ultimate solution is to give up tobacco, once and for all. It requires a bit of firm determination and resolve. One can take the aid of professional advice in this as well, including assistance from several NGO's and organizations. **(Table 2)**

**Table 2: Websites/links dedicated towards quitting tobacco**

| | |
|---|---|
| ***1*** | ***https://www.who.int/activities/quitting-to-bacco*** |
| ***2*** | ***https://www.mayoclinic.org/healthy-lifestyle/quit-smoking/in-depth/nicotine-craving/art-20045454*** |
| ***3*** | ***https://www.webmd.com/smoking-cessation/ss/slideshow-13-best-quit-smoking-tips-ever*** |
| ***4*** | ***https://www.cdc.gov/tobacco/quit_smoking/how_to_quit/benefits/index.htm*** |
| ***5*** | ***https://www.nhs.uk/live-well/quit-smoking/10-self-help-tips-to-stop-smoking/*** |

On the downside, despite the ostensibly vigorous commitment of some in the tobacco industry toward a smoke-free and tobacco free world, all major tobacco companies continue to aggressively advertise cigarettes and often clandestinely fight anti-tobacco efforts around the world. While there have been reductions in smoking rates in the United Kingdom, Australia, Brazil, it is largely offset by the increasing consumption in many countries with weaker tobacco control regulations. [7]

While the best thing is having never ever smoked, the second best thing is to take a pledge to abstain from it- for all times to come. There is no better gift for ourselves, our family and our community brethren

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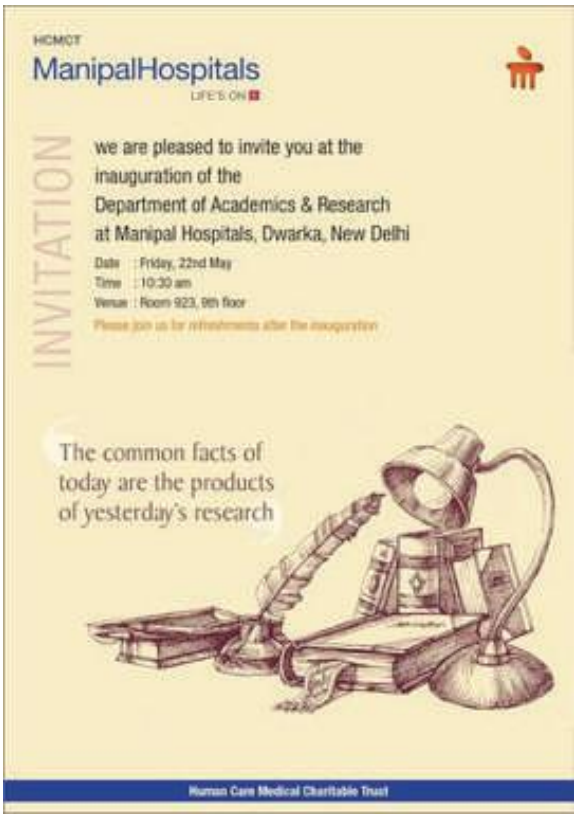
## INAUGURATION OF THE DEPARTMENT OF ACADEMICS & RESEARCH





# Financial Planning: What a Doctor should know

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## INTRODUCTION

Financial Planning is a process of creating a discipline to safeguard one's net worth or income creation by conserving saving and investing. The primary goal is to have a safe and secured financial future, and post retirement, smooth transfer of the assets to the next generation.

Three primary phases involved are:

A. Creation of Income and assets simultaneously securing and conserving them
B. Accumulation & consolidation of existing assets & income so that it appreciates and grows.
C. Wealth transfer planning – Preparing a will that transfers the assets to the beneficiary.

The basics of financial planning are the same for everyone but the ratio, proportion and designing varies from person to person. Their age, health, profession, income, needs and liabilities, dependence and family is kept in mind while designing a healthy portfolio. Attitude towards money also decides wealth creation. Simplicity and discipline has always been a winner.

Financial planning for doctors is different in comparison to other professionals. There are many reasons for the same.

A. They start earning late because of their academic requirements.
B. They are into a skilled profession so the emphasis on risk cover protection against disability and death is very important
C. Their profession exposes them to various infections and medical hazards.
D. Taxation behaves differently for consultants and salaried doctors.
E. Time and a busy schedule bars them from taking care of their financial health research online, for which a customized need base financial road map is required.

The process of designing a financial portfolio requires expertise and a strong grip, knowledge of the various financial instruments which your financial advisor is equipped with. Your financial advisor is like a coach who is monitoring your financial health and helping you take the right financial moves.

Financial planning involves carefully designed techniques and strategies similar to how a Doctor would prescribe medicines to patients after knowing their symptoms, current situation and medical history, same way with the help of below steps a Financial Coach would design a portfolio

A. It involves assessing current status, availability of resources, income, shortcomings, mind sets and requirements
B. An advisor helps you build a goal focussed approach along with considering your aspirations and dreams for the future
C. A good financial plan helps you fill the gap between what you have and what you want.
D. Helping the customer implement these strategies and to get the portfolio active.

There are various financial instruments in the market and selection may be different for every individual based on his/her goal, time horizon, product suitability, risk appetite, annualized returns, income creating span in mind and most importantly tax implications.

## WHY IS INSURANCE A SMART FINANCIAL STRATEGY?

Insurance is the foundation of financial planning and the most important part of a healthy portfolio. Insurance transfers the financial and legal risks to a third-party which would come into picture in case of any unfortunate event and compensate for financial losses.

Insurance helps in creating an umbrella to protect the unearned income by paying a small part of the income. Here a Financial Coach would help customize a suitable plan with adequate amount of sum assured to be purchased, adding value and further safety by endorsing these policies under HUF, MWPA making them un-attachable and safeguarding the rights of the beneficiaries free from any legalities. Doctors and Professionals are exposed to legal risks and liability requires this endorsement the most.

Effectively four types of situations are there when "I" is an Insurance Company comes forward and delivers for the goals as maturity and claims in case of events.

a. "Kids' education, I pay" – This refers to Education
b. "You fall sick, I pay" – This refers to Medical Insurance and Income Protection Planning
c. "You retire, I pay" – This refers to Retirement Planning
d. "You die, I pay" – This refers to Life Protection Planning

## WHY DO WE NEED INCOME PROTECTION?

Everything today is built on potential income especially considering the current pandemic situation. Losing the ability to earn and build income is the potential reason why a person can lose income.

1. Loss of employment or economic downturn
2. Loss of income due to bad health
3. Loss of income due to death

There are 3 basics – Food, Clothing and Shelter and all are based on income. Income decides the food we eat, the clothes we wear and the house we live in. Two ways to get income are either we work our whole life or our accumulated wealth churns out income for us.

## Three Risks

a. Environmental Risk – e.g. COVID-19, natural disaster or economic downturn, loss of job
b. Health Risk – Permanent disability, Critical illness, incapacitation to perform
c. Death – Absence of income generating individual would create vacuum for the dependants

## I. Life Insurance

Life Insurance planning is divided into 3 different categories:

1. **Term Insurance Plans** - Pure risk plans
2. **Endowment Plans** - Goal specific plans
3. **Whole-Life/Annuity Plans** - Retirement plans
4. **Unit Linked Plans** - Equity specific plans

A term insurance plan purely prepares the customer against death, these covers are lower in premium and deliver money post death. Whereas, saving plans have an edge, they secure your milestone goals with wavering off your premium and policy delivering the same pay-outs as they were designed. For example, in a child's education plan, parents are contributing towards the saving discipline to create a corpus for their child's higher education. During this course of saving, in case of an unfortunate absence of the payer/proposer, the saving plan takes care of the cost of education. Simultaneously, the policy premiums are paid by the company and the maturity is delivered to the child as it was planned.

## II. Health Insurance

A good and adequate Medical Insurance is a must for every individual especially doctors who are highly exposed to hazardous conditions. Medical plan purchases should have a high benefit programme with no exclusions, waiting periods and co-payment issues in later years.

## III. Critical Illness Cover

This compensates the income loss during the occurrence of critical or terminal illnesses and major critical ailments or in case of incapacitation to earn income. This is different from medical insurance and gives a lump sum amount in case of occurrence of an event amongst listed events.

## IV. Professional Indemnity Insurance

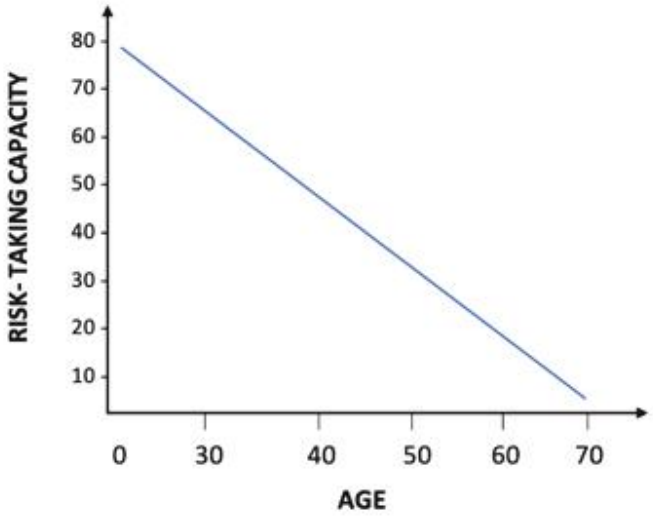
Professional Indemnity Insurance is a must for every professional be it a doctor, architect or any other profession where a minute error can put someone into a litigation. This safeguards future net worth against any kinds of litigation and medical license security.

## V. Mutual Funds

This is an excellent way to participate in the equity market and accumulate your investments and savings and make it work like a venture capital but also involves some risks due to the nature of the market. Financial advisory plays a very important role in selecting and managing the funds. New purchase, addition, selling, redemption, timely switching and profit booking are a part of financial coaching. Since doctors are involved in their profession, they do not have time and expertise to monitor markets and their trends. So, it is always advisable to have a personal financial coach to take care of their portfolio.

## VI. Stocks and Direct Equity

This instrument is dependent on the risk taking capacity of the investor and involves high risk also. Complete knowledge and patience can do wonders. By investing in these instruments, the investor becomes the owner in a company amounting to the shareholding that he/she possesses.




## VII. Bonds

They are fixed interest rate papers issued by the Government or Companies. They pay a fixed maturity amount with a safety rate that varies from company to company.

## VIII. Public Provident Fund (PPF)

A good tax-saving tool which gives 80CCC tax exemption from taxable income. The maximum limit to invest is INR 150,000 per annum. It has a fixed rate of return of 7.1%. The tenure is fixed for 15 years and one can do a partial withdrawal in the mid-term of the investment.

## IX. Real Estate

One of the most favourite categories of asset with low returns, poor liquidity and lots of complications involved.

Things To Remember While Selecting The Financial Instrument

1. Liquidity – How fast can the investment be converted into cash. As age increases, more liquidity should be in hand.
2. Volatility – How risky is the asset as an instrument. Is the price change expected suddenly or unexpectedly?
3. Yield – How much return can you expect from the investment?
4. Tax Efficiency – How the liquidation, final proceeds or maturities would be treated at the end of the tenure. Whether they would be added in your income, or tax exempted.

| Instruments | Liquidity | Volatility | Yield | Tax Efficiency |
|---|---|---|---|---|
| Property | Illiquid | Market Dependant | Stable Returns | Taxable |
| Equity/ Stocks | Liquid | Higher Risk | Higher Returns | Taxable @10% |
| Bonds | Liquid, Market Dependant | Safe | Stable Returns | Taxable |
| PPF | Lock-in Period –15 yrs | Safe | Stable Returns | Non-Taxable |
| Commodities | Market Dependant | High Risk | Higher Returns | Taxable |
| Insurance | Pre-defined at the time of purchase | Very Safe | Stable Returns | Non-Taxable |

Investment strategy must be based on Income Generation ➔ Income Accumulation.

Based on the risk appetite, there are 4 different personalities of investors.

A. **Aggressive**
B. **Balanced**
C. **Cautious**
D. **Defensive**

An **Effective Financial Coach** would help you in:

A. Designing your goal
B. Understanding your current situation along with your income expenditures and liabilities
C. Calculate the cash surplus
D. Assess your risk capacity and understand your personality (Disciplined/ Undisciplined/ Spendthrift/ Conservative)
E. Design your financial plan
F. Help you implement these strategies and bring the plan into action
G. Conduct half-yearly and annual reviews to monitor the progress.
H. Keep on increasing your bar so that your financial plan outperforms

The 3 Sectors of life span to be financially protected and planned and this process can be managed and planned by your Financial Coach.

A. Sustenance of the lifestyle (basic food & shelter) – Taking care of expenses that are recurring. This needs creating a back-up or a contingency fund through instruments which can be liquidated easily.
B. Goals – These are milestones which all of us have and make us dream big.
   - Short-term goals – Buying a car, world tour, jewellery, renovating a house, etc.
   - Mid-term goals – Buying a house, upgrading your vehicle, starting a venture, etc.
   - Long-term goals – Higher education for children, child's marriage, etc.
C. Retirement – Ensure that one is saving money into an annuity which provides the couple with an income as soon as one retires. Income in retirement is an asset. Assets in retirement can become a liability.

Financial Tips for Doctors

1. Increase your financial knowledge to help you plan better for you and your family's future.
2. Start saving regularly. The sooner the better. Try to save at least 20% of what you earn.
3. Avoid buying property on a mortgage as it takes a lot of your income in form of interest, unless a plan has been chalked out with your financial advisor to clear off the loan. Cash flow is very important. Although the house would be an asset on your balance sheet, your liabilities and commitments would increase.
4. Unexpected situations can ruin the plans. Ensure you are in a position to handle these risks by doing regular financial reviews with your financial advisor.
5. Car purchase should be done thoughtfully as this is a depreciating asset.
6. Ensure early saving into an Annuity which provides you with adequate income as you retire.
7. Reserve a part of your savings from your income before you start spending any of it. Do not take any unnecessary loans or liabilities unless it is a need of the hour. These loans can dent your cash flows and affect your peace of mind.
8. Marriages are made in heaven but the cost of the ride can dent your pocket, so the wedding should be kept simple.
9. Check inflation!! Don't keep huge chunks of money in bank accounts for contingencies. Keep an adequate amount in the bank and invest the remaining amount in liquid funds to get better returns and instant liquidity.
10. If you invest in the stock market, watch it with caution and be ready to take action. If you do not have the knowledge and expertise, hire someone (financial coach) and pay them a fee.
11. Do not have the notion of showing-off by having a huge property and an expensive car.

12. "Where there is Wealth, there are Advisors!" It is advised to have a "Letter of Wishes" in place to ensure the deliverance of the wealth to the beneficiaries whom it belongs to in the absence of the owner.
13. Life Insurance should be bought keeping in mind protection and continuation of family lifestyle in the absence of the income generating member. Returns are obvious to come on maturity to accomplish the goal for which it was bought. It is a lot more than just an investment and calculation of percentage of return. It is a risk management tool to protect the future income.
14. The future plan should be very clear especially in the area of career, life goals, expenses and investment strategy.
15. Build an emergency fund which covers approximately 6 months of your expenses.
16. Health & Wealth – Ensure keeping both these on top priority. Loss of either one can be really dangerous. Get regular check-ups done by professionals in both these areas.
17. Old Age is Real, do not overestimate your working capacity. You need some form of guaranteed income when you are in your retirement years. Age has a funny way of taking a toll on your ability to work.
18. It's a saying, "You should have a lot of gold in your pocket when you have silver on your head". Retirement is going to be your longest vacation. Plan wisely and be prepared to enjoy it.

## WEALTH TRANSFERS AND IMPORTANT ASPECTS OF FINANCIAL PLANNING

- Your financial advisor also helps you in segregating your net worth into human wealth, financial wealth and intellectual wealth.
- They help you to enhance, protect and to transfer by creating a proper succession plan.

## CONCLUSION

To conclude with, "You can put a price to everything but not a good night's sleep"

## HAPPY INVESTING!

Shalini Kohli ia a financial coach with over 21 years of experience in Risk & Financial Consultancy. She works very closely in areas of securing unearned income and making your money work harder for you post retirement rather than you working to create it. She can be reached at +91 9810890661 and shalinikohli21@gmail.com

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## INAUGURATION OF THE DEPARTMENT OF ACADEMICS & RESEARCH

# A Review on Covid 19 Vaccination in Cancer Patients - A High Priority Group

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## INTRODUCTION

SARS CoV 2 (COVID 19) pandemic has affected a large percentage of the global population and the second wave of Covid-19 in India has seen a significant rise in the number of recorded deaths. The death toll since the starting of the pandemic in India has crossed 3 lac by May 2021, but now there is light at the end of the tunnel in the form of the ongoing vaccination programme. The ICMR in April 2021 stated that out of 1.1 Cr beneficiaries who were administered Covaxin, only 0.04% each were found to be infected after 1st and the second dose. Likewise, with Covishield, only 0.02% tested positive after 1st dose and 0.03% after 2nd dose.

Amongst the subset of population who have a higher probability of moderate to high-risk illness are the cancer patients who have now heaved a sigh of relief with the ongoing vaccination drive. There are some important efficacy and safety concerns in this patient category. However various guidelines from US, [1,2] European [3] and Indian oncology (to be published) societies emphasize the benefits of getting immunized as early as possible. Since none of the phase 3 vaccine trials have included Cancer patients in significant numbers, following are the consensus-based statements from various associations and experts.

## IMMUNE SYSTEM PROFILE IS DIFFERENT IN CANCER PATIENTS

In general, cancer patients maybe in three categories: patients with active disease on treatment, those with chronic disease after specific treatment and patients in the survivorship phase.

In the “survivorship” and “chronic disease” phases (patients who are on low dose therapy to control cancer) vaccination seems essential and doable because of near normal immune responses. The question is more difficult in patients with active disease on anticancer therapy for whom vaccination could have reduced efficacy. The various consensus statements show that patients having a solid tumor malignancy would build up a better response to a Vaccine as compared to patients of acute leukemia on treatment. That said, vaccination should still be strongly considered in a patient of acute leukemia because the limited immune response to the first dose gets better after the second dose.

## TIMING OF VACCINATION DURING CANCER TREATMENT

Vaccination should be considered at least a couple of weeks prior to surgery as most cancer surgeries are elective. However, the time between the vaccination and the surgery can be shortened after discussion with the surgeon in case of urgency. A gap of at least a few days is necessary so that a postoperative febrile episode can be differentiated from a vaccination related febrile illness. Postoperatively, the vaccine can be given a week after surgery if the recovery is uneventful. [1,3]

For patients on chemotherapy, [1,3] vaccination can be considered prior to starting chemotherapy; or between the cycles, when there is a recovery of the Neutrophil count. Patients on Immunotherapy like Check point inhibitors and Targeted therapy, or on Radiation therapy should get themselves vaccinated as soon as a vaccine is available to them.

For patients undergoing Stem cell transplant / CAR-T cell therapy, [1,2] the vaccination is to be considered after a gap of at least 3 months from the procedure.

There should be a discussion with the oncologist prior to receiving the vaccine whenever the patient is on any active therapy.

## THE BEST VACCINE

Currently with 2 available vaccines in India both the vaccines provide similar efficacy in preventing moderate to severe illness and hence whichever is available should be taken.

## SIDE EFFECTS AND PRECAUTIONS

Since all the large trials had excluded cancer patients, we do not have a published data on side effects of these vaccines on this group of patients. However, there are no reports of any unusual or excessive side-effects in cancer patients who have been vaccinated so far across the globe. It is advisable to check complete blood count (CBC) prior to vaccination, especially for patients on chemotherapy. For patients of breast cancer, they should take vaccination on the opposite arm in order to prevent any inflammatory enlargement of axillary lymph nodes which may interfere in staging of newly diagnosed patients and to avoid increasing their chances of lymphedema in already treated patients.

Once vaccinated, cancer patients have decreased risk of morbidity from COVID-19 disease as compared to non-vaccinated cancer patients. They should be managed in the same way as any other patient would be managed, with a close monitoring for any complications of COVID 19. Another important aspect is to make sure that the caregivers of the patient should also get themselves

vaccinated as soon as they become eligible for the same because they may serve as carriers of COVID-19 thus putting the patient at risk. It would also help to build herd immunity which plays an important role.

## KEY-POINTS

- Vaccines against COVID-19 appear to be safe for cancer patients
- Timing of vaccination depends upon cancer status and type of ongoing treatment
- Surgical patients - one week prior to or one week after surgery. In case recovery is delayed, vaccination should be delayed.
- Chemotherapy - A few days to a week before commencing chemotherapy or between the cycles when white cell counts have recovered.
- Radiation & hormone therapy - anytime if health & white cell count is fine.
- Three months after Bone marrow transplant and CAR-T cell therapy.

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## INFORMATION CORNER

**List of Webinars done (Jan – June 2021)**

| |
|---|
| Sign N Symptoms N Second Wave Of Covid |
| Infectious Diseases |
| Variants Of Covid |
| Myths N Facts About Vaccination |
| Covid Vaccine |
| Lifestyle Disease |
| Chair Ergonomics |
| Cancer Awareness |
| High Bp And Anger |
| Mental Health |
| Diet And Lifestyle |
| Work Life Balance |
| Effects Of Covid On Mental And Physica Well-Being On Individual |
| Ergonomics |
| Aneuploidy Screening- Facts & Myths- What A Gynecologists Should Know |
| Diabetes Awareness |
| Stress Management |
| Know About Cancers |

# Central Venous Obstruction Management Strategies: A Case Series

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## INTRODUCTION

End stage chronic kidney disease patients are usually dialysis dependent. Of these, the hemodialysis dependent group need vascular surgery consultation for repeated vascular access. These patients usually have repeated temporary vascular access like the Hemodialysis catheter inserted in the central vein or longer term catheters like permacath. The permacath provides long term and high flow access that is required for hemodialysis.

Since these catheters remain in the central veins for a prolonged duration, the constant friction with the vein walls can lead to stenosis or narrowing at the points of maximum movement, usually the tip. This leads to subsequent development of central venous hypertension. Patients with central venous hypertension might remain asymptomatic and only manifest when they undergo a procedure like an arteriovenous fistula creation. This leads to increased flow through the veins leading to increased flow through an area of previous narrowing. The lesion that was inert now manifests clinically.

Patients present with swelling of the upper limb and face and flushing with or without respiratory distress. These cases of central venous hypertension need a high index of suspicion to be diagnosed and treated appropriately. [1]

Identifying the need to recognize this under diagnosed entity, we decided to study the cases of central venous hypertension presenting to the vascular surgery department. This study aims to look at the profile of the patients presenting with central venous obstruction and the management options (type and number of interventions required to give symptomatic relief to such patients) available and offered to them.

## METHODOLOGY

The study was an observational cross sectional case series that was conducted in the Department of Vascular and Endovascular Sciences, Manipal Hospitals, Dwarka, Delhi from December 2018 to March 2021.

Manipal Hospital Delhi is a private trust based hospital that caters to the semi-urban and urban population of Delhi and NCR region. All patients presenting to the department with symptoms suggestive and diagnosed with Central Venous Obstruction were included for the study.

All patients were taken up for interventional procedure in the Catheterization lab after the pre requisite investigations. It was interesting to note that all patients had Chronic Kidney disease and were on Hemodialysis.

After informed consent all patients were taken up for the procedure under local anaesthesia. All patients underwent the procedure that was done by a single primary vascular surgeon with his team.

Systemic heparinization according to creatinine clearance was administered in all of them. Contrast agents like omnipaque or visipaque were usually administered for the venography in the study group. Post procedure patients were monitored in the Cardiac care unit and then shifted to the ward. All patients were discharged within 24 hours of the procedure.

Data Collection was done retrospectively from the Hospital information system and the catheterization lab reports of the procedure done by a single data retriever. Data was collected in the excel format and analyzed.

## RESULTS

Data was collected from December 2018 to March 2021. Over a period of 27 months, 77 Interventional vascular procedures were done in the catheterization lab, of which 21 were done for central venous obstruction (27.3%).

Mean age of the patients presenting with these complaints and undergoing procedures was 60.3 years with a standard deviation of 9. **(Table 1)**. The procedures were more in males than females.

All patients had Chronic Kidney disease with history of multiple central venous access placements before developing the central venous hypertension.

A total of 21 procedures were done in 15 patients, of which 86 % procedures were venoplasty. Four patients underwent venoplasty followed by stenting of the central vein. In three patients the lesion could not be negotiated.

Four patients required repeat procedures for central venous hypertension in intervals ranging from 3 months to 11 months. One patient underwent the procedure three times, each of the time there was an instent stenosis and angioplasty was done. **(Table 2)**

**Table 1**
**Characteristics of the patients and veins undergoing venography and venoplasty for central venous obstruction**

| Parameters | Total procedures, n=21 |
|---|---|
| Age in years (mean , SD) | 60.3 (9) |
| Gender, n (%) | |
| Male | 14 (66.7) |

| Parameters | Total procedures, n=21 |
|---|---|
| Female | 7 (33) |
| Comorbid conditions, n(%)<br>Diabetes mellitus<br>Hypertension<br>CKD<br>CAD | <br>12(57)<br>16(76.2)<br>21(100)<br>3(14.3) |
| Multiple previous venous access ( >1), n(%) | 21(100) |
| Stenosis involving the segment of the central vein (Areas depicted in the Figure 1), n(%)<br>1) Superior Vena cava<br>2) Brachiocephalic<br>3) Subclavian<br>4) Instent | <br>1(4.7)<br>13(62)<br>2(9.5)<br>3(14.3) |
| Venoplasty done, n(%)<br>Lesion could not be negotiated, n(%) | 18(86)<br>3(14.3) |
| Stenting of the central vein done, n(%) | 4(19) |
| Access route accessible for angioplasty, n(%)<br>1) Femoral access<br>2) AV fistula proximity access | <br>17((81)<br>12(57) |
| Access route converted from femoral to AV fistula proximity access, n(%) | 10(47.6) |

**Table 2**
**Findings and time to recurrence of patients requiring repeat procedures**

| Patients with recurrence of symptoms | First presentation findings | Interval to Second presentation (months) | Interval to Third presentation (months) |
|---|---|---|---|
| Patient 1 | Left brachiocephalic Instent stenosis | 11 | 7 |
| Patient 2 | Tight long stenotic segment in left subclavian vein | 5 | 4 |
| Patient 3 | Features of central venous hypertension but patent SVC and brachiocephalic | 12 | |
| Patient 4 | Long segment tight stenosis of left brachiocephalic and subclavian | 3 | |

**Figure. 1**
**Anatomy of the thoracic central veins (image taken from the following reference paper 2)**

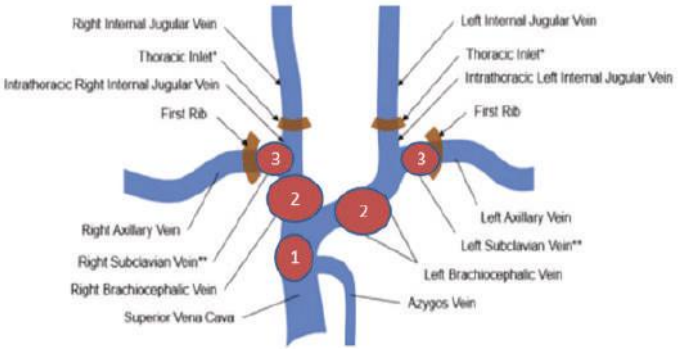



Figure 2 shows the venography and stenting images of the patient who presented with left upper limb swelling and facial puffiness. There was a chronic total occlusion of the left subclavian vein which was diagnosed by accessing the left AV fistula vein site access and the femoral access route as shown in the first two images. Post venoplasty and stenting the patient was relieved of the symptoms and good flow was reestablised.

**Figure 2**
Patient 1: Chronic Total occlusion of left subclavian vein.
Left Subclavian vein venoplasty and stenting with 12 x 60 mm self-expanding stent done.

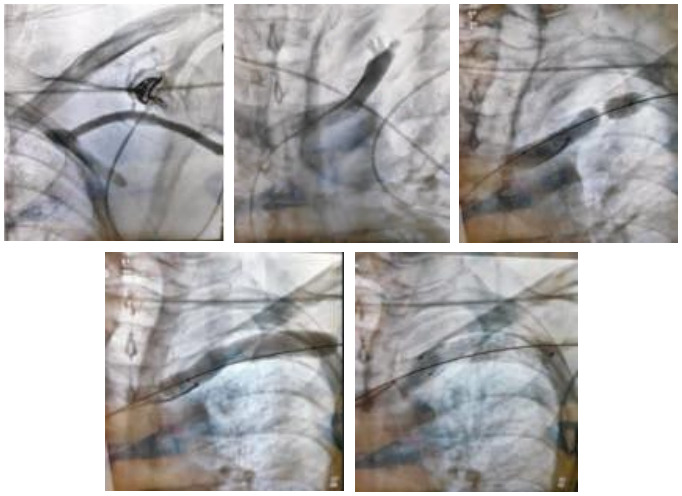
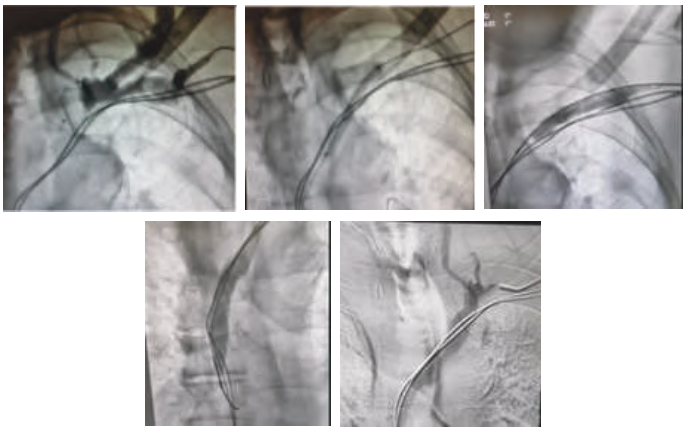


Figure 3 depicts another case where the patient presented with clinical symptoms of left upper limb swelling and facial swelling with collaterals on the chest wall. He was noted to have a long segment stenosis of the left brachiocephalic, left subclavian and Superior vena cava. He had a previous history of cardiac rhythm device placed in the left subclavian. He also required double access to cross over the lesion, through the femoral route and the left transbasilic vein route.

Post venoplasty, good improvement of flow was noted and his clinical symptoms and signs were also relieved. Patient presented again in three months' time with recurrence of symptoms. He again underwent venoplasty of the brachiocephalic, SVC and subclavian veins, following which symptoms were relieved.

**Figure 3**

Patient: 2: Long segment stenosis of the left brachiocephalic, left subclavian and Superior vena cava noted. Serial dilatation followed by venoplasty of the entire area done using 14 x 40 mm balloon. Post plasty good flow noted.



## DISCUSSION

The results of the 21 procedures shows that all of them had previous vascular access. This reiterates the fact that long term venous access [3] makes the vein more prone to narrowing and the resultant development of central venous stenosis. [4] All our patients had more than one previous vascular access. The duration of venous access which qualifies for long term definition is for > 6 weeks as per the article by Galloway et.al.

Right brachiocephalic and brachiocephalic/ SVC junction area narrowing were seen in majority of our cases. Subclavian vein stenosis was relatively rare. This could be due to the fact that most of the temporary hemodialysis catheters and permacath were inserted in the Right IJV or left IJV. This is similar to the study done by Tedla et. al, who has done a detailed mapping of the prevalence of these central venous narrowing in their chronic kidney disease patients. [5]

Cardiac rhythm devices inserted into the central veins were also noted to be an identified risk factor for the development of central venous stenosis. [5] One of our patients also had a cardiac rhythm device induced narrowing in the left subclavian vein.

Patients who underwent venoplasty with or without stenting require repeat procedures at different intervals of time. Four of our patients required repeat procedures at intervals of 3 months to 11 months. Our findings were similar to the findings of other studies. In the study done by Ozyer et. al, stenting was found to be useful in angioplasty resistant lesions though stenting had lower patency rates when compared to angioplasty alone. [6] Follow up studies done by Bakken et al, done for a period of 2 years post procedure showed patency rates to fall by half at the end of one year in patients undergoing angioplasty alone and this happened at 6 months for the group which underwent stenting. [7]

Patients who had a stent, pacemaker or a permacath in situ were noted to have lower patency rates in our study. These were also identified to be risk factors for recurrence by Tedla et al. [5]

Most of the cases of central venous stenosis can be managed by angioplasty. There are very specific indications for stenting like angioplasty resistant lesions, completely occluded lesions and rapid recurrence after angioplasty as shown in the study done by Verstandig et.al. [8] Even in our series only four patients underwent stenting.

There are concerns raised regarding accessing the AV fistula vein site for the angioplasty of the central veins. It was interesting to note that in 10 of our 21 procedures we had to convert the trans-femoral route to the AV fistula vein site route for the central venous procedure. As the area of the narrowing was commonly at the brachiocephalic and SVC junction it was usually non-negotiable through the femoral access route requiring the change in access site. We found this to be a safe option in all our patients. The possible explanation for this could be that the fistula vein access site is along the flow and this might be enabling the crossing over of the area of narrowing. This is in contrast to the femoral route access which would be against the flow and therefore the difficulty to negotiate the areas of narrowing.

Review of literature as well as our study revealed long term indwelling catheter in the central vein to be one of the risk factors for the development of central venous stenosis. We would therefore prefer the “Arteriovenous fistula first approach” for the patients presenting to us. Catheters can be reserved to bridge the gap to fistula maturation alone. Studies and vascular access guidelines also recommend “Fistula first and catheter last” approach. There is increasing awareness of the need to have multidisciplinary teams to have a “Right access for the right patient” [9] working towards a more patient centered approach to minimize these complications.

## CONCLUSION

Repeated use of Central venous catheters and long indwelling catheters make CKD patients prone to develop central venous stenosis. This can be evaluated with right investigations & treated if recognized early.

There needs to be a high index of suspicion to pick up the clinical signs of central venous stenosis. Options of central venoplasty with or without stenting can be offered to such patients for symptomatic relief. “Fistula first and catheter last” & “right access for the right patient” needs to be our goal when managing patients with chronic kidney disease requiring hemodialysis access.

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**Poems Dr. Smita Mishra**

# "सत्ता की महामारी"

सत्ता आपको बहला रही है ,
नासमझ उम्मीदों को, सहला रही है!
मालूम है उसे कि आपके सपने,
आपकी सच्चाई से ऊपर है,
जानती है वो कि, आपके अंदर ,
बसता है , एक जुआरी,
बस उसको दिखा दो ,
तीन एक्के की बाजी ,
और वो सम्मोहित सा चल देगाय
सच्चाई ईमानदारी की पोटली को,
दरकिनार रख कर ,
सदीयो के संसकारो को प्रणाम कर,
बोलने लगेगा नफरत की जबान,
फेकेंगा पथर और उछालेगा
नारा, जिससे उसका ना था वास्ता,
ना कभी होगा!
क्या कहता किसानी का समूह,
कोरोना–काल मे सड़कों पर बैठ कर?
मुद्दे कहाँ और क्या हैं, जिंदगी या मौत?
तो क्यों नहीं चीत्कार और पुकार,
उठी थी हफ्तों पहले?
क्यों नहीं किसी ने गिने थे,
अस्पताल के बिस्तर, आक्सीजन
के सलेंडेर या रेमदिसिविर की वायले?
क्यों नहीं दिखते हैं,
3 लाख मे बिकते टोसिलिजनाबय
क्यों नहीं कोई झगड़ता है,
गुणवत्ता पर , मास्क और पीपीई की!
क्या कोरोना ही है आज का ,
मोहम्मद गोरी जो चल आया है,
जयचंदो के सहारे, एक बार फिर!
दिख रहा है, नकली रेमदिसिविर
की इंदोर वाला कारखानाय
प्रदेशों की सरकारें ,
जो रोक रही है जाँचे कोरोना की,
और जो रोक रही है , इस्तेमाल,
दवाई, आक्सीजन, और,
अस्पताल के बिस्तरे का ।
ये राजनीतिक लड़ाई है,
विज्ञापनों में लड़ी जाएगी!
आपके राजनीतिज्ञ रिश्तेदार की,
सिफारिश भी आपको ,
आई सी यू बेड नहीं दिलाएगी!
इंसान का तन है, नेट की रेसिपी,
ना खाने में , ना दवाई मे,
काम आएगी!
सम्भालिये, बचिये, काल्पनिक
दुनिया के ठेकेदारों से,
राजनीति, नाटक कारों सेय
आप की दुनिया आपकी ही,
मेहनत से सँवरेगीय
नेता आपके सेवक है , शासक नहीं,
इसी समझ से जिंदगी ,
चल निकलेगी!
ये सत्ता की महामारी है,
जिसने आपको अफीम बन कर,
सहारे की आदत लगाई है,
आज अब इससे भी
उबरने की बारी आई है!

स्मिता.....,,

# COVID AND THE EYE

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## INTRODUCTION

COVID-19 pandemic has been raging throughout the world for close to a year and a half now, affecting millions of people all over the world. By and large, eyes have mercifully been spared to a large extent by the scourge involving almost every organ and organ system of the body.

## INVOLVEMENT OF THE ANTERIOR SEGMENT

The most common ophthalmic manifestation of SARS-COV-2 infection is conjunctivitis, which can present at any stage during the course of the disease. Mild conjunctivitis manifesting as conjunctival congestion is common and is one of the major ocular manifestations in COVID-19 positive patients. [1] In fact, in a few cases it may be the presenting complaint with which the patient may present to the unsuspecting Ophthalmologist. Thus, for ophthalmologists, the important consideration is that, in the current scenario, one should have a high index of suspicion for COVID-19 in patients presenting with conjunctivitis.

Ocular surface manifestations of COVID-19 can also be delayed (after a week). Immune response is considered to play a major role in the delayed development of signs, and responds well to topical steroids under antibiotic cover and lubricants.

## INVOLVEMENT OF THE POSTERIOR SEGMENT

Posterior segment involvement has varied manifestation and are actually vascular, inflammatory, and neuronal changes triggered by the viral infection but not specific to COVID-19. [2]

### Retinal Vascular Occlusions

Infection with SARS-CoV-2, the virus that causes COVID-19, is known to induce a hypercoagulable state with resulting venous thromboembolism. [3] Central retinal vein occlusion (CRVO) is commonly seen in association with a hypercoagulable state, which may contribute to the pathogenesis of retinal vein occlusion (RVO). [4] There are multiple case reports from different parts of the world, including India where patients have presented with features of Central retinal Vein Occlusion in the post-COVID period. Clinical picture varies from mild to severe, with corresponding visual loss. The treatment is in the form of Intravitreal Anti-VEGF injections in case of CRVO with significant macular edema.

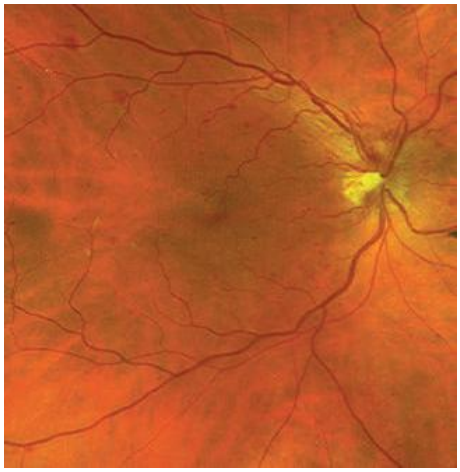

**Fig. 1**
Mild CRVO. Magnified view of the macula shows disc edema, scattered dot and blot hemorrhages, and cotton-wool spots.

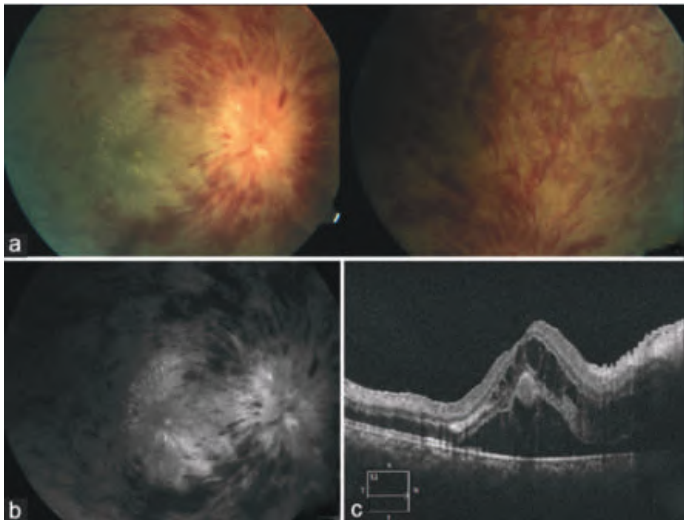


**Fig. 2**
CRVO. a) Color and (b) red-free fundus images of OD showing optic disc edema and multiple hemorrhages in all quadrants with a macular star. (c) Optical coherence tomography scan of macula shows neurosensory detachment and cystoid macular edema. [5]

Other retinal vascular diseases reported include Central Retinal Artery Occlusion (CRAO), [6] Acute macular neuroretinopathy (AMN), [7] paracentral acute middle maculopathy (PAMM). [8] While CRAO presents with severe loss of vision, AMN and PAMM usually present with scotomas and some loss of visual acuity.

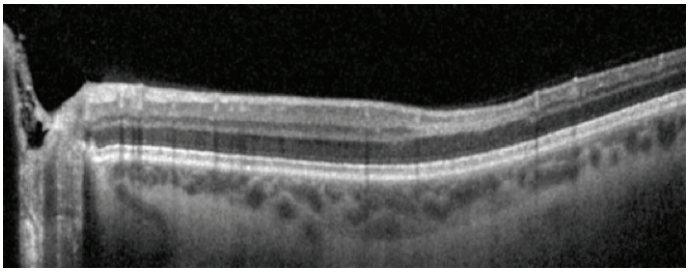

**Fig. 3**
Focal area of hyper-reflective change in the inner and outer plexiform layers with inner nuclear layer volume loss consistent with paracentral acute middle maculopathy. [8]

**Other retinal findings seen in patients with COVID-19**

Pereira et al., from Brazil, reported retinal findings in patients admitted with severe COVID-19. The findings included peripheral retinal hemorrhages, macular hyperpigmentation, retinal sectoral pallor, peripapillary flame-shaped hemorrhages, hard exudates, and cotton wool spots. All the patients were on prophylactic or full intensity anticoagulants to counter the prothrombotic condition in severe cases of COVID-19. But the superadded or primary effect of pre-existing comorbidities, ICU admission, and vasoactive drug support was not taken into account. The retinal findings, thus, cannot be solely attributed to the viral infection. [9]

## NEURO-OPHTHALMIC MANIFESTATIONS OF COVID-19

Neuro-ophthalmic manifestations are not common and at present, there are only isolated case reports which have been published. The neuro-ophthalmic manifestations include optic neuritis, [10] papillophlebitis,[11] Adie's tonic pupil, [12] acute hypokinetic rigid syndrome with transient opsoclonus, [13] Miller Fisher Syndrome (MFS) and cranial nerve palsy, [14] neurogenic ptosis, [15] and CVA with vision loss. [16]

## ORBITAL MANIFESTATIONS OF COVID-19

Rhino-Orbital-Cerebral Mucormycosis (ROCM) is a devastating complication emerging in COVID treated patients, especially those with diabetes mellitus, who were on treatment with corticosteroid therapy for COVID. The increasing incidence of ROCM in the setting of COVID-19 in India and elsewhere has become a matter of immediate concern. [17]

The COVID-19 care teams must be aware of the warning symptoms and signs of ROCM. If a patient currently under active treatment for COVID-19 or on follow-up after completion of treatment exhibits any of the symptoms and signs listed in **Table 1**, there should be a very high index of suspicion for ROCM, and an immediate ophthalmology and otorhinolaryngology consultation is warranted. [18]

- Nasal stuffiness
- Foul smell
- Epistaxis
- Nasal discharge - mucoid, purulent, blood-tinged or black
- Nasal mucosal erythema, inflammation, purple or blue discoloration, white ulcer, ischemia, or eschar
- Eyelid, periocular or facial edema
- Eyelid, periocular, facial discoloration
- Regional pain – orbit, paranasal sinus or dental pain
- Facial pain
- Worsening headache
- Proptosis
- Sudden loss of vision
- Facial paresthesia, anesthesia
- Sudden ptosis
- Ocular motility restriction, diplopia
- Facial palsy
- Fever, altered sensorium, paralysis, focal seizures



**Table 1**
Warning Symptoms and Signs of Rhino-orbito-cerebral Mucormycosis

A rapid and cohesive team effort by the various specialities is needed to quickly diagnose and manage the disease. Diagnostics (radiology, pathology, microbiology), Medical specialities (Internal Medicine, Pulmonology, Neurology, Infectious disease, Critical Care) and Surgical Specialities (Otorhinolaryngology, Ophthalmology and Neurosurgery) need to be on the alert for the early diagnosis and prompt management.

Following management protocol **(Fig. 4)** has been suggested by Honavar S. based on disease severity. [19]

Other orbital manifestations which have been reported include acute dacryoadenitis, [20] orbital pain, [21] orbital cellulitis. [22]

## CONCLUSION

Ocular manifestations my present at different times during the course of COVID-19 infection. A timeline of same has been depicted in Fig. 5. [2] Whether the manifestations listed are actually due to the SARS-CoV-2 virus, or due to the immune response of the body is yet to be determined. Large scale population based studies with appropriate standardizations are needed to further establish the myriad manifestations of COVID-19 in the eye.

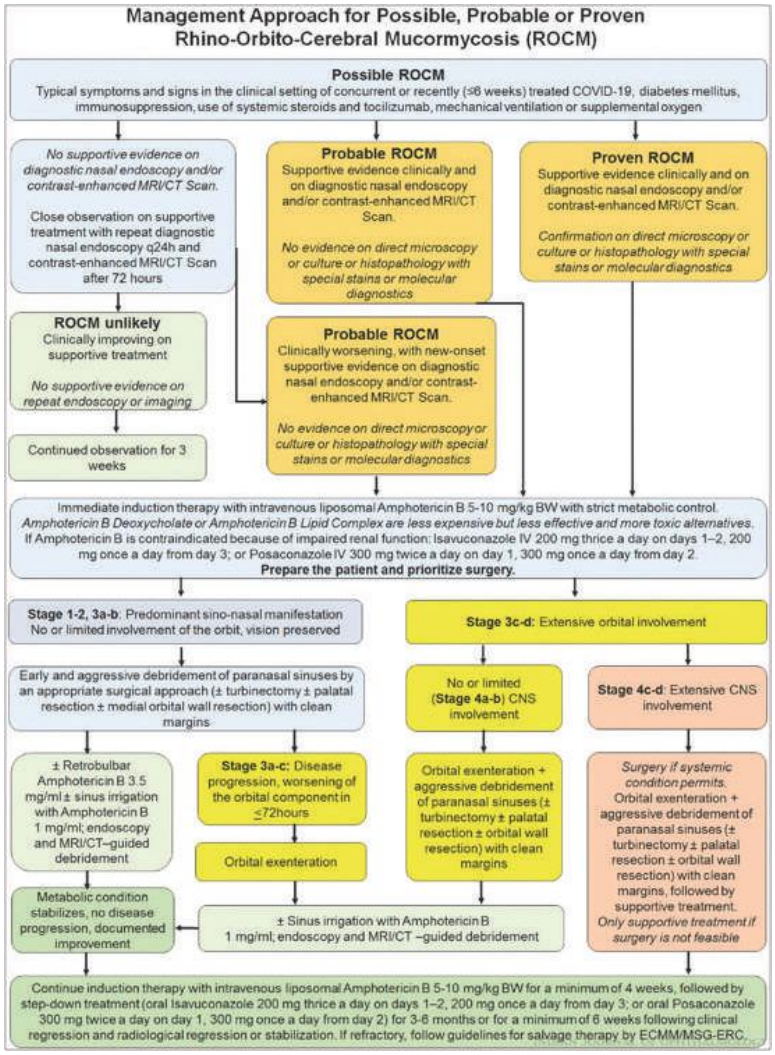


**Fig. 4**
Management algorithm for Rhino-Orbito-Cerebral Mucormycosis (ROCM)

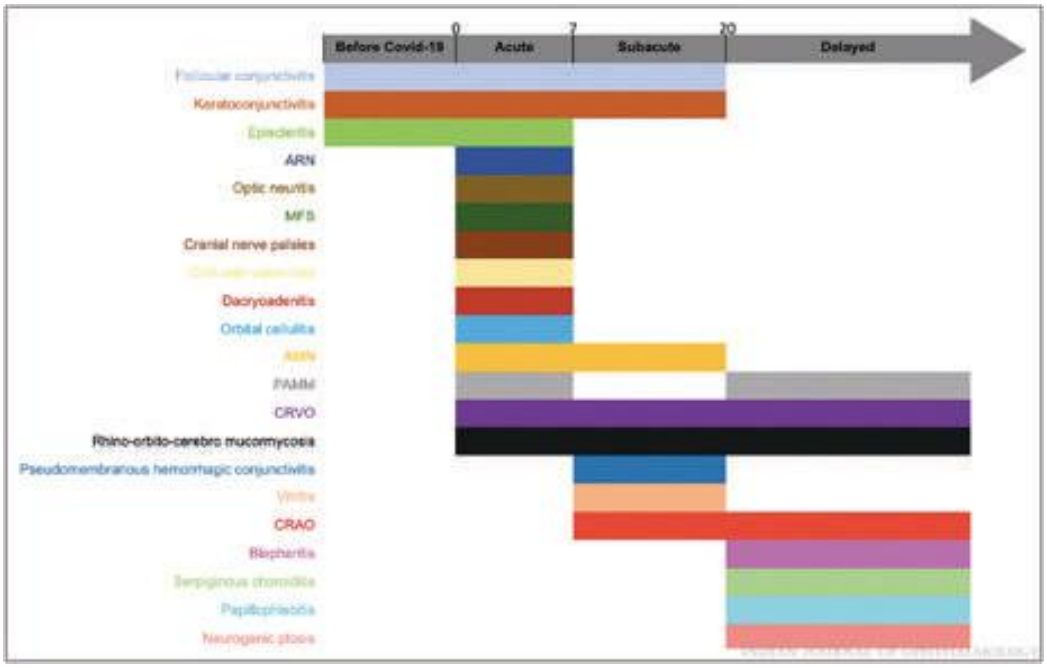


**Fig. 5**
A broad timeline of the different ophthalmic manifestations of COVID-19. They can be divided into those which present with ocular symptoms initially (before COVID-19), within the first week of infection (Acute, Day 0-day 7), between the second and third week since the onset of COVID-19 symptoms (Subacute, day 7-day 20) and those which present as late sequelae of the infection (Delayed, after 20 days) [2]

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# DIAGNOSTIC DILEMMAS IN HYDROPS FETALIS

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## Case history

A 33 year old second gravida was referred for routine obstetric sonography. There was no history of malformation, recurrent abortions, hematological or genetic disorder in the family. On ultrasound the fetus was found to have increased nuchal translucency, bilateral cystic hygroma, omphalocoele and features of hydrops **(Fig 1 & 2)**. Fetal prognosis and possibilities of chromosomal disorder, single gene disorder, malformation, and infection were explained to the woman. Chorionic villous sampling to know the karyotype of the fetus was suggested which was refused by the patient. NIPT (Non-invasive Prenatal Test) was done which was high risk for Trisomy 18. Due to her religious beliefs she was committed to the pregnancy. She was again seen at 16 weeks which showed hydrops fetalis. One week later she again came with pain abdomen and ultrasound was suggestive of intrauterine fetal death. Labour was induced and products of conception (POCs) were sent for microarray testing which confirmed Trisomy 18. A final diagnosis of Trisomy 18 (Edward Syndrome) was made and counselling was done to explain the recurrence risks and need for follow up in the next pregnancy

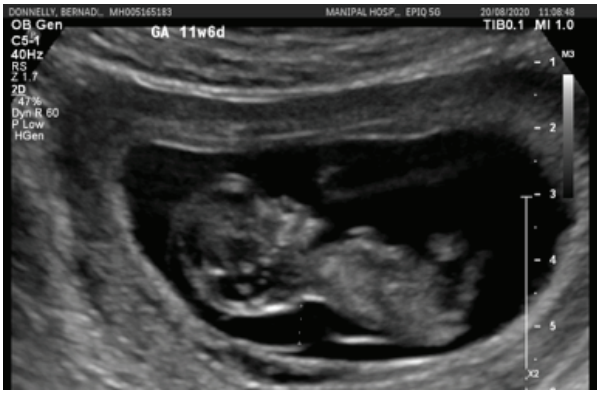



**Fig. 1**
Hydrops in the Fetus

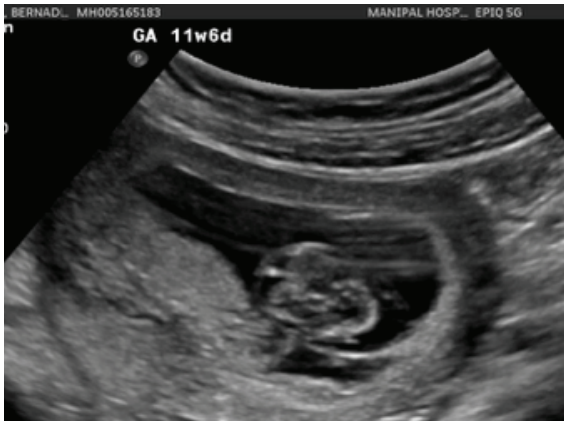



**Fig. 2**
Cystic Hygroma

**INTERPRETATION**

The cytogenomic microarray analysis showed a gain involving all markers of chromosome 18 (**77.9 Mb**), indicating trisomy for this chromosome. Trisomy 18 (Edwards syndrome) is characterized by intrauterine growth retardation and a low birth weight. Affected individuals may have heart defects and abnormalities of other organs that develop before birth. Clinical correlation is indicated.

**Note:** Maternal Cell Contamination test result: "Negative".

**Test result of most common anomalies**

| CONTENTS | RESULT |
|---|---|
| **Autosomal Aneuploidies** | |
| Trisomy 21 (Down syndrome) | Negative |
| Trisomy 18 (Edwards syndrome) | Positive |
| Trisomy 13 (Patau syndrome) | Negative |
| Other autosomal aneuploidies | Negative |
| **Sex Chromosome Aneuploidies** | |
| Monosomy X (Turner syndrome) | Negative |
| XYY (Jacobs syndrome) | Negative |
| XXY (Klinefelter syndrome) | Negative |
| XXX (Triple X syndrome) | Negative |
| **Triploidy** | Negative |
| **Clinically significant Genome-wide copy number variations** | |
| Gains | Negative |

**Fig. 3**
Microarray report of POC suggesting Trisomy 18

## DISCUSSION

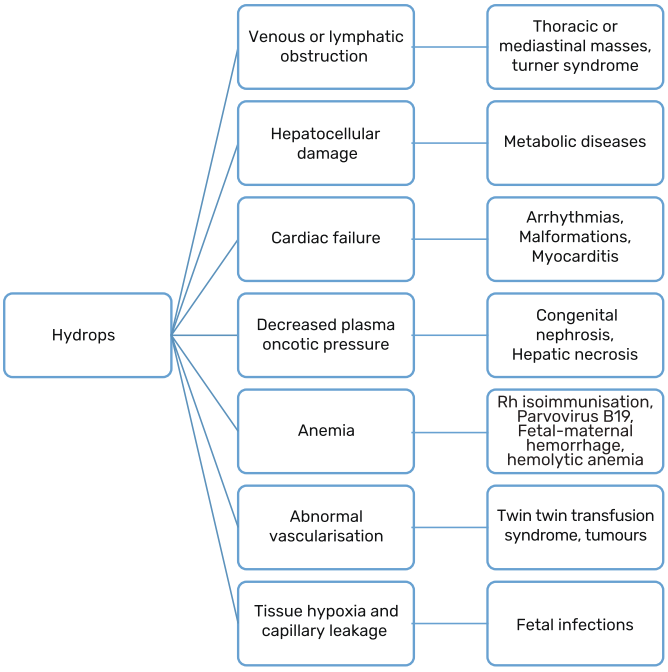
Hydrops fetalis occurs when there is abnormal fluid accumulation in at least two body cavities or in the soft tissues of the fetus. It is classified as immune if it occurs secondary to maternal allo-immunization to red cell antigen and non-immune if it occurs due to other causes. The incidence of non-immune hydrops fetalis is estimated to be approximately 1 in 3000 pregnancies. [1,2]

### Etiology of hydrops fetalis

Immune hydrops occurs due to circulating antibodies against red blood cells in the mother. It is most commonly due to Rh-D disease. Hydropic fetus represents the end stage in the disease process and is associated with worse prognosis than if hydrops is absent.

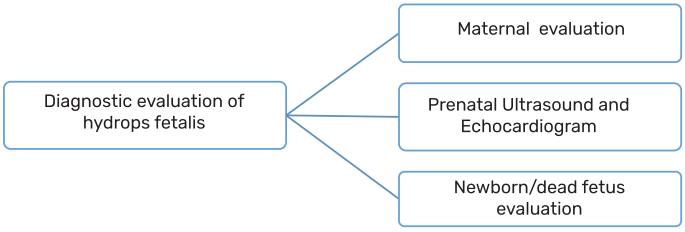
There are over 120 etiologies related to the causation of non-immune hydrops. These can be broadly classified as Cardiovascular disorders (most frequent), Chromosome abnormalities (second most frequent), Recognizable syndromes, Hematologic disorders, Twin pregnancy, Metabolic diseases, [3] Structural malformations like Thoracic, Genitourinary, Gastrointestinal and hepatic anomalies, Neurological abnormalities, Certain Maternal diseases, Placental and cord abnormalities, Intrauterine infections. Despite this exhaustive list around 22% of all cases remain idiopathic.

### Pathophysiology of hydrops fetalis [4]




**Prenatal evaluation of a case of Non-immune hydrops**

Systematic prenatal evaluation is important not only for the management of the current pregnancy but also for future genetic counselling




- Prenatal Ultrasound Evaluation

| | |
|---|---|
| Detailed ultrasound | 1. Distribution of fluid collection may give a clue to the etiology |
| | 2. Ultrasound markers of aneuploidy suggest a cause |
| | 3. Degree of polyhydramnios and cervix assessment to exclude risk of premature rupture of the membranes or preterm labor |
| | 4. Systematic fetal anatomy assessment |
| | 5. Fetal bladder visualization to exclude urinary ascites |
| | 6. Bone length, curvature, density, and presence or absence of fractures to exclude skeletal dysplasia |
| | 7. Stigmata of congenital infection like microcephaly or intracranial calcifications |
| Fetal Echocardi-ograhy | Structural and functional assessment of fetal heart to evaluate structure, rhythm, and function |
| Colour doppler study | MCA PSV velocity to detect fetal anemia<br>Umbilical vessel indices, venous Doppler should be included |
| Amniocentesis | For FISH and Karyotype, Microarray, PCR for viral antigens, cultures for syphilis, CMV, toxoplasmosis wherever relevant, AFP levels, Metabolic testing (whenever relevant) |
| Fetal blood sampling | For rapid karyotype, complete blood count, platelets, blood group, coomb test, electrophoresis, viral IgM, PCR, G6PD and metabolic testing(whenever relevant) |

- Maternal evaluation

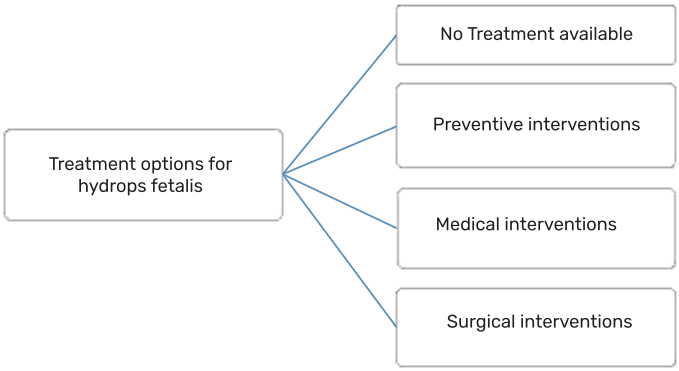
| | |
|---|---|
| Medical history | Diabetes, Hypertension, Anemia, SLE, Thyroid disorder, h/o any drug intake |
| Obstetric history | H/o consanguity, abortions, recurrent hydrops, Twin pregnancy, fever with rash, Severe Preeclampsia, Diabetes |
| Blood tests | 1. Blood group and Indirect coombs test |
| | 2. CBC and indices |
| | 3. HPLC |
| | 4. Kleihauer-Betke count |
| | 5. Blood sugar |
| | 6. Blood chemistry for red cell enzymes deficiency (G6PD, pyruvate kinase) carrier |
| | 7. Infection screening (VDRL, TORCH IgM, IgG, Parvo virus, GroupB sterptococcus, Listeria |
| | 8. Autoantibody screen for SLE, Anti Ro-Anti-La Antibodies |

C. Evaluation of newborn/dead fetus with hydrops

| | |
|---|---|
| Cardiovascular evaluation | Echo, ECG |
| Chest evaluation | Chest- X ray chest, pleural fluid examination |
| Blood indices | CBC, DLC, Platelet count, Blood group, Coombs test, Peripheral smear, HPLC |
| Gastroinestinal evaluation | X ray and USG abdomen, LFT, peritoneal fluid examination |
| Renal evaluation | Urine examination, KFT |
| Genetic tests | Karyotype, Microarray, Skeletal Xray |

| | |
|---|---|
| Infections | Specific IgM and IgG testing for parvo virus, syphilis, CMV, Toxo, HSV, Rubella |
| Autopsy | Including placental examination |

**Treatment Options for Non immune hydrops**




| Prenatal interventions | Medical interventions | Surgical interventions |
|---|---|---|
| 1. Thalassemia screening of parents by CBC, HPLC | 1. Anti-arrhythmic drugs (transplacental digoxin, flecanide for tachyarrythmia, Betamimetics for bradyarrythmia | 1. Intrauterine transfusion for RH isoimmunised pregnancy, Parvovirus induced fetal anemia, Feto-maternal hemorrhage |
| 2. Genetic counselling for Autosomal recessive and dominant disorders | 2. Penicillin therapy for Syphilis | 2. Pleurocentesis for pleural fluid drainage to prevent pulmonary hypoplasia |
| | 3. Antiviral drugs (Acyclovir for HSV, gancyclovir for CMV) | 3. Laser coagulation of feeding vessel in pulmonary Sequesteration, Sacrococcygeal teratoma, Chorangioma |
| | 4. Spiramycin for toxoplasmosis | 4. Thoraco-amniotic Shunt placement in macrocystic CCAM, pulmonary cyst, pleural effusion |
| | | 5. Serial Amnioreduction or endoscopic laser coagulation of communicating placental vessels in Twin twin transfusion syndrome |
| | | 6. Open fetal surgery in sacrococcygeal teratoma, solid lesion of chest |

**Recurrence Risk**

| | |
|---|---|
| Fetal defects, infections, Sporadic cases | No increased risk |
| Autosomal recessive (e.g. metabolic disorders) | 25% risk in every pregnancy |
| Autosomal dominant disorders | Not increased unless one of the parent is a carrier (50% risk of recurrence) |
| Chromosomal defects | risk is increased especially if one of the parent is a translocation carrier |
| RH isoimmunised pregnancy | Increased risk with each subsequent pregnancy |

## SUMMARY

Etiology of the Hydrops defines the ultimate outcome. In a proportion of cases, cause remains unidentified. Fetuses with pleural effusion are associated with poorer outcome owing to lung compression and pulmonary hypoplasia. Conditions which are amenable to medical or surgical therapies have markedly improved prognosis. Majority of other cases have guarded prognosis because of no effective treatment.

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# ONCOLOGICAL APPLICATIONS OF 18F-FLUORODOPA PET/CT: A BRIEF REVIEW

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## INTRODUCTION

18F-FluoroDOPA PET has been utilised since the 1980s for evaluation of the nigro-striatal pathway in patients with Parkinson's disease and other movement disorders. 18F-FluoroDOPA is an analog of L-DOPA which is the precursor of dopamine. Subsequently, this novel radiotracer allows the imaging of the dopaminergic metabolic pathway in various neuroendocrine origin tumours in the human body. In addition, structural homology with precursor amino acids allows 18F-FluoroDOPA to be transported through the L type neutral amino acid transporter and thus be used as an amino acid imaging radiotracer in imaging other malignancies such as gliomas. [1]

Over the past decade, clinical evidence of 18F-FluoroDOPA PET/CT utility in various cancers has been generated. Studies have predominantly concentrated upon and have found utility for FluoroDOPA PET/CT in the following oncological indications:

### A. Pheochromocytomas and paragangliomas

Pheochromocytomas and paragangliomas are histologically similar tumours arising from adrenal medulla and autonomic ganglia present in the body. These tumours are often benign, but frequently tend to be symptomatic secondary to hormonal secretion or due to mass effect. This usually requires definitive treatment in the form of surgery. Imaging thus plays a crucial role in diagnosis, localization and staging (in case of malignant) of these tumours.

Functional imaging secondary to its high specificity can provide additional information over conventional imaging for differentiation of these tumours from other differentials and for evaluation of disease extent. Molecular imaging radiotracers such as 123I-MIBG and 68Ga-somatostatin receptor (SSTR) targeting peptides such as Ga-68 labeled DOTANOC and DOTATATE have reported good sensitivities for the same. [2,3]

On evaluation, high sensitivity in excess of 90% with very high specificities has also been reported for localization using FluoroDOPA PET/CT, predominantly in Pheochromocytoma and Thoraco-abdominal paragangliomas. Studies have also reported significant outperformance by FluoroDOPA PET/CT compared to 123I-MIBG and marginal outperformance of 68Ga-SSTR peptide based PET/CT. [4-6] Therefore FluoroDOPA PET/CT when available is considered as a first choice investigation for pheochomocytomas and thoraco-abdominal paragangliomas, with the exception of SDHB mutation associated tumors. Higher false negative rates using FluoroDOPA in SDHB mutation patients has led for preference of FDG PET/CT in the same. [7]

Similarly, good detection rates for head & neck paragangliomas have also been reported. However, detection rates are lower in comparison to 68Ga-SSTR peptides, but nonetheless superior to conventional imaging. [6] This has been ascribed to the differing origins of thoraco-abdominal (sympathetic ganglia) versus head and neck (parasympathetic ganglia) paragangliomas. In addition, a correlation between detection rate and SDH mutation status has also been found in patients. [6,8,9]

### B. Well-differentiated neuroendocrine tumours

Neuroendocrine tumour (NET) includes both pancreatic neuroendocrine tumours (pNETs/PETs) and NETs in other locations, including gastrointestinal NETs (GI-NETs) (carcinoids) and bronchial NET's.

NETs present many unique problems in their management, because they differ from adenocarcinomas in their pathogenesis, diagnosis, clinical presentations, and treatment approaches despite histological similarities.

In regards to PET molecular imaging, well-differentiated neuroendocrine neoplasms are usually slow-growing and usually non-FDG avid. This requires the utilisation of other radiotracers for the localisation and staging. Prominent radiotracers used for this indication include somatostatin receptor targeted agents (68Ga-SSTR peptides) and 123I-MIBG among others. [10,11]

Use of FluoroDOPA PET/CT in various studies such as those by Haug et. al. (12) and Ansquer et. al. (13) report varying sensitivities for the same in this indication. This can be accounted for by the relatively lower sensitivity of 18F-FluoroDOPA PET/CT in neuroendocrine neoplasms of foregut and hindgut origin. In tumours arising from the midgut, 18F-FluoroDOPA PET/CT has been reported to be marginally superior to somatostatin receptor targeted (SSTR) PET/CT.

Therefore the guidelines suggest use of 18F-FluoroDOPA PET/CT in patients with midgut origin neuroendocrine neoplasms. [7]

In addition, certain neuroendocrine histologies such as insulinomas are frequently non-localized on 68Ga-SSTR peptide imaging. 18F-FluoroDOPA PET/CT has been found to be very useful for localization of insulinomas by the same and is a useful alternate investigation.

Similarly, use of FluoroDOPA PET/CT in pediatric patients with congenital hyperinsulinism for differentiation between focal and diffuse histology has been validated. FluoroDOPA PET/CT is considered the preferred imaging modality for the same. [7,14].

### C. Neuroblastoma

Neuroblastoma is the most common extra-cranial solid malignancy in children. Almost half of the patients may present with metastasis at presentation. In the past decades, MIBG (123I-meta-Iodobenzylguanidine) scan has emerged as the standard nuclear medicine investigation used in neuroblastoma.

In this malignancy however, recent clinical evidence suggests that 18F-FluoroDOPA PET/CT might offer improved sensitivity and disease localisation compared to MIBG scans. [15] Data for this use is a relatively limited but whatever data is present is very encouraging with regards to the use of18F-FluoroDOPA PET/CT in neuroblastoma. Further generation of data documenting utility in improving staging, treatment response and prognostication may further lead to improved outcomes for patients.

A reference case is shown in Figure 1 showing utility of FDOPA PET CT scan in Neuroblastoma.

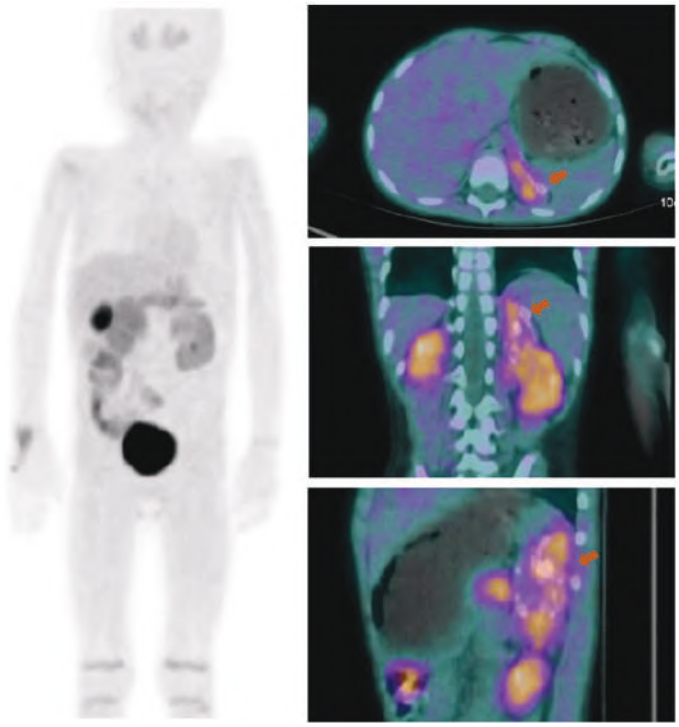

**Figure 1**
Patient with neuroblastoma, with metabolically active recurrence (arrow) visualized on 18F-FluoroDOPA PET/CT images.

### D. Medullary carcinoma thyroid

Molecular imaging of the various subtypes of thyroid cancer is predicated by the underlying histology. Differentiated (papillary and follicular) thyroid cancers are predominantly imaged using radioiodine and FDG PET/CT. However, owing to the neuroendocrine origins of medullary thyroid cancer, imaging using FluoroDOPA and 68Ga- SSTR peptide PET/CT has also been studied. These studies have reported good sensitivity rates upto 80% for FluoroDOPA PET/CT with high specificity (16). Further analysis has reported improved yield from FluoroDOPA PET/CT when selection of patients with predominant calcitonin secretion and with calcitonin doubling times < 24 months. [17,18] Conversely, patients with predominant CEA secretion may benefit more from FDG PET/CT imaging.

A reference case is shown in Figure 2 showing utility of FDOPA PET CT scan in treatment response evaluation in medullary carcinoma thyroid.

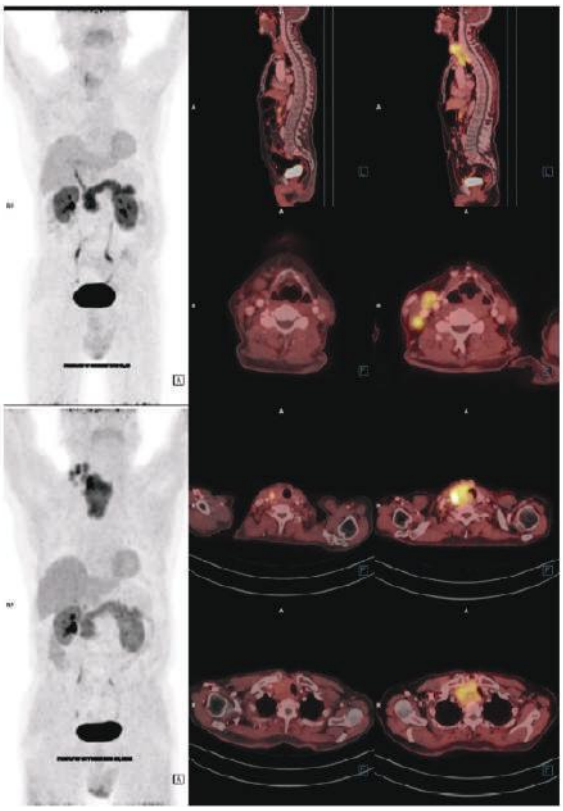

**Figure 2**
Partial response in a patient with medullary carcinoma thyroid on Lenvatinib evaluated using 18F-FluoroDOPA PET/CT imaging.

### E. Gliomas

Contrast enhanced MRI is currently the standard of care for imaging of gliomas. However, it is not without its own limitations. Evaluating disease extent of non-enhancing gliomas and imaging of post-treatment (surgery or radiotherapy) patients can be challenging.

18F-FluoroDOPA PET/CT has also been found useful in these situations. At a molecular level, uptake of FluoroDOPA in gliomas occurs secondary to the transport of 18F-FluoroDOPA through the L- type neutral amino acid transporter. Thus, for the imaging of gliomas 18F-FluoroDOPA PET/CT can be considered form of amino acid imaging and does not require disruption of blood-brain barrier.

Imaging with FluoroDOPA PET has been found useful in evaluation of disease extent for surgical and radiotherapy planning (19,20). However, it is with regards to evaluation of post-treatment recurrence where 18F-FluoroDOPA PET/CT really shows very high sensitivity and specificity with consistent outperformance of contrast enhanced MRI imaging. [21] Studies have reported as many as 33% of patients may have change in management in this setting secondary to the use of 18F-FluoroDOPA PET/CT. In addition, recent data suggests improvement in radiotherapy outcomes if planning is done based on FluoroDOPA PET imaging. [22]

Giving credence to its utility, RANO (Response assessment in neuro-oncology criteria) working group guidelines also advocate its use as a tool for initial diagnosis, disease extent, response evaluation and in suspected recurrence of gliomas.

## CONCLUSION

F-18 Fluorodopa PET CT is an excellent imaging modality for the evaluation of neuro-endocrine tumours and gliomas in specific clinical settings as described above. With its recent commercial availability, it is expected that this imaging modality will see far-wider oncological application in the coming decade.

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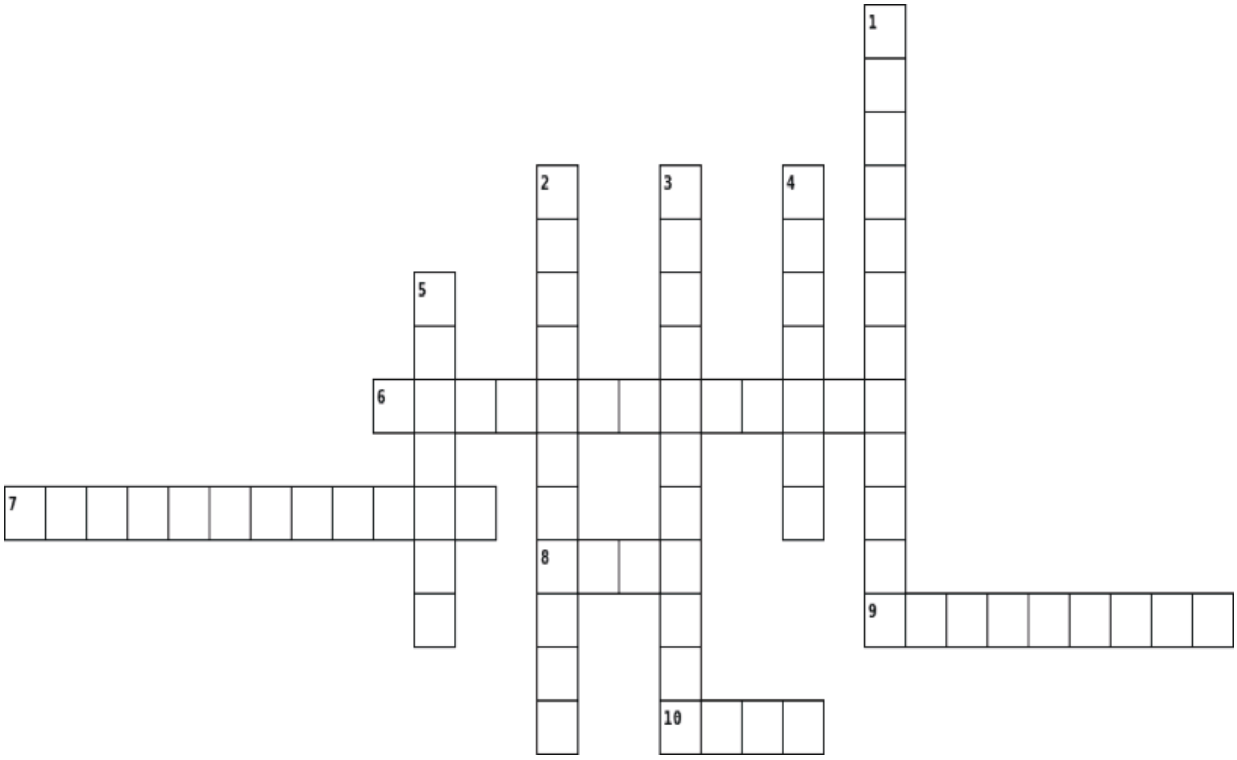
# CROSSWORD

## DID YOU READ THE JOURNAL SCAN: LET'S SEE !

**Dr Peush Bajpai, Medical Oncology**




**Across**

| | |
|---|---|
| 6. | The **Lambda variant** of this drug accelerated viral decline in outpatients with COVID-19 |
| 7. | This **Fluoroquinolone** if used with Rifapnetine and other ATT drugs cut down treatment for pulmonary Tuberculosis to **4 months**. |
| 8. | In this trial, **Voxelotor** was associated with an increment in Hb levels and lesser complications in sickle cell anemia. |
| 9. | This helps in postoperative small bowel obstruction. |
| 10. | This mutation is common in hairy cell leukemia |

**Down**

| | |
|---|---|
| 1. | Route of administering TEZEPELUMAB therapy in severe uncontrolled asthma. |
| 2. | These cells (differential cell counts) were monitored during Tezepelumab therapy |
| 3. | This drug was recently used in a phase 2 trial of Hairy cell leukemia with Rituximab and gave encouraging results. |
| 4. | This drug was non-inferior to vitamin K antagonists in the treatment of cervical artery dissection. |
| 5. | This is a major risk factor for adverse outcomes after infection with SARS-CoV-2 |

# RADIATION THERAPY AND ITS ROLE IN MANAGING BENIGN DISEASES

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## INTRODUCTION

Radiation therapy (RT) uses high energy x-rays or gamma rays to damage DNA of cells via direct or indirect mechanisms. [1] While radiation is primarily used for treatment of malignant tumors, there are also a considerable number of benign tumors and non-neoplastic diseases for which RT is a potential treatment option. [2] Probably the first benign disease to be successfully treated using radiation was a hairy mole. The year was 1897 and this eventually led to use of x-rays in treating many other benign diseases. This article aims to highlight the mechanism of action of radiation, various indications of radiation in benign conditions, dose of radiation used and toxicities.

## MATERIAL & METHODS

Two basic hypothetical mechanisms are exploited while treating benign disease with RT. First is the anti-proliferative effect of RT. [3-5] This effect is duly used to reduce the risk of heterotopic ossification after hip replacement or recurrence of pigmented villonodular synovitis (PVNS) following synovectomy. Second is the anti-inflammatory effect which can be used in several inflammatory conditions like thyroid eye disease. [6] Other mechanisms include cellular gene and protein expression (eczema), inhibition of fibroblast proliferation (keloids), inhibition of inflammation in lymphocytes (pseudo tumor orbit).

The RT doses used for treating most benign conditions are well below the range used to treat cancer. For example, a so-called 'anti-inflammatory dose' of RT is around 20 Gray (Gy) in ten fractions and acute toxicity usually is not a problem at these low dose levels.

Rationale for RT in benign conditions include:

1. To control invasive and aggressive growth (desmoids)
2. To avoid cosmetic disfiguration and functional loss (keloids)
3. Use in potentially life threatening complications (juvenile angiofibroma of face, AV malformations)
4. Use in Non-malignant diseases causing pain or other serious symptoms when other modalities of treatment have failed or may induce more side effects.

**Table-1**
Summary of Dose-Fractionation Schedules in various Benign Conditions [7-9]

| Site | Disease | Dose | Fractions | Toxicity |
|---|---|---|---|---|
| Head and Neck | Paraganglioma | 45 Gy<br>12-20 Gy | 25<br>1 | RIC in brain, SNHL |
| | Juvenile nasopharyngeal angiofibroma | 30-45 Gy | 5-10 | Cataract, xerostomia, hypopituitarism, RIC |
| | Pleomorphic adenoma | 50-60 Gy | 25-30 | RIC |
| | Sialorrhea | 20 Gy<br>10 Gy<br>7.5 Gy | 4<br>2<br>2 | RIC (hence not an advisable option in children) |
| Eye | Thyroid eye disease | 20 Gy<br>10 Gy | 10<br>10 | Retinopathy (hence contraindicated in diabetes & hypertension), cataract, RIC |
| | Orbital pseudo tumor | 20 Gy | 10 | Cataract, RIC |
| | Pterygium | 20 Gy<br>10 Gy<br>35 Gy<br>30-35 Gy | 1<br>2<br>5-7<br>1 | Scleromalacia, lid adhesion, cataract, rarely scleral ulcer |
| | Macular degeneration | 24 Gy | 4-5 | Cataract, RIC |
| | Choroidal hemangioma | 20 Gy | 1-2 | Cataract, RIC |
| Central Nervous System | Meningioma (WHO grade I) | 50-55 Gy (EBRT)<br>14-15 Gy (SRS) | 25-30<br>1 | RIC |

| | | | | |
|---|---|---|---|---|
| | Cerebral AV malformations | 16-20 Gy | 1 | Radiation necrosis, hemorrhage, RIC |
| | Trigeminal neuralgia | 70-90 Gy | 1 | RIC |
| | Vestibular schwannoma | 45-56 Gy<br>12-14 Gy (SRS)<br>25 Gy (FSRT)<br>30 Gy (FSRT) | 25-30<br>1<br>5<br>3 | RIC |
| | Chordoma | 65-70 Gy (IMRT)<br>15-40 Gy (SRT) | 33-35<br>1-8 | - |
| | Pituitary adenoma | 45-50 Gy (non-functioning adenoma)<br>50.4-54 Gy (ACTH, GH secreting)<br>20 Gy- SRS (Prolactinoma) | 20-25<br>28-30<br>1 | RIC |
| | Craniopharyngioma | 54 Gy<br>18 Gy (FSRT) | 28-30<br>3 | RIC |
| Musculo-skeletal | Dupuytren's disease of hand | 30 Gy (in two phases of 15 Gy each)<br>21 Gy | 10<br>7 | RIC (skin cancer), anhidrosis, skin athropy |
| | Heterotopic ossification of hip | 7 Gy | 1 | RIC |
| | Plantar fibromatosis | 30 Gy (in two phases of 15 Gy each) | 10 | Dryness, RIC (skin cancer) |
| | Plantar fasciitis | 3-6 Gy | 6 | Dryness, RIC |
| | Peyronie's disease | 9-30 Gy | 4-5 | - |
| | PVNS | 35-40 Gy | 15-20 | - |
| | Vertebral hemangioma | 36-40 Gy | 18-20 | - |
| | Aneurysmal bone cyst | 30 Gy | 15 | - |
| Skin/Soft tissues | Keloid scarring | 5-10 Gy<br>12 Gy | 1<br>3 | RIC, site specific side effects |
| | Langerhans cell histiocytosis | 5-10 Gy (child)<br>6-15 Gy (adult) | 2-5<br>3-6 | - |
| | Lentigo maligna | 45 Gy<br>50 Gy | 10<br>15 | RIC |
| | Hidradenitis suppurativa | 10 Gy | 6-7 | - |
| | Psoriasis | 6-8 Gy | 3-8 | - |
| | Chronic eczema | 4-5 Gy | 4-5 | - |
| | Gynecomastia induced by endocrine therapy used in treatment of prostate cancer | 10-12 Gy | 1 | RIC |
| | Desmoid tumor | 50-55 Gy (PORT)<br>60-65 Gy (Gross disease) | 20-30<br>30-33 | - |
| Functional disorders | Temporal lobe epilepsy (intractable) | 24-25 Gy | 1 | - |

RT- Radiation therapy, PVNS- Pigmented villonodular synovitis, Gy- Gray, AV- Arteriovenous, RIC- Radiation induced cancers, SNHL- Sensorineural hearing loss, EBRT- External beam radiation therapy, IMRT- Intensity modulated radiation therapy, SRS- Stereotactic radiosurgery, FSRT- Fractionated stereotactic radiotherapy

Radiation induced cancers have been a matter of concern in the past, especially in the context of benign diseases. With the advent of new radiation technology such as intensity modulated radiotherapy and image guided radiotherapy, the precision of radiation has much improved and consequently, the risk of radiation induced malignancies has come down dramatically.

## CONCLUSION

To summarize, there are many benign conditions where radiation therapy is actively utilized. For some of the benign conditions, the role and usefulness of radiotherapy has declined, likely due to increased availability of alternative medical therapies, advancements in surgeries, and concerns about the very small but potential risk of radiation-induced cancers. All clinicians need to be aware of these conditions, so that timely intervention by a radiation oncologist can be done.

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**Physician Assistant exam cleared by Shelbin, Shalini and Nikhil (Degrees awaited)**

# MULTIDISCIPLINARY APPROACH IN CLINICAL MANAGEMENT OF SARS CoV2 - ROLE OF PHYSIOTHERAPY

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## ABSTRACT

The breakneck spread of Covid 19 (SARS CoV-2) disease has created an unprecedented public health crisis across the globe. Involvement of respiratory system during the acute stage of infection, especially with the onset of adult respiratory distress syndrome (ARDS) requires admission to critical care settings. Physiotherapy intervention comprising physical and pulmonary rehabilitation program is a crucial component for Covid 19 patients in facilitating functional recovery and providing pulmonary care which must be a part of multidisciplinary approaches in acute as well as later care keeping in mind the sequelae resulting in dysfunctions post discharge. The aim of this review is to gain insights on the role of physiotherapy in multidisciplinary care during and after the hospital stay by applying various pulmonary and physical rehabilitation interventions. However considering multidisciplinary approaches in clinical practice, role of physiotherapy cannot be overlooked to accomplish respiratory function and exercise tolerance during and after Hospitalization.

## INTRODUCTION:

Millions of people are infected globally with the severe acute respiratory distress syndrome caused by coronavirus2, which is better known as Covid 19 (SARS-CoV-2) disease. In the second wave of Covid 19 (SARS-CoV-2) pandemic in India most of the patients have been admitted in hospitals for acute care ranging from moderate to severe respiratory symptoms. It is very likely that the patients who are infected with SARS-CoV2 requiring supplemental oxygen, NIV (Non-invasive ventilation) or MV (Mechanical Ventilation), may have difficulty in breathing and probably immobile that is often a leading cause to muscle loss and joint pain. These patients may also have neurological deficits, balance impairment along with throat speech dysfunctions therefore in the management of Covid 19 (SARS-CoV-2) multidisciplinary approach may play great role in overall clinical management. [1]

Considering early physiotherapy intervention may play a great role in recovery from impairments caused during acute, subacute and post discharge in maintaining continuity of care, reducing the hospital dependency and improving quality of life. [2] In nutshell, physiotherapists play a crucial role by providing acute pulmonary care, applying neural-facilitation techniques, electrical muscle stimulation [19] and accomplishing overall body conditioning. This reality is further reinforced by the World Health Organization (WHO), a statement which recommends that physiotherapists should be a component of patient centred care. [3]

Unfortunately, in India physiotherapy care is grossly lacking and being given less priority. However a multidisciplinary approach can therefore enhance the functional independence, improved pulmonary function and helping patients to combat the Covid related sequelae. The purpose of this review is to gain insights on the role of physiotherapy in multidisciplinary care during and after the hospital stay by applying various pulmonary and physical rehabilitation interventions.

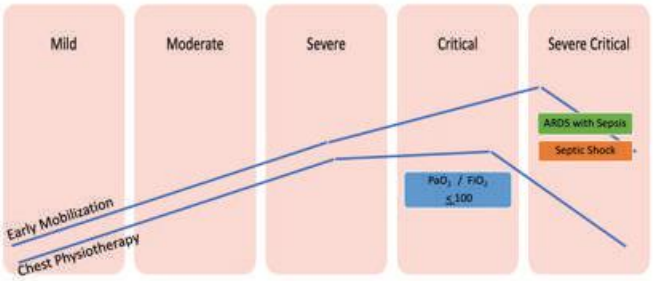


**Figure1**: Describing the role of physiotherapy at deferent stages and severity of disease.

## CLINICAL PRESENTATION OF Covid 19 (SARS-CoV-2) PHYSIOTHERAPY PERSPECTIVES:

Covid 19 (SARS-CoV-2) syndrome can be divided broadly into the 2 phases-the acute phase where patient predominantly have the respiratory manifestation, dyspnoea on exertion, and later phase where patient have sequelae of either the neurological deficits, balance impairments along with prolonged hospitalization/ICU stay. Other clinical issues such as deep vein thrombosis, intubation related iatrogenic dysphagia and cognitive dysfunctions should not be overlooked.

Few of recent literature also suggested that COVID-19 (SARS-CoV-2) virus at later stages affects the central nervous system. Patients having more severe respiratory manifestation, have a higher rate of neurological symptoms. [4]

## POST DISCHARGE SEQUELAE OF Covid 19 (SARS-CoV-2)

Patient journey of recovery from critical illness should not stop post hospitalization as patients may have residual impairment even after discharge, known as post

Covid syndrome, post-intensive care syndrome (PICS) resulting in chronic disability. [5] COVID-19 (SARS-CoV-2) patients, who are either admitted for severe respiratory failure or have neurological symptoms, may be left with long-term neurological impairments. [6] It has been shown that majority of COVID-19 (SARS-CoV-2) patients at discharge have motor and cognitive symptoms. [7]

## ROLE OF PHYSIOTHERAPY IN MANAGEMENT OF COVID

As per WHO, rehabilitation is "a set of interventions designed to optimize functioning and reduce disability in individuals with health conditions, in interaction with their environment". It is emphasised that the physiotherapist along with other healthcare professionals should be included in the multidisciplinary team for acute management as well as management of sequelae of COVID-19 (SARS-COV-2). [8] Physiotherapist can integrate, coordinate patients requirements pertaining to physical rehabilitation and other relevant clinical needs using the valid and reliable measurement scales such as Cumulative Illness Rating Scale (CIRS), including the Cumulative Illness Rating Score Comorbidities Index (CI) and the Cumulative Illness Rating Scale Severity Index (SI). [9] CIRS-CI was calculated assigning to each item a score between 0 (none) and 4 (extremely severe), total score reflecting the mean value of the first 13 items. CIRS-CI was obtained by the sum of the items with score ≥3. Length of stay (LoS) in referring hospitals, use of mechanical ventilation, either invasive or NIV, and arterial blood gases that helps to with other healthcare providers. [8] The potential role of physiotherapist is to enhance or maintain pulmonary function, minimising the short & long term effects of restricted mobility or physical inactivity during acute care hospitalization. [10] This may be achieved by early screening and assessment of possible cardiopulmonary, neuromotor and functional impairment caused by Covid virulent.

These impairments can be evaluated using BARTHEL Index, 4 min standing to sitting static and dynamic scales and 6 min walk/1 minute step-up test. [11]

European Respiratory Society- and American Thoracic Society-coordinated international task force suggests that hospitalised patients with COVID-19 (SARS-CoV-2) should receive rehabilitation at/around the bedside (critical care and/or ward based) until safe for discharge to the home environment. Most of the experts recommended strongly (55%) or conditionally (37%) for hospitalised patients with COVID-19 (SARS-CoV-2) receiving rehabilitation at/around the bedside (critical care and/or ward based) until safe discharge to the home environment. [1]

Progressive Exercise principle applied to patients with chronic lung diseases and concepts of pulmonary rehabilitation can be applied in post-COVID-19 patients. In view of reduced cardiac and lung function post Covid, a maximum score of 4/10 on Borg Scale CR10 for shortness of breath and fatigue during the post-acute rehabilitation phase is recommended. [12]


**Figure-2**: Modified Borg Scale for assessment of perceived exertion level.

They also recommended that patients with COVID-19 (SARS-CoV-2) should be encouraged to do regular daily activities in the first 6–8 weeks after hospital discharge and should be encouraged to do low-/moderate-intensity physical exercise at home (rather than high-intensity physical exercise) in the first 6–8 weeks after hospital discharge if a formal exercise assessment with measures of exertional desaturation has not been conducted. [1] "Subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate aim the improvement or maintenance of physical fitness". [13] All the interventions and activities must be performed to avoid or reduce the risk of droplet production and spread of infection. [14]

Post discharge Covid physical rehabilitation can be continued at home, outpatient, or tele- rehabilitation basis where physiotherapist provide the tailor-made exercises prescription -aerobic and resistance training (frequency, intensity, type, and time), monitoring of vitals and oxygen support, energy conservation techniques-pacing, planning, prioritizing, and positioning. [15] This will help patients to cope up with the physical fatigue, functional dependency and close monitoring of the patient's performance. [14,15]

## DISCUSSION

Throughout Covid outbreak phase both national and regional authorities have taken many measures to curb the spread during this phase. Physiotherapists all over India are constantly striving to help patients in hospital setting and outpatient rehabilitation to improve their lung functions, reduce demand of supplemental oxygen and prevent physical deconditioning. It has been reported that post-COVID patients can have an impaired physical functioning when they are discharged home, even after early mobilization. [13]

Physiotherapy along with a multidisciplinary approach is known to benefit a large population of patients with pulmonary and systemic involvement. Physiotherapy at or around bed in ICU will focus on prevention of secondary complications & maintain pulmonary hygiene. In moderate cases in ward setting physiotherapy will focus on positioning, neuromuscular facilitation of ventilatory muscle, airway clearance using ACBT & PEP

vibratory therapy, lung volume expansion exercises, electrical muscle stimulation [19], energy conservation technique and maintaining muscle strength which is further supported by recent literatures. [16]

Pulmonary rehabilitation in the post-acute period may work towards improvement in exercise capacity. In patients with interstitial lung disease, exertional desaturation is a key feature and is often more severe than that seen in other pulmonary conditions. [17]

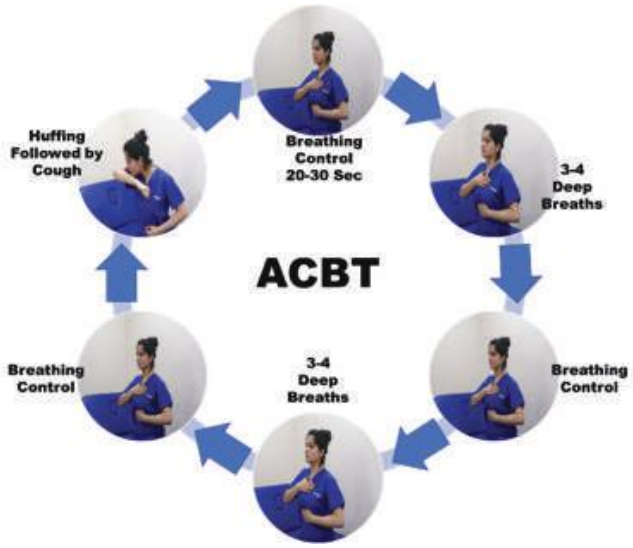


**Figure-3**: Demonstrating the ACBT technique for airway clearance.

A recent study state that 36.4% patients demonstrated neurological conditions. Italy has reported many patients suffering from vascular events, such as ischemic strokes and thrombosis, as a consequence of viruses targeting the coagulating mechanisms and need physiotherapeutic interventions. [18]

**Figure-4**: Acapella PEP Vibratory Therapy Device.

The rehabilitation guidelines are based on expert consensus using previous evidence databases pertaining to ARDS, MERS & SARS. It is recommended that the physiotherapy intervention must be based on a thorough assessment of patient condition, severity of disease and other comorbidities, and physiotherapist professionals must make a sound decision based on assessment findings.

## CONCLUSIONS

Physiotherapists can play a pivotal role in multidisciplinary care and help in the early recovery of patients with COVID-19 by delivering early pulmonary care and early mobility interventions at all stages including home isolation, acute hospital care, intensive care, and post discharge.

Patients who get discharged from acute care should be screened for residual pulmonary, neuromotor, musculoskeletal, cognitive, speech and swallowing dysfunctions by a multidisciplinary team. Physiotherapy interventions include pulmonary rehabilitation, aerobic exercises for physical conditioning, passive/active mobilization, muscle strength training, static and dynamic balance training for balance dysfunction, and joint proprioceptive training. Patients must also be evaluated for the ability to carry out activities of daily living and appropriate training/advice must be provided. Other clinical issues, like post intubation iatrogenic dysphagia must not be overlooked, neuropsychological and cognitive issues, should also be addressed by a multidisciplinary team.

Multidisciplinary care including physiotherapy must be continued after discharge from hospital-based care to an outpatient or home based setting, using either in-person or virtual mode.

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## Future Plan for the Department of Academics

# A Case Of Right Parietal Gliosarcoma Abutting Motor Cortex- Resection Of Tumour Aided By Intra-Operative Motor Cortex Mapping By Direct Brain Stimulation

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**Keywords:** Gliosarcoma, Intra-operative motor cortex mapping, fMRI, DTI, Tractography

## INTRODUCTION

Primary Gliosarcoma is a rare tumour of the central nervous system that remains poorly studied, possibly due to its infrequency, and also because it is often under-reported and misdiagnosed as Glioblastoma Multiforme (GBM), due to both having similar radiological features. [1] The recommended primary management of gliosarcoma is surgical removal of the lesion, but due to the propensity of gliosarcomas to originate from the parieto-temporal region of the brain, [2] the risk of damage to crucial motor cortex fibres during tumour removal is high. However, by using modern techniques such as functional MRI (fMRI), diffusion tensor imaging with tractography, and intra-operative direct electrical stimulation, the motor cortex can be mapped in great detail, thereby aiding the surgeon in selecting the approach with the least risk.

In this report, we discuss an interesting case in which the neoplasm was found to be encroaching onto the motor cortex, but post-operative neurological deficit was minimised through the use of pre-operative and intra-operative motor cortex mapping.

## CASE REPORT

The patient was a 75 year old male and a known case of hypertension, coronary artery disease post CABG, and chronic kidney disease, being managed with antihypertensive and antiplatelet medications. He initially presented with complaints of tingling over the left side of his body for past 1 month. There was no history of headache or weakness. The patient was conscious, oriented, and hemodynamically stable, and examination of the motor system was normal. Initially, the patient was given symptomatic treatment and advised NCV of all 4 limbs and MRI Brain. NCV found no abnormalities, but MRI Brain reported the presence of an irregular space-occupying lesion in the right parietal region with surrounding edema. Contrast Enhanced MRI Brain with MRS and FDG Full Body PET scan were subsequently performed. CEMRI Brain with MRS suggested that the lesion was of high grade mitotic etiology. **(Fig. 1)**

PET scan revealed no metastatic lesions, and confirmed that the primary lesion was lobulated, metabolically active and heterogenously enhancing, with few foci of calcification.

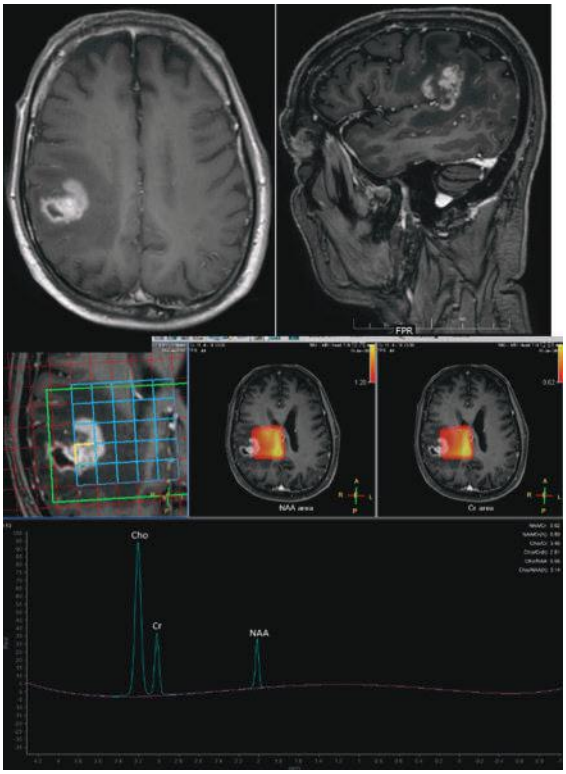


**Figure 1**
Pre-operative CEMRI Brain (above) with visible irregular space occupying lesion in the right parietal region, and MRS peaks (below) suggesting high mitotic etiology

At this point, surgical removal of the right parietal space-occupying lesion was decided upon. After obtaining cardiac and pre-anaesthesia clearance, the patient was admitted. Given that the tumour was located near the motor cortex, there was a high chance of devastating hemiplegia post-operatively. Hence it was decided to go for functional MRI Brain with motor stimulation (right and left finger tapping) along with

Diffusion Tensor Imaging (DTI) and Fibre Tractography. Motor stimulation of the left hand showed activation of the right motor cortex without any activation in the left, and vice versa, however right motor cortex showed marked reduction in activation as compared to the left. **(Fig. 2A)** DTI with tractography showed antero-medial and superior displacement of the right cortico-spinal tract by the lesion and surrounding edema. **(Fig. 2B)** Hence the surgical approach chosen was posterior and inferior to the lesion, so as to avoid damage to the cortico-spinal tract.

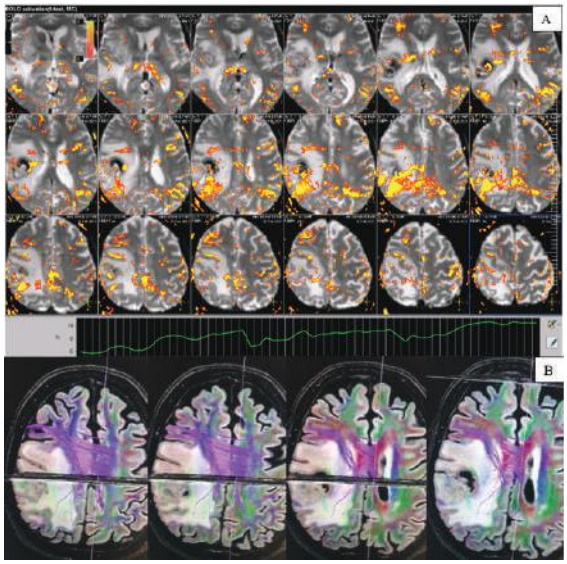


**Figure 2**
Pre-operative fMRI (A) showing activation of motor cortex and DTI (B) showing displacement of right cortcico-spinal tract by tumour and surrounding edema

As the patient was elderly and had multiple comorbidities, the risk of anaesthesia was high and awake surgery could not be attempted. Potassium levels were found to be high pre-operatively, which was managed in conjunction with Nephrology team. After proper optimization, the patient was taken up for surgery under general anaesthesia with atracurium and noradrenaline infusions, which allowed for the intra-operative use of direct electrical stimulation to the cortex. Electrodes were used to stimulate areas of the brain cortex, and any particular motor response was noted, and motor cortex was mapped accordingly. **(Fig. 3A and B)**

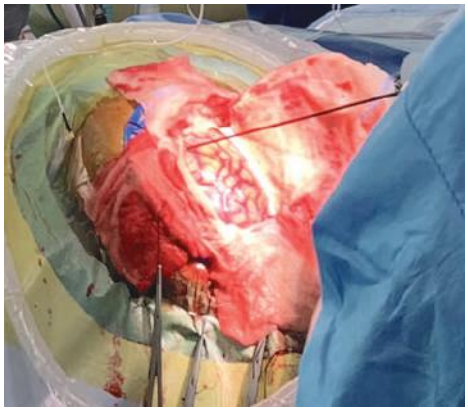

**Figure 3A**
Direct electrical stimulation being applied to brain intra-operatively

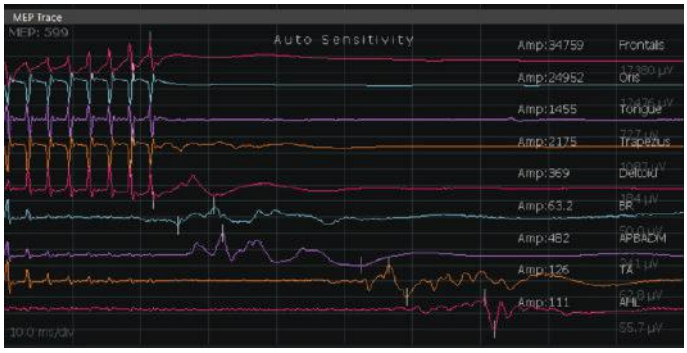


**Figure 3B**
Intra-operative motor evoked potentials seen in left side muscles upon applying electrical stimulation to right motor cortex

This allowed the surgeons to identify and avoid motor cortex fibres while resecting the tumour. The lesion was found to be firm to hard in consistency with areas of calcification. It was removed completely in the form of 5 pieces, which were all sent for histopathological examination. **(Fig. 4)** The remainder of the operation was completed without any complications.

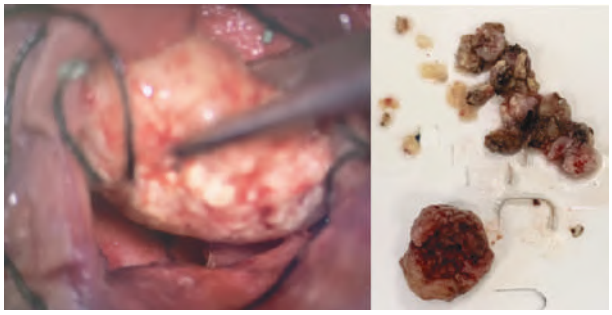

**Figure 4**
Intraoperative photos showing tumour being removed from cranial cavity (Left) and all pieces of tumour completely removed (Right)

Post-operatively, the patient was shifted to ICU for monitoring and kept sedated, intubated and on ventilator support. He was taken off sedation and extubated on POD-1, following which he maintained saturation on room air and had a GCS of 15/15. NCCT Head was done on the same day, which revealed post-operative changes with complete removal of the lesion and no alarming findings. **(Fig. 5)** The patient was found to have developed left sided hemiparesis, with a power of 4/5 in left upper and lower limbs, which was probably related to edema due to retraction. The patient was started on regular out-of-bed physiotherapy and was discharged soon after, with instructions to continue physiotherapy exercises.

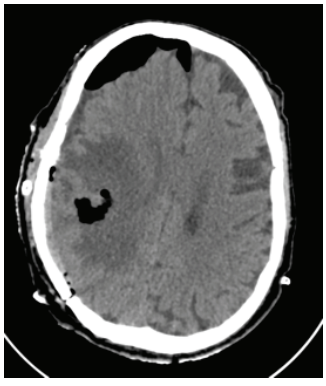

**Figure 5**
NCCT Head done on POD-1 showing post-operative changes and intracerebral cavity with no tumour remnants

The patient came for regular dressing changes to the OPD. The surgical wound healed well, and sutures were removed on POD-14. By this time, histopathological analysis had been completed and the lesion was reported to be comprised of glial cells involving gemsitocytes, along with spindle cells, osseous metaplasia, and occasional necrotic foci. Immunohistochemistry was done for definitive diagnosis, which confirmed the neoplasm to be Gliosarcoma, WHO grade IV, IDH-1 negative. Following this, the patient was given hyper fractionated radiotherapy with concurrent chemotherapy with temozolomide over a span of 3 weeks, as per consultation with Radiation and Medical Oncology teams. Follow-up MRI done 2 months post-op showed post-operative changes with no tumour recurrence. In his most recent follow-up, the patient had started the advised chemoradiation course. He had no new complaints, and his left hemiparesis had improved- power in both left upper and lower limbs had increased to 4+/5. Right upper and lower limb power had remained at 5/5, and the patient was able to walk independently.

## DISCUSSION

Gliosarcoma is described as a "well-circumscribed lesion with clearly identifiable gliomatous and mesenchymal components" by the WHO, and is classified as a variant of GBM. [3] The glial component is typically some form of astrocytoma, whereas the mesenchymal component is far more variable. [2] In this particular case, it was in the form of osseous metaplasia. Gliosarcomas are most often seen in the 5th to 7th decades of life, with a male preponderance. [3] The most common symptoms at presentation include weakness and related reduction in motility, headache, and visual problems. [4] Recommended treatment guidelines remain the same as that for GBM, which includes surgical removal of the lesion followed by radiotherapy, with or without a concurrent chemotherapeutic regimen of temozolomide. [3] Prognosis of gliosarcoma is poor, with studies showing median overall survival after treatment to be around 14 months. [1,3] This neoplasm also has a tendency to metastatise, which contributes to its poor prognosis, [2] although fortunately for this patient metastasis did not occur. Post-operative morbidity is also significant, and is mostly due to a combination of damage to nerve tracts by the neoplasm or during surgery, and tumour recurrence, further making the already shortened lifespan miserable.

Non-invasive pre-operative mapping of the motor cortex has significantly improved post-operative neurologic status in patients with gliosarcoma. Various methods are available, but those used in this case were functional MRI Brain and diffusion tensor imaging with tractography. Functional MRI (fMRI) is a type of imaging dependent on blood oxygen level dependent sequences, and is mainly used to map the motor and language regions of the cortex. [5] For motor mapping, the patient is instructed to perform simple movements such as finger tapping. This will cause the corresponding motor cortex area to become active and use more oxygen, delineating it on fMRI. [5] This type of scan can help identify the motor cortex area in a broad sense, but it is unsuitable for mapping out specific white matter tracts. For this, we have used the imaging modality known as diffusion tensor imaging (DTI) with tractography. DTI is a form of MRI which maps the diffusion of water across cell membranes in three dimensions. [6] This allows the mapping out of the location and course of white matter tracts, and hence help ascertain if the neoplasm has infiltrated motor tracts, or has merely displaced them. [6] This allows DTI to be a prognostic indicator as well as a useful pre-operative tool.

Intra-operative motor cortex mapping has become a valuable tool, as it allows surgeons to make informed decisions on the extent of tumour resection as and when required in real time. In this case, surgery with continuous neuromonitoring was performed. Direct electrical stimulation was given to the cortex and motor evoked potentials were monitored. This allowed for quick and accurate identification of cortico-spinal tract fibres while on table, so they could be largely avoided when resecting the lesion.

## CONCLUSION

Primary gliosarcomas have been found to have an extremely poor prognosis across several studies, [1-4] and their propensity to affect the motor cortex complicates surgical removal of these lesions. However, through the combined use of pre- and intra-operative mapping techniques, even these difficult tumours can be safely removed and result in a patient with minimal muscle weakness who is able to walk independently. These techniques can be expanded and used in many other neoplastic pathologies such as GBM, and their positive impact on patients' post-operative condition ensure that they will remain an integral part of neurosurgical procedures in the years to come.

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**Poems Dr. Smita Mishra**

# "कल के लिए"

जो गुजरा , वो वक्त था,
जो ठहरा रहा वो प्रश्न थाय
सृष्टि और भगवान का,
कि उद्दण्ड और आवेशित इंसान,
क्या तुम सीखोगे पाना
थोड़ा कम और बाटना थोड़ा
ज्यादा?
दिखाना थोड़ा कम, और
समझना थोड़ा ज्यादा?
प्यार बसता है दिल ,
उतरता है नजरों में ,
जरूरी नहीं, हिलाना हाथ को,
गलबहिया दोस्ती कीय
एक बार दिल मे मोहब्बत
की शमा जला कर,
अपनी ही आँखों का कमाल देखो,
उनकी भी है एक भाषा,
जो बातें कर लेती हैंय
अब तो सूरज को करने
दो राज और हवाओ को
कमरे में घुसने दो ,
अपने कदमों को बांध लो
दयोढ़ी से, अपने घर को,
अपने से जुड़ने दो!
थम जाओ जरा , बाहर की
खट खट से बचना,
वो जो तुम्हें दोस्त बन
बुला रहा है, अनजान,
आवारा कोरोना –जिंदगी
की डोरे उलझा रहा है!
ये वक्त है, सम्भालने ,
समझने का, कदमों
को रोक रखने का,
तुम्हीं हो मालिक तुम्हारे
भविष्य के,
कोरोना तुम्हारा धैर्य
आजमा रहा है!
आओ , थमे, रुके,
चेहरे को ढके,
रखें हाथों को
जीवाणु रहित, और
एक लक्ष्मण रेखा खींचे,
कल की जिंदगी के लिए!

स्मिता

# A RARE CASE OF HYPEREMESIS GRAVIDARUM LEADING TO INTRAUTERINE FETAL DEMISE

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## ABSTRACT

Hyperemesis gravidarum (HG) refers to intractable vomiting during pregnancy that leads to weight loss and volume depletion resulting in ketonuria and/ or ketonemia. It may lead to many maternal and fetal consequences including dehydration, electrolyte imbalance, metabolic disturbance and nutritional deficiency which may require hospitalization. Its incidence is 0.5-2%. [1] We present a case of a 30 year old primigravida who has severe hyperemesis gravidarum from the early weeks of pregnancy and was resistant to all standard management. She was managed with a multidisciplinary approach and was supported with intravenous fluid management .Despite appropriate management she had intrauterine fetal demise at 14 weeks of pregnancy. She had relief in symptoms and also her general condition improved after she aborted.

## BACKGROUND

It is estimated that 70–80% of pregnant women experience NVP [2]. It usually starts between fourth and seventh weeks of pregnancy and resolves by the 20th week of pregnancy. Hyperemesis gravidarum is defined as severe nausea and vomiting causing weight loss of 5% or more of pre-pregnancy weight, dehydration and electrolyte imbalance. Although there is an association between hyperemesis gravidarum and human chorionic gonadotropin (hCG) levels, the underlying mechanism is still not fully understood. As per NORD (National Organization for Rare Disease), currently the most evidence exists for the placenta and appetite hormone GDF15 as playing the role in ethology of hyperemesis gravidarum. Genetic evidence also supports a role of hormone receptor GFRAL and FGR. Outdated theories include the pregnancy hormone HCG, Vitamin B deficiency, hyperthyroidism and maternal fetal DNA levels.

Serum electrolyte and acid-base abnormalities may include hypochloremic alkalosis, hypokalemia, and hyponatremia. Other abnormalities such as mild elevation in amylase, lipase, and liver function enzymes are also associated with hyperemesis gravidarum. This case was challenging to manage as her nausea and vomiting were associated with deranged liver function tests and severe ketosis, resistant to all available standard treatments.

## CASE PRESENTATION

We present a case of a 30 year old primigravida who presented in emergency at 13 week + 4 day period of gestation with complaints of difficulty in swallowing since 1 day and nausea/ vomiting on and off since early pregnancy. She was married for 2 years. This pregnancy was a spontaneous conception. Injectable antiemetics and antacids were given and advised hospital admission but she refused for admission. Patient came to emergency the very next day with severe nausea and vomiting upto 7-8 episodes per day. Urine ketone was 4+. Patient was admitted and given iv fluids, injectable antiemetics and antacids. Strict monitoring of vitals was done and investigations sent.

Liver enzymes were markedly raised so gastroenterology opinion was taken .Ultrasound showed fetal bradycardia with a gestation of 14 weeks and was suggestive of impending fetal demise. Patient was informed of the same. With appropriate medical management her frequency of vomiting decreased. She had intrauterine fetal death and spontaneously expelled the fetus the next day. Her symptoms subsided in 1 to 2 days and liver enzymes returned to normal within a week.

## INVESTIGATIONS

- **Day 1**

Serum electrolytes – Sodium-140 mmol/l, Potassium-2.2 mmol/l, Chloride-104.8 mmol/l.

Total protein – 5.4 gm/dl, Serum albumin – 3 g/dl, Serum globulin – 2.4 g/dl

Plasma ammonia – 112.6 mcg/dl (elevated)

- **Day 2**

Kidney function tests – BUN-3 mg/dl, Serum creatinine – 0.49 mg/dl, Serum uric acid – 1.8 mg/dl

Serum calcium – 7.4 mg/dl, Serum phosphorus – 0.7 mg/dl, Serum Sodium – 133 mmol/l, Serum Potassium – 2.5 mmol/l, Serum magnesium – 1.5 mg/dl

Total protein – 5 gm/dl, Serum albumin – 2.8 g/dl, Serum globulin – 2.2g/dl, INR – 1.05

- **Day 3**

CBC: HB – 10.5g/dl, WBC – 16210/cumm, Neutrophils – 80.1%, Lymphocytes – 12.2 %, Monocytes – 7.2 %, Eosinophils – 0.3 %, Basophils – 1.20 %, Platelet – 186000/cumm

Serum electrolytes – Sodium-137 mmol/l, Potassium – 3.6 mmol/l, Chloride – 104.9 mmol/l.

Total protein – 5.8gm/dl, Serum albumin – 3.2 g/dl, Serum globulin – 2.6 g/dl

Blood culture-no growth in aerobic culture after 48 hrs of incubation

• **Day 4**

Total protein – 5.2gm/dl, Serum albumin – 2.7 g/dl, Serum globulin – 2.5g/dl

Serum Potassium – 3.3 mmol/L

**Patient had deranged LFT.**

| | DAY 1 | DAY 2 | DAY 3 | DAY 4 |
|---|---|---|---|---|
| Total Bilirubin | 2.70 mg/dl | 1.60 mg/dl | 1.10 mg/dl | 0.80 mg/dl |
| Direct Bilirubin | 2 g /dl | 1.30 g /dl | 0.90g /dl | 0.10g /dl |
| Indirect Bilirubin | 0.70 mg/dl | 0.30 mg/dl | 0.20 mg/dl | 0.70 mg/dl |
| SGOT | 264 IU/L | 177 IU/L | 172 IU/L | 164 IU/L |
| SGPT | 394 IU/L | 313 IU/L | 314 IU/L | 260 IU/L |
| ALP | 118 IU/L | 115 IU/L | 119 IU/L | 94 IU/L |
| Total Protein | 5.4 gm/dl | 5 gm/dl | 5.8gm/dl | 5.2 gm/dl |
| Serum Albumin | 3 g/dl | 2.8 g/dl, | 3.2 g/dl | 2.7 g/dl |
| Serum Globulin | 2.4 g/dl | 2.2g/dl | 2.6 g/dl | 2.5 g/dl |

She was investigated for any other potential causes that could be causing or contributing to nausea and vomiting. Also, she was reviewed by the gastroenterology team around the time of onset of nausea and vomiting to ensure that no surgical cause such as acute cholecystitis, intestinal obstruction, etc. was resulting in uncontrolled nausea and vomiting. Gastro-duodenoscopy was done which was normal. Urine ketone was 4 + at the time of hospital admission, after expulsion of fetus reduced to 3+. One week post discharge it was reduced to nil.

## TREATMENT

She was initially treated with regular intravenous antiemetics including metoclopramide, and ondansetron, along with intravenous hydration. She was given multivitamin injections in iv fluids. Injectable Ceftriaxone was started. In view of deranged LFT, Tab Udiliv and Inj glutathione were started. Potassium supplementation given in iv fluids in view of hypokalemia. Unfortunately after some initial response, there was no significant improvement in her persistent nausea and vomiting. She had intrauterine fetal demise and after expulsion of the fetus her symptoms started subsiding and her liver functions became normal in a weeks' time.

## DISCUSSSION

Nausea and vomiting are not uncommon in pregnancy. In most of the cases, it does not require hospital admissions, and self-resolves by the second half of pregnancy. Its severe form, hyperemesis gravidarum, which is associated with weight loss, however, can sometimes be very challenging resulting in frequent hospital admissions, and in rare cases like this leading to intrauterine fetal demise.

The pathogenesis of hyperemesis gravidarum is multifactorial. The risk factors described for hyperemesis gravidarum include young age, black or Asian ethnicity, socioeconomic deprivation, nulliparity, female fetus, multiple pregnancy, history of hyperemesis gravidarum in a previous pregnancy, thyroid and parathyroid dysfunction and type 1 diabetes. The differential diagnosis of patients with hyperemesis gravidarum is wide and includes infections, metabolic, gastrointestinal, neurologic, and iatrogenic causes. [3] Common diagnoses such as gastroenteritis, cholecystitis, hepatitis and biliary tract diseases, drug abuse/misuse, migraine headaches as well as more rare causes such as diabetic ketoacidosis, intracranial lesions leading to increased intracranial pressure and intestinal obstruction, should also be considered. Hyperemesis gravidarum is often associated with failure to respond to outpatient management and often requires hospitalization.

HCG is often stated as the most likely cause of HG. This is because the highest incidences of HG occur at the time HCG has its peak level and because HG has a higher incidence in conditions said to be associated with elevated HCG levels, namely twin and molar pregnancies, pregnancies of female fetuses and those with Down syndrome. [4] How HCG can cause HG remains unclear, but proposed mechanisms include a stimulating effect on the secretory processes in the upper gastrointestinal tract (GIT) or by stimulation of thyroid function because of its structural similarity to thyroid-stimulating hormone (TSH)

Increased levels of estrogen and estradiol are known to cause nausea and vomiting in pregnancy. [5] It has been suggested that patients with hyperemesis are probably more sensitive to estrogen effects than asymptomatic pregnant women. [6] However, some studies have reported negative results regarding the association between elevated estrogen levels and the development of hyperemesis. [7]

Some studies have suggested that Helicobacter pylori (H. pylori) infection may play a role in hyperemesis, but the data is inconclusive and the explanation of association between H. pylori infection and hyperemesis gravidarum is unclear. [8] For explanation, it was reported that, increased level of steroid hormones and human chorionic gonadotrophin during pregnancy lead to changes in the pH and motility of gastrointestinal tract. These changes favor activation of H. pylori infection. Other explanation is impaired defensive mechanisms against H. pylori. [9]

In a study on hyperemesis gravidarum and its effects on fetal outcome conducted by Hallak M et al between 1984 and 1991, 138 patients were diagnosed with hyperemesis gravidarum and they demonstrated that none of the fetus of the patients who have suffered from hyperemesis gravidarum had FGR, prematurity or any anomaly. [10]

In another study done by Veenendaal et al on consequences of hyperemesis gravidarum for offspring,

they concluded that hyperemesis gravidarum is associated with higher female/male ratio offspring and higher incidence of LBW, SGA and premature babies. [11]

In none of the studies there was an adverse fetal outcome, but in our case report, inspite of managing the patient as per standard conservative treatment protocol, severe hyperemesis gravidarum was associated with adverse fetal outcome in the form of intrauterine fetal demise.

## INFERENCE

1. In most cases of severe hyperemesis gravidarum, there is no significant side effect on the fetus but the possibility of intrauterine fetal demise can't be ruled out.
2. The pathogenesis of hyperemesis gravidarum is still not fully understood and the underlying mechanism cannot be explained by one factor only.
3. Complicated cases of hyperemesis gravidarum should be managed by a multidisciplinary team involving obstetricians, gastroenterologists, dietitians and psychiatrists.
4. Hyperemesis gravidarum can cause derangement in liver function tests,starvation ketosis ,and rarely intrauterine fetal demise.
5. The role of other treatment options like antipsychotic drugs for hyperemesis gravidarum needs further studies and research.

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**Crossword Key:**

| DOWN | ACROSS |
|---|---|
| 6 PEGINTERFERON | 1 SUBCUTAEOUS |
| 7 MOXIFLOXACIN | 2 EOSINOPHILS |
| 8 HOPE | 3 VEMURAFENIB |
| 9 SEPRAFILM | 4 ASPIRIN |
| 10 BRAF | 5 OBESITY |

# DOLICHOCOLON - An unusual cause of a common problem.

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Key words: Chronic abdominal pain, constipation, dolichocolon.

## INTRODUCTION

Dolichocolon is an inborn anatomic variant, where redundancies may involve the entire colon or may be limited to certain areas as the hepatic flexure, transverse colon, splenic flexure and the sigmoid colon which also happens to be the most commonly affected region [1,2,3]. The incidence is 1.9% - 28.5% but the prevalence is not known. The redundant colon presents as an unusually lengthened large bowel forming extra loops, tortuosities and kinks.

## CASE REPORT

A 30 yr old female patient presented to gastroenterology OPD with complaints of left lumbar region pain, bloating, long standing constipation and nausea & vomiting since 2 days. On examination, mild tenderness was elicited in the left lumbar region on palpation.

Basic relevant investigations – TLC, LFT and KFT were normal. The urine routine reported presence of 10-15 WBC and slight turbid appearance. USG abdomen was reported normal. Since her pain did not subside, she was advised NCCT whole abdomen with oral contrast.

## OBSERVATION

The CT scan reported normal position of stomach and duodenum. The DJ flexure was on the left. Proximal jejunum was in the right upper abdomen. Ileal loops were in the lower abdomen. The superior mesenteric vessel congruity was maintained thereby ruling out malrotation. The cecum was seen deep within the pelvis on the right **(Fig. 1)**. Ileo-caecal junction and appendix were normal. The ascending colon, hepatic flexure and proximal third of transverse colon were delineated with oral contrast.

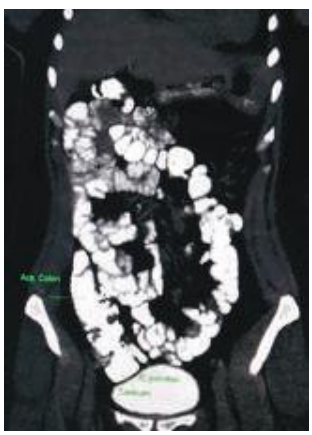


**Fig 1** : Long ascending colon

The distal transverse colon coursed caudally towards the left iliac crest **(Fig. 2a & 2b)**. The splenic flexure, descending colon and sigmoid colon were redundant. Oral contrast was seen ascending in the loaded descending colon **(Fig 3)**.

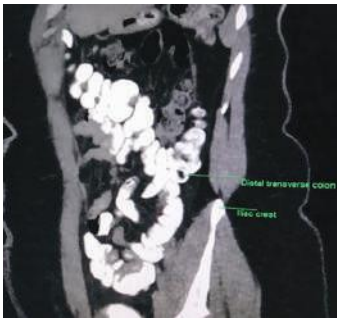



**Fig. 2a**
Downward sloping transverse colon towards left crest

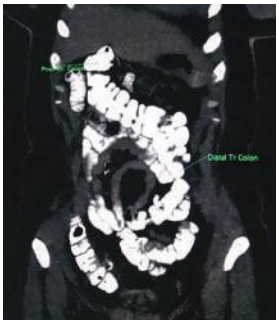



**Fig. 2b**
Transverse colon reaching left iliac

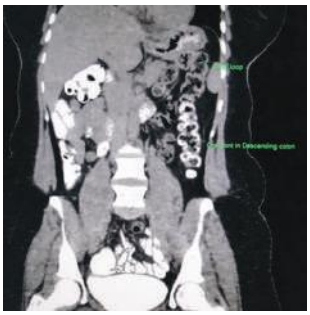


**Fig. 3**
Redundant descending colon

The lumen thereafter contained fecal matter and further on had air mixed with fecal matter. Two extra colonic loops were seen at the splenic flexure **(Fig. 4)**. The sigmoid colon was partially collapsed and rose well above the line between the iliac crests **(Fig. 5)**. It almost reached the stomach bed and was displacing the jejunal loops to the right. Based on these findings a diagnosis of fully developed dolichocolon with a persistent descending mesocolon was offered.

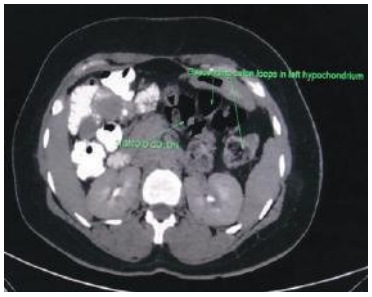


**Fig. 4**
Extra loops at splenic flexure pushing jejunum to right.

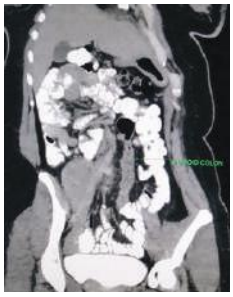


**Fig. 5**
Redundant sigmoid colon reaching the stomach bed

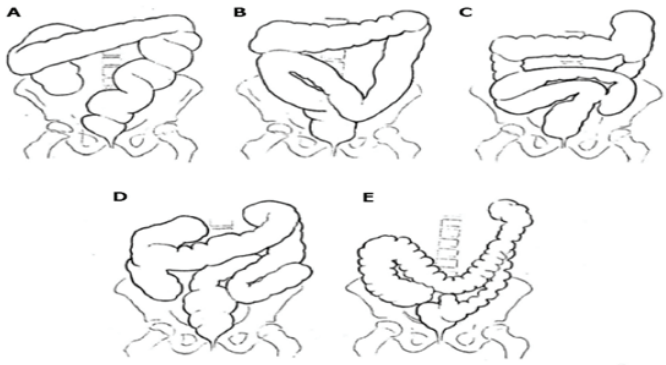
## DISCUSSION

Dolichocolon was first visualized by Kienböeck [4] in 1912 using bismuth and named dolichocolon (dolicho-, Greek: long) by Lardennois and Auborg [5] in 1914. The length and mobility of colon have great clinical implications [1,6,7]. The sigmoid and descending colon are known to present redundant loops that are reported as dolichocolon in the literature [1,2,3]. A redundant colon is defined as one that is too long to fit into its owner's body without undergoing reduplication [3]. The redundancy may involve the entire colon or it may be limited to certain segments of the colon, but the distal segment especially the sigmoid colon is the most commonly affected as regards its length, position and shape [1,2,3].

A redundant loop of sigmoid colon has tremendous clinical significance [6,7]. It may hinder both the instrumentation and diagnosis of imaging examinations [6,7,8]. Hence, it is crucial for surgeons, obstetricians and radiologists to be aware of this variation since its awareness determines the accurate radiographic diagnosis and surgical outcomes (6,7). It may be asymptomatic or it may lead to urinary (increased urinary frequency), digestive (constipation, indigestion, abdominal discomfort, loss of weight, abdominal pain and tenderness) and vascular complications [6,7,8,9,10]. Infact, rectosigmoid endometriosis has the same clinical presentation as dolichocolon [11].

Embryologically, a long colon results from failure of zygosis of its mesocolon with the parietal peritoneum. As a result of this, the elongated colon is not fixed to posterior abdominal wall and can swing free on a long mesentery which makes it susceptible to a potential risk for volvulus [1,6,7,8,12,13,14]

The dolichocolon was characterized by the following criteria: a sigmoid loop rising over the line between the iliac crests, a transverse colon below the same line and extra loops at the hepatic and splenic flexure. A fully developed dolichocolon occurs when all redundancies are present simultaneously as was observed in our case [10,15,16].




Different types of dolichocolon. A-C: Redundancies in the sigmoid; D: Generalized redundancies; E: Low transverse colon. From Caffey [15], 1961.

The dominating symptoms of dolichocolon are a triad of constipation, abdominal pain and bloating [17,18]. Colon transit time is prolonged and increases significantly with increased number of redundancies [19]. Radiologically, the redundant colon is characterized by the criteria mentioned above. The diagnosis is established by a barium enema or CT-colonography. Treatment is conservative or surgical in case of volvulus or refractory constipation [20].

Our patient was managed conservatively as her scan did not show signs of bowel obstruction or volvulus. She was treated for UTI and her symptoms resolved during hospital stay. She was discharged with advice to seek medical help if symptoms recurred.

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## Saraswati Puja

# ROBOTIC ATRIAL SEPTAL DEFECT CLOSURE: A CASE REPORT

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## ABSTRACT

Atrial septal defect (ASD) is one of the most common congenital heart defect. The treatment options for this pathology are percutaneous devices or surgical closure. However, some of the ASDs are not suitable for device closure. Currently, robotic surgical techniques allow surgeons to close ASDs in a totally endoscopic fashion with high success and low complication rates. We present a case of 30 year old female patient with ostium secundum ASD with deficient inferior margins, who underwent Total Robotic ASD closure successfully.

## INTRODUCTION

Atrial septal defect (ASD) is one of the most common congenital heart defect [1]. This pathology can be treated with percutaneous devices with a low rate of early post-procedural complications [2]. However, ASDs with unfavourable anatomy and the type of ASD other than the secundum are not suitable for transcatheter closure. Moreover, there are important device-related late complications of transcatheter ASD closure including device migration, device malposition, cardiac erosion or perforation leading to tamponade and death, atrioventricular block and bacterial endocarditis [1–4]. Currently, robotic surgical techniques allow surgeons to close ASDs in a totally endoscopic fashion with a high success rate and a low complication rate [1]. The robotic technique can be applied to ASDs with different anatomical sizes and also to both secundum and sinus venosus type defects. Moreover, since this technique does not require implantation of any prosthetic material, it may offer patients a safe long life that is free from any device-related complications.

We report a case of 30 year old female patient with ostium secundum ASD with deficient inferior margins, who underwent Total Robotic ASD closure successfully.

## CASE REPORT

A 30 year old female patient presented to the cardiology department with dyspnoea on exertion since 6 months. On examination, she had ejection systolic murmur in pulmonary area and wide fixed split second heart sound. Transthoracic echocardiography revealed ostium secundum ASD of size 2.1 cm with deficient inferior margin and left to right shunt. Patient was planned for Robotic ASD closure using Da Vinci Xi surgical system.

Anaesthesia was induced and patient was intubated using standard techniques. External defibrillation pads were placed on the chest wall. A chest roll was placed under the right shoulder, the right arm placed at the side of the operation table. The patient was placed in a slightly right lateral decubitus position. After systemic heparinization, an outflow cannula (Biomedicus 17 Fr, Medtronic, Tijuana, Mexico) was inserted percutaneously into the left internal jugular vein and positioned into the superior vena cava. Inflow cannulas (Biomedicus 17 Fr, Medtronic, Tijuana, Mexico) were inserted into the right femoral artery, and an outflow cannula (V FEM 22 Fr, Edwards Lifesciences, Irvine, CA, USA) was inserted into the right femoral vein. At the anterior axillary line, endoscope was inserted through the fourth intercostal space, the arms of the robot were inserted through second and sixth spaces and the working port was placed in the fourth space. **(Fig. 1 & 2)** Photo Insufflation of carbon dioxide was used with 8 mmHg pressure and a flow rate of 6 l/min.

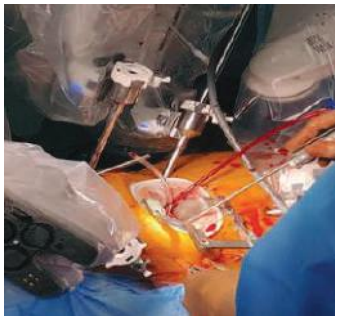

**Fig. 1**

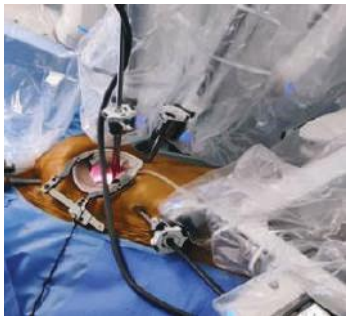

**Fig. 2**

**Port sites for Robotic ASD closure**

Cardiopulmonary bypass (CPB) was initiated, and the vena cava were snared. Aortic occlusion was performed using a Chitwood cross-clamp via the second intercostal space, and antegrade Del- nido cardioplegia was administered directly through the working port with long cannula. A right atriotomy was performed, and the secundum ASD was confirmed. The ASD was closed directly with CV- 5 Gore-Tex continuous running suture. The knots were tied with a knot pusher through the working port. **(Fig. 3 & 4)** After cross-clamp release and meticulous intracardiac de-airing, the patient was weaned from CPB, hemostasis was done and wound was closed in layers after chest tubes insertion.

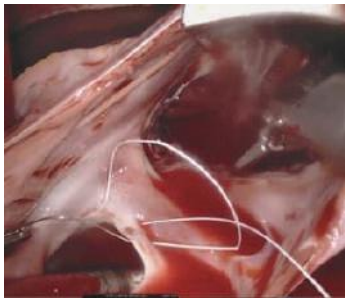

**Fig. 3**

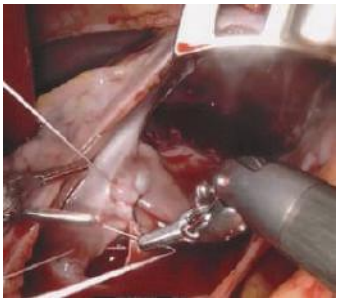

**Fig. 4**

**Robotic ASD closure using CV 5 Gore-Tex continuous suturing.**

The integrity of the ASD closure was confirmed by TEE. The cardiopulmonary bypass and aortic cross clamp times were 142 and 62 min, respectively, and the blood loss volume was 80 ml. Patient was shifted to recovery room and was extubated the next day. The chest tubes were removed and the patient was mobilised on the first post-operative day. The patient was discharged on 5th post-operative day and she resumed normal routine life with excellent cosmetic results.

## DISCUSSION

Although surgical ASD repair with conventional median sternotomy is effective and is associated with low morbidity and mortality, a minimally invasive approach that does not utilize sternotomy is desirable for a variety of reasons. Over the past decade, the significant advantages of minimizing surgical trauma by reducing incision size and eliminating rib-spreading have resulted in a tremendous increase in the number of minimally invasive cardiac surgical procedures being performed [1]. This consideration has led to the development of the mini-thoracotomy technique with sub-mammary incision.

In parallel, recent advances in transcatheter closing devices has resulted in a shift from surgical repair to interventional closure for treatment of secundum and patent foramen ovale types of ASD. However, the presence of a large ASD or multiple ASDs with an insufficient surrounding tissue to anchor the closure device is associated with higher procedural failure rates. Recurrence of the intra cardiac shunt, dislodgement of the occluder and breakage of the device have also been described [5, 6].

Alternatively, total endoscopic robotic surgery can be offered for ASD closure regardless of ASD size, location and shape. Some authors have already reported that robotic surgery can be performed with mortality and morbidity rates similar to those associated with open-chest operations [7, 8], and avoidance of thoracotomy or sternotomy has yielded potential benefits in terms of less pain, less blood loss, very small incision (cosmetically better), faster recovery and quick return to a normal lifestyle.

## CONCLUSION

In conclusion, total endoscopic robotic ASD repair using the Da Vinci Xi surgical system in a patient with ostium secundum atrial septal defect, was achieved safely with good clinical results and excellent cosmetic outcomes

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# SELF-EXPANDABLE METALLIC STENT FOR MALIGNANT SMALL BOWEL OBSTRUCTION IN A PATIENT WITH ADVANCED COLON CANCER WITH ILEOSTOMY

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## INTRODUCTION

Colorectal cancer is the second most common cause of cancer in women, and the third most common in men. [1] Approximately 20% of colorectal cancer patients presents with unresectable locally advanced or metastatic disease. [2,3] The majority of these tumors are clinically silent for long periods of time or manifest with non-specific symptoms, such as dull, crampy abdominal pain, abdominal distention, fecal occult blood, nausea, vomiting and change in flatus's emission in the previous 24 hour. Obstruction is the first main sign of disease in 8-29% of colorectal cancer patients given its insidious growth and could be due to recurrence or progression of disease. [4.5] Malignant small bowel obstruction is a dire complication of intrinsic disease or extrinsic compression from abdominopelvic tumors. In some studies, this complication is said to occur in 10%-28% of all colorectal cancers. [6,7,8]

The pathogenesis of obstruction may be the direct effect of the malignancy, as a secondary effect from cancer-related treatments, or from non-malignant causes. Because the small intestine is relatively inaccessible to routine endoscopy, diagnosis of small intestinal neoplasms is often delayed for months after onset of symptoms. Peritoneal carcinomatosis results from tumor cells in the peritoneal cavity. Tumor cells may come from a primary tumor in the peritoneum but in most cases come from the metastasis of abdominal and pelvic malignancies

In this report, we present a case of Malignant Small Bowel Obstruction in a patient with Advanced Colon Cancer with Ileostomy

## CASE STUDY

A 59-year-old male patient, K/C/O Ca Ascending colon came to the ER with complaints of distention of abdomen for 3-4 days, poor stoma output since 1 day and low backache.

Past medical history: He is a k/c/o CA Colonic-ileocecal mass operated 9 months ago – exploratory laparotomy followed by decompression of the dilated small bowel loops with subtotal ileo-colectomy with end ileostomy and colonic mucous fistula. He was diagnosed to have metastatic omental carcinoma progressive in nature, chemo-refractory after four cycles of CAPOX + Bevacizumab, KRAS mutation + MMR-wild type. Patient had earlier presented in the ER with multiple episodes of vomiting and loose stools since 2 days. He was vitally stable but tachycardiac.

Examination: Vitals: BP-80/50mmHg, P-88/min, RR-18/min, SpO2 94% in RA, RBS-116 mg/dl, Temp 36.6* C, No pallor, icterus, cyanosis, lymphadenopathy, JVP not raised. Systemic examination: Chest: B/L intermittent crepts+, CVS: S1+S2+, P/A: tense, diffuse tenderness, ileostomy bag in situ, CNS: Patient conscious, weak, obeying commands, moving all limbs. H/O Allergies: NKDA, Medications: NAD.

Investigations: CBC: Hb 8.6g/dl, TLC 11750, PLT COUNT 476000, KFT: BUN 15mg/dl, S. Creat 1.12 mg/dl, Na 135mmol/l, K 3.4mmol/l, LFT: T.Bil 0.2mg/dl, D. Bil. 0.1mg/dl, ALP 130U/L, AST 10U/L, ALT 15U/L. X-ray abdomen showed multiple air-fluid levels in the abdomen ?suggestive of subacute intestinal obstruction with surgical staples in-situ. CT Enterography shows right hemi-colectomy status with distal ileostomy .Fluid filled proximal jejunal loops were grossly dilated with air fluid levels (bowel obstruction). Distal jejunal and proximal ileal loops were collapsed with cocoon formation (adhesion) with surrounding loculated ascites. A dilated ileal segment distal to adherent bowels was seen with abrupt luminal narrowing with collapsed distal ileal loops beyond dilated segment (transition zone). Right kidney revealed persistent nephrogram with poor contrast excretion and dilated renal pelvi-calyceal system and proximal ureter (acute obstruction).

His past PET CT done 5 months ago was suggestive of right colon not being seen post right hemicolectomy status with evidence of ileo-colostomy and colonic mucosa fistula in the right iliac fossa region, metabolically active nodular parietal peritoneum thickening in the right iliac fossa region, small bowel loops in the region mildly hypermetabolic thickening in the parietal peritoneum abutting the anterior abdominal wall mildly hypermetabolic lymph node in the protected space on the left side likely metastatic as compared to the previous PET CT scan done on 9 months ago -there is an increase in size and number of pelvic mesenteric lymph nodes previously noted, metabolically active nodular setting along the parietal peritoneum abutting the small bowel loops in the right iliac fossa is new and the parietal peritoneum in the midline abutting the anterior abdominal wall is also new-progressive disease.

He was initially managed conservatively with Nil per mouth, Ryle's tube decompression, but the intestinal obstruction persisted. Surgical opinion was taken but they didn't advise for any surgical management in view of unresectable and advanced colon cancer. Hence, it was decided to do ileoscopy and if possible put a SEMS stent across the stricture.

Ileoscopy was done using ultra-thin scope (GIF-XP190N, Olympus America Inc, PA, USA). Multiple strictures were noted in the ileum and crossed after 2 failures on 2 days with a gap of 3 days. On the first 2 attempts the stricture was crossed using Terumo guidewire (xxx) but the SEMS could not cross the stricture. Next time the SEMS crossed one stricture but not the second stricture. Finally in the third attempt, the stricture was crossed using ultra-thin scope and the guidewire was placed after crossing the stricture with the ultrathin scope. SEMS (Wallflex Duodenal 12cm, Boston Scientific, USA) uncovered (12cm) was placed under endoscopic and fluoroscopic guidance. He responded well to the SEMS placement.

There was constant stool/gas flow after stent deployment and his abdominal distention also reduced. His diet was slowly advanced from liquid diet to soft low fiber diet as tolerated. The rest of his post-operative hospital stay was unremarkable and the patient was discharged in a stable condition after 48 hours of SEMS placement. The patient was followed up and he expired one and half months after stent placement due to the progression of the colon cancer, without clinical signs of re-obstruction.

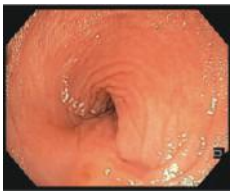

**Fig. 1a**

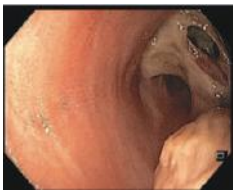

**Fig. 1b**

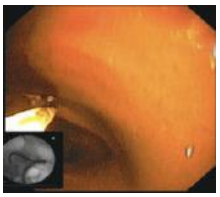

**Fig. 1c**

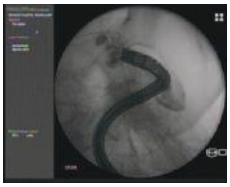

**Fig. 2a**

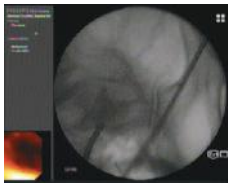

**Fig. 2b**

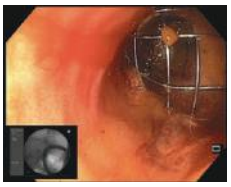

**Fig. 2c**

**Fig 1a:** Small bowel normal mucosa

**Fig 1b:** Small bowel infiltration and stricture

**Fig 1c:** Scope crossed the stricture

**Fig 2a:** Ultra-thin scope in small intestine thru the ileostomy

**Fig 2b:** SEMS deployed in the small intestine – fluoroscopic view

**Fig 2c:** SEMS deployed in the small intestine – Endoscopic view

## DISCUSSION

Malignant gastrointestinal obstruction (MGO) is a frequently faced complication of primary gastrointestinal cancer or various metastatic cancers, manifesting as a stricture of the gastrointestinal tract. The appropriate management strategy for such malignant SAIO is difficult to identify, because of the narrow range of available treatment options or low performance status of terminally ill patients. [9] Treatment of the patient with MGO is a challenging clinical scenario as decision making needs delicate balance between pros and cons of intervention. It is influenced by the level of obstruction, clinical stage of cancer, overall prognosis, and presence of ascites as well as patient's performance status. [10] There are no satisfactory criteria to select patients appropriate for surgery. [11] When there are several obstacles in the small bowel, extensive resection or bypass may be necessary even if these may induce severe complications. [12,13,14] Few studies focus on the role of endoscopic prosthesis in the palliative management of obstruction with peritoneal carcinomatosis. [15,16]

Palliation for malignant gastro-intestinal and biliary obstruction with SEMS deployment shows long term outcome of 70% stent patency until death, and most re-obstructions could be addressed endoscopically. [17] Success rates concerning the resolution of obstruction do not seem significantly different between obstructions by primary tumor or by carcinomatosis. [18,19] The overall survival of the patients who do not undergo surgery is rather poor with less than 25% of the patients alive at 5 years. [20] Approximately one-half of patients who underwent ''curative'' resection for localized disease will eventually die of metastatic disease. [21] About 10%–30% of the colorectal cancer patients at diagnosis could only receive palliation and approximately 40% of patients, treated with curative intent, develop recurrence that, for the vast majority, cannot be treated with curative intent. [22] To the best of our knowledge till now, very few cases of malignant terminal ileal stricture with metallic stent placement have been reported. [23-27] SEMS has also been used as a bridge to surgery with good outcomes as it is much less invasive. [28-30]

A deep small bowel enteroscopy is limited, and three endoscopy systems are now available – double balloon endoscopy (DBE), single balloon endoscopy and spiral endoscopy. [31,32] Some studies showed more technical success when either the endoscopic or the combined technique is used compared to only radiography. [33,34] Lee et al [35] reported 19 patients with malignant small bowel strictures who underwent SEMS insertion. Clinical success rate noted was 84% but patients with malignant distal small bowel strictures/ adhesions were not included in this study.

So the stenting can be performed using either the through-the-scope (TTS) or the over-the-guide wire (OTW) technique. Ross et al [36] reported a case of carcinomatous distal duodenal stenosis treated with SEMS placement using DBE technique with the TTO technique. Lennon et al [37] performed the same procedure using spiral endoscopy. This way can be used to treat deeper malignant small bowel blockages, but studies that are known have only used it for distal duodenum, proximal jejunum, or surgically –reconstructed intestines. [37]

Moreover it is seen that using stents of different

diameters do not make much difference technically, clinically or in likelihood of adverse events. [41-44] Some studies have even shown contradictory results regarding ideal stent length. [41] It is advised to use a stent that is long enough to bridge the stricture and to extend atleast 1.5-2 cm on each side of the lesion.

Study conducted by Young et al [45] noted that the surgery group had significant reduced quality of life if compared with the stent group from baseline 1 to 2 weeks (p=0.001 and p=0.012, respectively) and from baseline to 12 months (p=0.01). Analysis of the same RCT revealed lower total costs for stenting than for surgery. [46] Placement of a self-expanding metallic stent has emerged as a favourable therapeutic approach, both as a palliative option (in patients with advanced or unresectable cancer) [47-49] and as a bridge to surgery (in patients with potentially curable disease). [50,51]

## CONCLUSION

Advanced metastatic CA Colon (post colostomy /CT/ RT/IT) with SAIO (multiple SB strictures) was managed using SEMS (uncovered, 12 cm). All stents remained patent until death in our case.

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## Monthly CME Planner Year 2021-23

*Date is scheduled on 3rd Wednesday of every month

| S.no | Department | Date |
|---|---|---|
| 1 | Anesthesia | 23-Jun-21 |
| 2 | Critical Care Medicine | 21-Jul-21 |
| 3 | CTVS/Cardiology Pacing and Electrophysiology/Interventional Cardiologist | 18-Aug-21 |
| 4 | Dental/ Derma | 15-Sep-21 |
| 5 | Emergency Medicine | 20-Oct-21 |
| 6 | ENT/Ophthalmology | 17-Nov-21 |
| 7 | Fetal Med/ Gynecology & Obstetrics | 15-Dec-21 |
| 8 | Gastroenterology | 13-Jan-22 |
| 9 | Internal Medicine/Infectious diseases/Diabetes and Endocrinology | 16-Feb-22 |
| 10 | Lab -Transfusion medicine/Clinical Biochemistry/Clinical Hematology/Pathology/ Microbiology | 16-Mar-22 |
| 11 | Liver Transplant & Hepat-Pancreatic & Biliary Surgery | 20-Apr-22 |
| 12 | Nephrology/Urology | 18-May-22 |
| 13 | Neurology | 15-Jun-22 |
| 14 | Neurosurgery | 20-Jul-22 |
| 15 | Nuclear Medicine | 17-Aug-22 |
| 16 | Orthopedics/Rheumatology/ Spine/ pediatric Ortho | 21-Sep-22 |
| 17 | Neonatology/Pediatrics &PICU/Pediatric Cardiology/Pediatric Orthopedics/Pediatric Gastro | 19-Oct-22 |
| 18 | Psychiatry/Pain Management/Psychology | 16-Nov-22 |
| 19 | Physical Therapy | 21-Dec-22 |
| 20 | Radio-Diagnosis & Imaging/ Intervention radiology | 18-Jan-23 |
| 21 | Respiratory Medicine | 15-Feb-23 |
| 22 | Surgery (Vascular Surgery/ Plastic surgery/ General/ Thoracic) | 15-Mar-23 |
| 23 | Oncology(Surgery/ medical/ radiation) | 19-Apr-23 |

# A CASE REPORT ON SEPSIS INDUCED CARDIOMYOPATHY IN EMERGENCY

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## ABSTRACT

Sepsis-induced cardiomyopathy is a reversible myocardial dysfunction that typically resolves in 7–10 days. It is characterized by left ventricular dilatation and depressed ejection fraction. However, many uncertainties exist regarding the mechanisms, characteristics, and treatment of this condition. This review attempts to summarize our current knowledge of sepsis-induced cardiomyopathy.

## INTRODUCTION

Sepsis is "a life-threatening condition that arises when the body's response to an infection injures its own tissues". [1] Despite significant advances in an organized treatment approach, it remains the most common cause of death in critically ill patients worldwide [2] and the most frequent non-cardiac diagnosis in the cardiac ICU. [3] Sepsis-induced cardiomyopathy (SICM), or sepsis-induced myocardial dysfunction (SIMD), is an increasingly recognized form of transient cardiac dysfunction in septic patients. Despite implications on patient outcomes, the critical care community has not given significant emphasis, and prominent critical care textbooks [4,5] do not have dedicated sections on SICM.

While no formal definitions exist for septic cardiomyopathy, most review articles & expert opinions agree on a few fundamental features of this unique form of cardiac dysfunction. **(Table 1)** One flaw is that to meet the criteria of reversibility, the patient must survive the episode. Given the high mortality with sepsis, this leads to bias which may affect both diagnosis and trials in SICM.

**(Table 1)**

| **Proposed Diagnostic Criteria for Sepsis Induced Cardiomyopathy** |
|---|
| **Acute & reversible, within 7-10 days** |
| **Global, biventricular dysfunction (systolic and/or diastolic) with reduced contractility** |
| **Left ventricular dilation** |
| **Diminished response to fluid resuscitation and catecholamines** |
| **Absence of acute coronary syndrome as etiology** |

## CASE REPORT

A 22 Yrs old male patient working as an Executive in the private sector was brought to our Emergency Department on 13th May 2021 at around 06:45 pm with complaint of moderate grade fever, generalized weakness, and throat pain since last 7-8 days. He was also complaining of difficulty in swallowing food (more for solid than liquid) and unable to move his neck for the last 4-5 days.

At the time of presentation, he was conscious and oriented to time, place, and person, GCS was E4V5M6, BP-60/40mmhg, HR-94/min, RR-14/min,RBS-121mg/dl, axillary body Temp-102 *F, SPO2-100% in room air. B/L pupils were 3mm, reactive to light.

On Primary Survey Airway was patent. Lungs were clear to auscultation. Abdominal examination revealed mild epigastric tenderness. Exposure of the patient didn't show any signs of physical injury or marks in the body.

Secondary survey and detailed examination from head to toe were unremarkable except for mild swelling over the right para pharyngeal area in the neck region and movement of neck restricted to the right side.

His initial ABG showed PH-7.442, PCO2-23.8mmhg, PO2-87.8mmhg, HCO3-19.2mmol/l, Lactate-2.7mmol/l, Ionized Calcium-1.05mmol/l, Na-128mmol/l, K-3.8mmol/l. ECG showed Sinus Rhythm with no ST-T changes.

Initially, he was given 1 litre NS IV bolus, then by checking the volume status of the patient by doing an ultrasound of IVC, another 1 litre of NS was given. Then he was started on Noradrenaline infusion after putting ultrasound-guided right internal jugular central line. Blood culture, Urine culture, Serum Procalcitonin were sent on an urgent basis from Emergency and broad-spectrum antibiotics were started given high CRP, low platelet count, and high D-dimer value. Patient already had routine blood investigation done in OPD basis on same day (CRP 25.94, D-DIMER 2205, TLC 13730, N-93%, Platelet count 86,000. The patient was then shifted to MICU on Noradrenaline infusion (@10ml/hr)

In the first 5 hrs of admission, the patient had decreased urine output (15ml/hr) and a Nephrologist consultation was sought but then his urine output improved and advised for USG whole abdomen. The patient had persistent tachycardia and hypotension on day 2 so, intubated and put on mechanical ventilator support.

On Day 2, 2D Echo screening done was suggestive of severe global LV hypokinesia, LVEF-20-25%, RA/RV/LV dilated, Moderate MR/ TR, Mild to moderate PAH, (RVSP 24 mm Hg + RAP), severe RV and LV systolic dysfunction. Troponin I and BNP levels were also raised. (Troponin -I 2.13, BNP 3790)

Because of poor LV function and dilated cardiomyopathy background in ECHO, Dobutamine infusion was started in due course of hospitalization. Given high Procalcitonin value and Sepsis, MP antigen, and dengue profile, scrub typhus was sent which came negative.

Serum Procalcitonin value was very high (PCT-Q 14.37

ng/ml) and all the cultures including blood, urine, and ET secretion came sterile. Because of poor myocardial function, intravenous immunoglobulin (IVIG) was planned and 120 gm transfused over 2 days.

The patient was maintaining SPO2 level of 98% with FiO2 40% and PEEP 8, with no fever and adequate amount of urine output on Day 2 of admission. Repeat 2D ECHO done on Day 4, was suggestive of global LV hypokinesia, LVEF 40%. All cardiac chambers were normal.

The patient started to show improvement by day 4 and was extubated later on the same day. Serial Procalcitonin levels showed declining trends and subsequently Noradrenaline and Dobutamine infusions were also tapered and stopped because of clinical improvement of the patient. Repeat 2D ECHO done on day 5 was suggestive of mild global hypokinesia with an LVEF 45-50%. The patient completely recovered on day 5 and was discharged in a good healthy condition on day 7 of admission.

## DISCUSSION

Given that there is no definitive agreed-upon definition or criteria, the diagnosis of SICM can be difficult. Moreover, it can be challenging to distinguish between cardiovascular system failure (i.e., distributive shock) and cardiac failure (i.e., SICM), and the two often coincide.

Clinical features that suggest the diagnosis include a prior history of heart failure, a "septic, cool extremities phenotype" on clinical exam, hemodynamic instability despite vasopressor therapy, failure to respond to a preload challenge, cardiac dysrhythmias, abnormal echocardiogram, low mixed venous oxygen saturation, and elevated cardiac troponins. [2,3] Herein we discuss diagnosis based on electrocardiogram, biomarkers, echocardiogram, and both invasive and non-invasive direct measures of cardiac output.

### Electrocardiogram

There are no diagnostic electrocardiographic (ECG) findings of SICM. The most common rhythms include sinus tachycardia and atrial fibrillation (AF). A 2019 meta-analysis concluded that new-onset atrial fibrillation occurs in patients without traditional risk factors for the development of AF suggesting that sepsis-induced cardiac changes lead to AF. [2] While the correlative relationship suggested by these studies links AF with SICM via similar pathophysiology, it does not lend itself to using AF as a diagnostic or prognostic tool.

### Biomarkers

### Troponin (cTn)

In septic patients, elevated cTn is correlated with a greater degree of left ventricular dysfunction, illness severity, and mortality. [6,7,2] In a meta-analysis of over 1200 patients with sepsis, 61% of subjects with elevated cTn had a twofold increased risk of death compared with patients with undetectable cTn. Multivariate analysis confirmed that increased serum cTn was an independent risk factor for mortality.

### Brain Natriuretic Peptide (BNP)

Natriuretic peptides also has prognostic value in sepsis. [1,3] A multi-center, randomized clinical trial of approximately 1000 patients with sepsis and septic shock showed that N-terminal pro-B-type BNP (NT-proBNP) and cTn were elevated in 97.4% and 84.5% of patients, respectively. The degree of biomarker elevation was highly correlated with the development of septic shock and mortality, but NT-proBNP predicted mortality in the ICU and at 90 days better than cTn. [7]

### Echocardiography

Echocardiography is the cornerstone for the diagnosis of septic cardiomyopathy. There is consensus and expert opinion that every hemodynamically unstable patient should receive critical care echocardiography (CCE). [4,5] These findings are summarized in **Table 2** and described in more detail below

## LVEF

It was initially thought that diagnosis could be made solely on a depressed LVEF. [6] A major problem with LVEF is that reduced afterload from the distributive shock may pseudo-normalize a depressed EF (coupling between contractility and afterload). This leads to under diagnosis of SICM when LVEF is used alone. We think that this explains the "paradox" of improved survival identified by Parker et al. [6] as a patient with profound shock (vasodilation) with a "normal EF" may do worse than one with less shock and a "low EF". [6,7] Therefore, LVEF in critically ill patients should be interpreted with the amount of inotropic/ vasopressor support & the degree of shock.

**Table 2**
**Echocardiographic findings in sepsis-induced cardiomyopathy**

| Parameter | Modality | Strengths | Weaknesses |
|---|---|---|---|
| LVEF | Two-dimensional echocardiography<br>- Semi-quantitative ("eye-ball")<br>- Quantitative | Easy to obtain (including point of care) and most clinicians are comfortable interpreting the information | Lacks sensitivity and specificity. May be "pseudo-normalized" with low afterload. Unclear prognostic role (low LVEF "paradox") |
| SV + CO | Spectral Doppler | Can be used to evaluate fluid responsiveness. May be prognostic. Relatively easy to obtain (point of care) | Lacks sensitivity and specificity. Alterations in preload, afterload, and contractility will cause variations which can make consistent interpretation difficult |

| | | | |
|---|---|---|---|
| RV dysfunction | Two-dimensional, spectral Doppler, tissue Doppler | Prognostic if present. TDI provides higher quality information | Lacks sensitivity and specificity. RV can be difficult to visualize. More advanced imaging techniques require formal echocardiography |
| Diastolic dysfunction | Two-dimensional, spectral Doppler, or tissue Doppler | More prognostic than LVEF alone. Basic information relatively easy to obtain, but TDI provides higher quality information | Lacks sensitivity and specificity. More advanced imaging techniques require formal echocardiography |
| Global longitudinal strain (LV + RV) | Speckle tracking | Highly prognostic. Very sensitive assessment of LV, RV, and diastolic dysfunction. Less inter-observer variation. Not dependent on physiology loading parameters | Requires special software and equipment. Requires high imaging quality (difficult in critically-ill patients). Lack of consensus on cut-off values |

LVEF: left ventricle ejection fraction, SV: stroke volume, CO: cardiac output, RV: right ventricle, TDI: tissue doppler imaging, LV: left ventricle

**Stroke Volume (SV) and Cardiac Index (CI)**

Both SV and CI can be calculated using left ventricular outflow tract (LVOT) diameter and the velocity time integral (VTI), but the measurement of these indices is hard to interpret in SICM because of the profound variations in preload, afterload, and contractility intrinsic to septic shock. Studies have, however, found that sepsis survivors have higher VTI and CI on ED presentation. [3]

**Right Ventricle (RV) Systolic Dysfunction:**

Approximately two-thirds of patients with sepsis and septic shock have RV dysfunction and, as stated above, it is an independent risk factor of 1-year survival. [3] Measurements of RV function includes the RV end-diastolic area in comparison to the LV, the RV fractional area change with tricuspid annular plane systolic excursion, tricuspid annulus tissue Doppler imaging (TDI), and the RV free wall TDI. A study suggested that the RV wall strain was the most important predictor of mortality in patients with SICM. [1] All patients with an RV global longitudinal strain (GLS) less negative than –13% died within 20 days. [1]

**Diastolic Dysfunction:**

LV diastolic function is very common in septic shock. The septal relaxation in TDI (a-wave, abnormal < 8 cm/s) was a very strong predictor of mortality in septic shock patients, after adjusting for severity of illness, comorbidities, and other echocardiographic indices. [3] Another study measuring the peak early diastolic trans-mitral velocity during the passive filling of the heart (E)/peak early diastolic mitral annular TDI velocity (e') showed a significant and independent predictor of mortality.

**Table 3**
**Management of sepsis-induced cardiomyopathy**

| Therapy | Mechanism of action | Pro | Con |
|---|---|---|---|
| Vasopressors | Vasoconstriction by alpha or beta adrenergic, vasopressin, or dopamine receptor stimulation | Physician familiarity. Well studied in septic shock. Alpha-adrenergic, dopamine, and vasopressin activity will help with decreased afterload. Beta and dopamine activity will increase contractility | Increasing afterload too much may "unmask" cardiac dysfunction (especially with isolated vasoconstrictive drugs phenylephrine and vasopressin). The beta-adrenergic and dopamine activity could increase myocardial demand leading to worsening cardiomyopathy and/or arrhythmias |
| Fluids | Increasing preload with increase stroke volume based on Frank–Starling relationships | Increasing stroke volume will increase cardiac output | Cardiomyopathy will shift the Frank–Starling curve and overaggressive fluid management can lead to worsening organ failure |

| | | | |
|---|---|---|---|
| Dobutamine | Beta-adrenergic selective agent | Physician familiarity. Most studied with proven improvement in cardiac parameters (i.e., CO) | Increased myocardial demand and vasodilation may worsen hemodynamics. Risk of arrhythmias. May not improve outcomes |
| Milrinone | Phosphodiesterase inhibitor increases cAMP | Increased contractility without adrenergic activity. No trials for SICM | Vasodilation. Limited by renal dysfunction. Risk of arrhythmias |
| Levosimendan | Calcium sensitizer and potassium channel activator | Helps with calcium signaling to increase contractility in an adrenergic-dependent manner so less oxygen demand | Vasodilation. Mixed information about mortality with the largest trial suggesting increased mortality |
| Beta blockers | Beta-adrenergic blockade | May help decrease the pathogenesis of SICM by decrease myocardial demand | Negative inotropic effect. Patients with cardiac dysfunction were excluded from the largest trials |
| Ivabradine | Selective inhibitor of the If channel | Lower myocardial demand without negative inotropic effect found in beta blockers | Possible worsened mortality, but data sparse and not specific to SICM |
| Methylene blue | Nitric oxide metabolism | Treats vasoplegia. Improves catecholamine responsiveness. May improve vasopressor requirement | No change in outcomes. Risk of serotonin syndrome. Can cause worsening oxygenation by pulmonary vasoconstriction. Hemolytic anemia in G6PD deficiency. Interference with pulse oximetry. Contraindicated with renal dysfunction |
| Mechanical support | Provide bypass or mechanical assistance of cardiac output | Provides aggressive supportive care until reversibility occurs | Invasive with relatively high risk of complications. Must choose right device |

## In our case

- The patient was not responding to initial crystalloid and started on Noradrenaline and Dobutamine infusion
- The patient was having high CRP, high TLC, high D-dimer value but cultures negative suggestive of high suspicion of viral sepsis over secondary bacterial infection.
- Initial 2D ECHO was suggestive of severe LV Hypokinesia with LVEF 20-25%. RA/RV/LV dilatation with RV systolic dysfunction and severe LV systolic dysfunction which subsequently improved after intravenous Immunoglobulin therapy.
- The patient was having neck swelling over the right para pharyngeal area on the day of presentation which subsided after broad-spectrum antibiotics. Contrast-enhanced CT of neck could not be done because of deranged renal parameters. (BUN 33 mg/dl, Sr Creatinine 3.05)
- The presentation of illness was acute onset and reversible within 7 days of hospitalization
- The absence of acute coronary syndrome as etiology could not be determined in this patient as being sepsis-associated clinical picture.
- The patient was asked to follow up in OPD after 7 days for neck swelling if reappears.

Hence all these relevant points are suggestive of diagnostic criteria for sepsis-induced cardiomyopathy (SICM)

## CONCLUSION

SICM is currently an under-recognized entity that has significant prognostic and mortality implications for our patients. Clinicians should consider the diagnosis in patients with sepsis-associated organ dysfunction and particularly septic shock requiring vasopressor therapy. Biomarkers can provide prognostic information and put SICM on the clinician's radar, but their diagnostic utility is limited. Echocardiography is currently the gold standard of diagnosis, and evaluation of global longitudinal strain is more sensitive and specific for SICM than LVEF or other common findings alone. Standard management includes the use of vasopressors, inotropes, and

judicious fluid resuscitation, but large studies validating these measures are lacking. Additionally, while there is growing evidence for other therapies for SICM, more data is needed to make any definitive recommendations about adopting them to everyday practice. Finally, a consensus statement on diagnostic criteria is currently lacking and is essential in future studies evaluating treatment.

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## करोना वार्ड का अनुभव

करोना वार्ड का अनुभव मेरा बहुत अच्छा रहा। मुझे अपने ऊपर गर्व है कि मैं नर्सिंग स्टाफ हूँ। सच में इस करोना ने यह सिखाया की बहुत सी जिन्दीगियाँ जो हमारी आंखों के सामने से ओजल हुई, उनके परिवार का दर्द, हम किस हद तक समझ पाए। करोना में हमें सहानुभूति के साथ काम करने का मौका मिला क्योंकि उस समय पेशेंट के साथ उसका कोई परिवार का सदस्य नहीं होता और उस समय हमें ही उसका परिवार बनना पड़ा। पेशेंट ने अपना आत्मविश्वास मानो खो सा दिया था, उसको अपने जीने की आशा समाप्त सी लगने लगी थी। उस समय उनका मनोबल सहयोग बढ़ाकर उनके अंदर एक जीने की इच्छा फिर से जागृत की। कुछ पेशेंट ऐसे भी मिले जो देख नहीं सकते, सुन नहीं सकते उनके साथ हमने बहुत धैर्य और नम्र भूमिका निभाई।

इस दौरान बहुत से मरीजों को कमजोरी थी, जो पेशेंट के गिरने का एक महत्वपूर्ण कारण बनी। उस समय में, हमने पेशेंट के लिए कुछ चुनौतियां लीं, जैसे पेशेंट की बेड की साइड रेल को ऊपर रखना, कॉल बेल पेशेंट के पास रखना और 2–3 घंटे में पेशेंट को जाकर देखना। कुछ पेशेंट करोना के कारण मानसिक तौर पर इतना डिस्टर्ब हो गए कि अपना कैनयूला, फोलीज, कैथिटर निकालने की कोशिश करने लगे और बहुत से पेशेंट ने तो गालियां भी दीं, लेकिन यह समय उनसे  लड़ने और उन पर गुस्सा करने का नहीं था, बल्कि उनको एक नई जिंदगी देने का था। भावुक और सशक्तिकरण सहयोग भी दिया पेशेंट को।

हॉस्पिटल मैनेजमेंट से भी बहुत सहयोग मिला जैसे PPE KIT- N95 मास्क, रिफ्रेशमेंट और इस महामारी में एक साथ टीम वर्क किया।

उमा मनराल

नर्सिंग टीम

# ECTOPIC PROSTATIC GROWTH MASQUERADING AS "BLADDER TUMOR" !!

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## INTRODUCTION

Ectopic prostatic tissue is a rare entity that is encountered in the lower male genitourinary tract, [1] most commonly at the trigone area and rarely at the bladder neck of periurethral location. [2,3,4] Though it is also reported in pericolic fat, anal canal, retroperitoneum, spleen and female genitourinary tract. Herein, we report an unusual case of intra-vesical benign ectopic prostatic tissue presenting as a submucosal growth at the trigone. Till date only four cases are reported in literature. [1]

## CASE REPORT

A 32 year old man presented in the Urology OPD with difficulty in passage of urine and denied any trauma/ past significant medical or surgical history. On evaluation, his bladder was palpable. Initial urine routine microscopy showed turbid urine with microscopic hematuria, trace proteinuria and no significant increase in pus cells. Urine culture was sterile. Non contrast CT-KUB showed tiny bilateral calculi with minimal urothelial thickening in the right renal pelvis (? Pyelitis) with a urethral calculus. Patient was catheterized to drain urine and Cystoscopy was planned for stone removal.

Cystoscopy incidentally showed a submucosal growth (dimensions 1.0 x1.0 cm) in trigone area of urinary bladder grossly mimicking a bladder tumor. **(Fig. 1)** The growth was resected and histopathological analysis of the tissue submitted showed several benign prostate glands focally dilated, with intact myoepithelial layer along with few urothelial cell nests (? Von Brunn's nest) with surrounding unremarkable muscle tissue. Immuno histochemical analysis showed strong positivity of these glands with PSA (prostate specific antigen), hereby confirming a diagnosis of ectopic prostatic tissue. **(Fig. 2)** The postoperative course was uneventful.

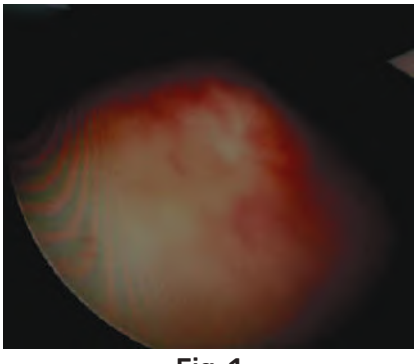
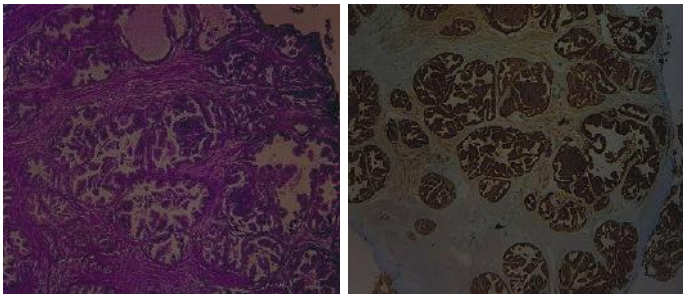


**Fig. 1**
Cystoscopy showed a smooth sessile mass at the trigone area in bladder



A B

**Fig. 2**
A: Sections show prostatic acini with focal dilation & intact myoepithelial cell layer (H&E, 4X)
B: Prostatic acini positive for Prostate specific antigen Immunostaining (PSA, H&E, 4X)

## DISCUSSION

Ectopic prostatic tissue in the urinary bladder is rare and predominantly occurs in young men in urinary bladder, trigone being the most common site. [3,4,5] Prostatic differentiation was confirmed on immunohistochemistry in our case, with acinar cells being strongly positive for PSA Source of ectopic prostatic tissue is not clear and numerous theories have been proposed like migration / misplacement of normal tissue, persistence of embryonic remnants and metaplastic change caused by chronic inflammation. [6] In our case, the first theory is more likely as there was no inflammation in the biopsy and embryonic remnants usually appear in the urethra and periurethral regions. So any growth in the bladder is to be biopsied to exclude bladder cancer. Ectopic prostatic growth is a rare but differential diagnosis of bladder tumor.

## CONCLUSION

These lesions may clinically mimic a bladder mucosal tumor. On a small biopsy, it may be confused with a well-differentiated adenocarcinoma. Hence, awareness of this entity is essential for both urologists and pathologists to prevent misdiagnosis of malignancy. Therefore these masses should be completely excised and histologically confirmed because preoperative confirmation of ectopic prostatic tissue is extremely difficult and cases of malignant transformation of ectopic prostatic tissue are known to be reported in literature. However these lesions are small with smooth surfaces unlike urothelial neoplasms which are usually papillary. Also ectopic prostatic tissue is histologically and immunohistochemically indistinguishable from normal prostatic tissue and most likely indicates the persistence of embryonic structures.

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# A DAY THAT CELEBRATED THE COURAGE OF OUR CAREGIVERS.

INTERNATIONAL NURSES DAY
12TH MAY 2021

# MIND YOUR MIND: TAKING CARE OF YOUR MENTAL WELLNESS

Ruchi Sharma
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"I suppose it is tempting, if the only tool you have is a hammer, to treat everything as if it were a nail."

-Abraham Maslow

## INTRODUCTION

Mental wellness is important for everyone. It does not imply staying happy all the time. However, learning to adapt and adjust to the ever-growing demands and stress is vital. Most of us have various 'coping mechanisms' or mental tools that we use for this purpose. But over reliance on the same set of strategies over time may lead to reduced efficacy of these mechanisms. So we need to update this 'psychological skill set' and create a mental toolkit for ourselves, which would empower us.

## NEED OF THE HOUR

During acute health crises, healthcare services are placed under excess pressure, making working life even more stressful than normal. [1] It is unfortunate that talking about one's mental health remains a challenge in our society. Studies have also shown that many doctors find it difficult to tell their colleagues or employers about their mental health difficulties. [2] The most commonly cited reasons are perceived stigma and anticipated damage to future career prospects. Not only do doctors find it difficult to share mental health concerns with colleagues, they are also often reluctant to get professional help. Research shows that many doctors would rather seek help from friends and family than look for psychological/psychiatric consultation. Furthermore, there is evidence that many doctors are even reluctant to disclose mental health problems to their friends and family. [3] In such a scenario, it is indispensable to learn new ways to cope and develop resilience.

Also, authorities and healthcare executives must show strong leadership and support for doctors and their families during the ongoing pandemic, and call for efforts to reduce mental health stigma in clinical workplaces. This can be facilitated by deliberately adding 'healthcare staff mental health support process' as an ongoing agenda to high-level management planning meetings.

## MINDFUL MIND FOR BETTER IMMUNITY

Improved mental health and resilience is a process and involves lifestyle changes. Some of these changes and activities may involve:

**A. Positive Affirmations:** When we find ourselves in a stressful situation, the voice of our 'inner critic' often leads to self- blaming and guilt. In such times we need to reassure ourselves and give positive affirmations such as:

- Recovery is a process, not a miracle. Be patient
- I deserve calmness and peace
- Sharing my worries makes me strong
- Setbacks do not equal failures
- I am allowed to set boundaries
- It is okay to rest and start again tomorrow.
- I am strong. This too shall pass.
- It is okay to seek help
- Everyone has problems and difficult times

**B. Chromotherapy:** Chromotherapy is also called color therapy which is the use of color and light to gently bring about homeostasis. [4] Some colors which can be used to uplift and relax yourself are:

- Red: boosts energy, beats fatigue, and increases libido
- Orange: A warm and cheerful color that can be used to free the mind and body from constriction. It stimulates creativity.
- Yellow: It can strengthen the nerves and stimulate creativity. It uplifts mood and eases depression. Yellow soothes muscle pain and improves bowel conditions.
- Green: The most balancing of all the colors as it represents nature and earth. can affect blood pressure, heal hormonal imbalance, and increase immunity.
- Blue: a cooling color that can calm strong emotions such as anger and aggression.
- Purple: It can lead to better sleep while calming emotional and mental stresses, along with reducing sensitivity to pain.

**C. Self- Care:** Various facets of self- care have been listed below. It is essential to choose activities in each sphere, based on our interests & beliefs, work on them & incorporate them into our daily schedules. This will help in achieving holistic wellbeing. [5]


## CONCLUSION

Mental wellness is not a luxury, it is a necessity. Especially in the current ongoing pandemic, a healthy mind is our greatest defense, as distress can lead to a weakened immune system. As Robert Schuller aptly remarked, “Tough times don’t last, but tough people do!”

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# CAN WE HAVE A STANDING OVATION FOR OUR NURSES PLEASE?

Vasanthi Hariprakash

Columnist & Founder-Editor, Pickle Jar

Beena may not have a lamp in her hand, but every 10 minutes in the night the lady quietly checks on those wounded by Covid, and have landed in her ICU ward.

Bed no. 7 is an easy patient; she has to check only his SP02 – the oxygen saturation levels; and generally keep an eye on him for sudden fluctuations. Young man, he will recover.

Oh that way, bed no. 13 is also a young guy? But he has comorbidities; diabetic for 4 years already, plus hypertension. His medicines' list that Dr. Asma gave, Beena has to follow very carefully, to give what pill at what time, how much and when, the next dose. The ward boy where is he, did he give this patient sponge bath?

Bed no. 2 worries her the most. When the lady came in, she looked like she will be sent home in 4 days. After her CT scan, she told Beena about her granddaughter who has to eat food only from her hands. "My phone is not here, Sister, otherwise I would have shown you her birthday picture in that red frill frock," she said in Kannada. And Beena smiled, her eyes glowing from inside her masked face and full PPE suit, top to toe.

Then suddenly, the next morning when she came in on duty, she saw doctors trying frantically to revive her heart function. Oh god, will she make it? That little girl, will she see her grandma again?

There are 22 beds in the ward that was changed just this March into a Covid ward; otherwise those beds in the cardiology department, they were vacant.

Until February, Beena and her colleagues actually had free time sometimes; they could sit and laugh, eat a Mysur Pak someone had kept in the nursing station. And once or twice a week, they all could make a group video call to Suchi who used to work here. Oh, that lucky girl Suchi! There was an opening last November in a Dubai hospital, she applied, she got, she left also, in one chartered flight the government had announced. Now, you know how much her salary is? Dirhams to Indian rupee if you convert – 1.2 lakh per month.

Can you imagine?

Riyadh, Rome - everyday on the 'Kochi Florence Nightingales' Whatsapp group, someone or the other is posting about 'Nurses wanted' ads. They said in America, the pay is 45 dollars an hour, really? But Beena sometimes didn't mind her 19,000-rupees salary; what she missed was the 3 days off that her foreign nurse friends got every week that too after night duty. That, and respect. Doctors don't shout at the nurses, patients there don't expect the nurse to be their bedsheet-folder, food-feeder, hairwasher, even bedpan-giver all at once. "Still I am lucky I am in this big city not village; imagine no ventilator no ICU, just me one nurse for 30 patients?" Beena shuddered.

You see, a nurse can't get attached to the patient. She was shocked when she got a message from the HR department of her hospital that the psychologist will take some 'sessions' for them. Some games organized specially. These new people in the corporate office, they don't have work or what – we nurses will now sit and play or what? Beena was irritated. But last week, Reji the fresher who just joined two years back and Manjunath (About him, a patient had said, Manju is so caring like a lady) were both called by the Head Nurse to be sent for counselling. Beena later learnt when she took off the suit, took a hot bath in the nurses bathroom and came out, that the two of them had broken down 3 days back, crying, "We did so much, looked after, made them do proning, and still four more people died today." Both are in their early 20s. Beena was also like that ten years back, very sensitive.

Now she has only her kids on her mind. Her husband is always so supportive, but last week he was worried. "You won't get Corona yourself no?" She laughed, "No you will have to cook for me for many more years." She heard a beep on her phone. "Aye Beena, your patient no. 2, Sarasamma? She is good to go home, took your number. Said she will send you her little girl's frill frock picture next week."

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Vasanthi Hariprakash is an award-winning radio anchor & journalist, columnist and audio-video content creator. Her dynamic career in the media has taken her across the bustling newsrooms of The New Indian Express, the quiet soundproof studios of Radio City Bangalore & All India Radio, on the field as a special correspondent for NDTV 24/7, and to faraway lands such as Laos and Vietnam as a documentary anchor for BBC World News.Recently she went from being broadcaster to a businesswoman, and is presently the Founder-Editor of Pickle Jar, an audio video and new-media content company that aims to tell stories of a vibrant changing India.

# PATIENT SAFETY IN COVID UNITS

Nomita Sarkar
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"An engaged nurse goes the extra mile to ensure safe, competent, and compassionate care

The current Covid wave made us more scared as we were managing sicker patients and occupancy also was more compared to the 1st wave.

It was very challenging for the entire nursing team to manage this patient's safety because the patient is sicker than the previous, higher in number, staff shortage due to staff falling sick, and introduction of new protocols and drugs.

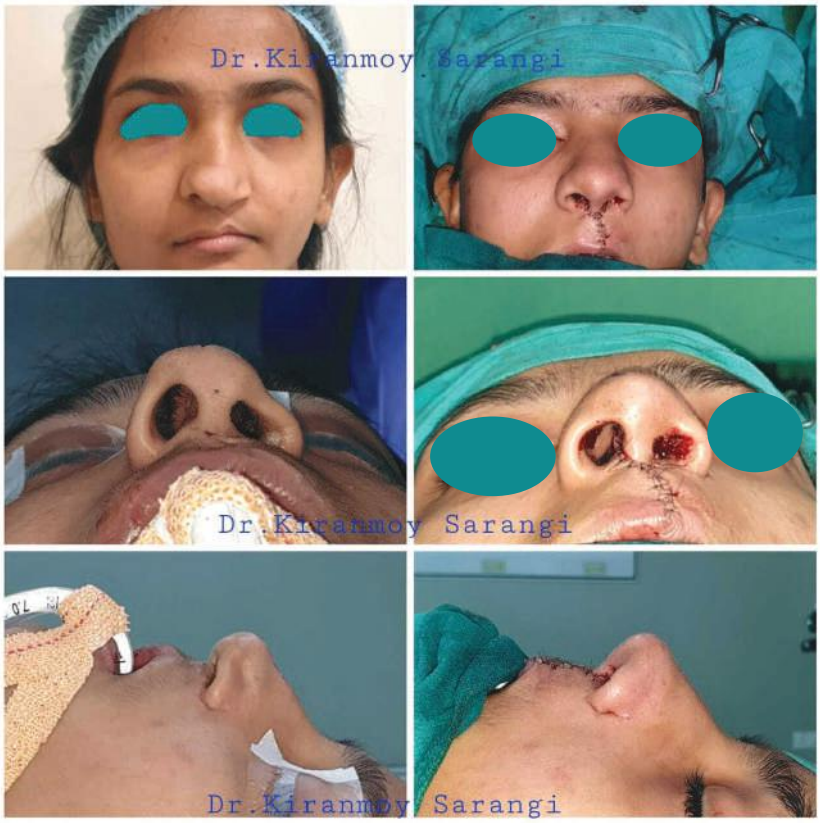
Meeting these challenges and yet maintaining quality care and patient safety was a tough task.

To overcome these issues we made efforts and continuously monitored to maintain quality patient care and patient safety in the following manner:-

- Cohorting the patients into different categories .. like sick patients in HDU with continuous monitoring with more skilled staff, milder staff in rooms and gender-wise also.
- We encouraged functional training due to the sudden rise in occupancy. The staff of high competency was managing medication part and medium and lower level competent staff were managing vitals and other bedside care.
- Junior staff were separately trained for COVID early warning signs for the prompt escalation.
- Continuous training by ICN for all staff on COVID protocols.
- Ensuring the easy availability of PPEs for all categories of staff.
- Ensuring the easy availability of all necessary equipment required for managing covid patients like–
  - Steamer
  - Pulse Oximeter
  - Nebulizer etc.
- Managing raised blood sugar levels due to the use of steroids in Covid patients by continuous monitoring and insulin sliding scale.
- Managing the mental health of patients and connecting them with their anxious families by updating the attendants about their patient's condition on daily basis., connecting video calls
  - To boost their mental health we have celebrated their special occasion.
  - Geriatric patients who were at risk for falls were given special attention by frequent rounds.
  - Patients who were continuously refused to take food, we have arranged video calls with their family to ensure they eat properly, as food is the first medicine.
- We have re-deployed the staff to overcome this crisis. OT staff were posted in HDU, ER, and wards as per their skill set and competency.
- Daily thorough checking of oxygen leaking and filling of oxygen cylinders to manage for the smooth functioning of the department during emergencies.
- We ensured all the patients are visited by the dietician and recommended customized diet as per their gender, comorbidities, and any other factors.
- High-risk drugs were reconciled during the cross audit by various senior staff.
- Ensured physiotherapy at least twice a day.
- Frequent proning of the patients.
- We taught the patients about breathing exercises and yoga to encourage effortless breathing.

# Aces of Plastic Surgery

Dr Kiranmoy Sarangi




Cleft Rhinoplasty with Lip Revision.


RTA with Pan-facial fractures ...ORIF with titanium mini plates and extensive soft tissue repair done

# JOURNAL SCAN

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## 1. Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma

Menzies-Gow A, Corren J, Bourdin A, et al. N Engl J Med. 2021 May 13; 384(19): 1800-1809. doi: 10.1056/NEJMoa2034975

### Abstract

#### Background

Tezepelumab is a human monoclonal antibody that blocks thymic stromal lymphopoietin, an epithelial-cell–derived cytokine implicated in the pathogenesis of asthma. The efficacy and safety of tezepelumab in patients with severe, uncontrolled asthma require further assessment.

#### Methods

We conducted a phase 3, multicenter, randomized, double-blind, placebo-controlled trial. Patients (12 to 80 years of age) were randomly assigned to receive tezepelumab (210 mg) or placebo subcutaneously every 4 weeks for 52 weeks. The primary end point was the annualized rate of asthma exacerbations over a period of 52 weeks. This end point was also assessed in patients with baseline blood eosinophil counts of less than 300 cells per microliter. Secondary end points included the forced expiratory volume in 1 second (FEV1) and scores on the Asthma Control Questionnaire–6 (ACQ-6; range, 0 [no impairment] to 6 [maximum impairment]), Asthma Quality of Life Questionnaire (AQLQ; range, 1 [maximum impairment] to 7 [no impairment]), and Asthma Symptom Diary (ASD; range, 0 [no symptoms] to 4 [worst possible symptoms]).

#### Results

Overall, 1061 patients underwent randomization (529 were assigned to receive tezepelumab and 532 to receive placebo). The annualized rate of asthma exacerbations was 0.93 (95% confidence interval [CI], 0.80 to 1.07) with tezepelumab and 2.10 (95% CI, 1.84 to 2.39) with placebo (rate ratio, 0.44; 95% CI, 0.37 to 0.53; P<0.001). In patients with a blood eosinophil count of less than 300 cells per microliter, the annualized rate was 1.02 (95% CI, 0.84 to 1.23) with tezepelumab and 1.73 (95% CI, 1.46 to 2.05) with placebo (rate ratio, 0.59; 95% CI, 0.46 to 0.75; P<0.001). At week 52, improvements were greater with tezepelumab than with placebo with respect to the pre-bronchodilator FEV1 (0.23 vs. 0.09 liters; difference, 0.13 liters; 95% CI, 0.08 to 0.18; P<0.001) and scores on the ACQ-6 (–1.55 vs. –1.22; difference, –0.33; 95% CI, –0.46 to –0.20; P<0.001), AQLQ (1.49 vs. 1.15; difference, 0.34; 95% CI, 0.20 to 0.47; P<0.001), and ASD (–0.71 vs. –0.59; difference, –0.12; 95% CI, –0.19 to –0.04; P=0.002). The frequencies and types of adverse events did not differ meaningfully between the two groups.

#### Conclusions

Patients with severe, uncontrolled asthma who received tezepelumab had fewer exacerbations and better lung function, asthma control, and health-related quality of life than those who received placebo. (Funded by AstraZeneca and Amgen; NAVIGATOR ClinicalTrials.gov number, NCT03347279)

## 2. Vemurafenib plus Rituximab in Refractory or Relapsed Hairy-Cell Leukemia

Tiacci E , De Carolis L, Simonetti E et al. N Engl J Med. 2021 May 13; 384(19): 1810-1823.

doi: 10.1056/NEJMoa2031298

### Abstract

#### Background

Hairy-cell leukemia (HCL) is a CD20+ indolent B-cell cancer in which a BRAF V600E kinase–activating mutation plays a pathogenetic role. In clinical trials involving patients with refractory or relapsed HCL, the targeting of BRAF V600E with the oral BRAF inhibitor vemurafenib led to a response in 91% of the patients; 35% of the patients had a complete response. However, the median relapse-free survival was only 9 months after treatment was stopped.

#### Methods

In a phase 2, single-center, academic trial involving patients with refractory or relapsed HCL, we assessed the safety and efficacy of vemurafenib (960 mg, administered twice daily for 8 weeks) plus concurrent and sequential rituximab (375 mg per square meter of body-surface area, administered for 8 doses over a period of 18 weeks). The primary end point was a complete response at the end of planned treatment.

#### Results

Among the 30 enrolled patients with HCL, the median number of previous therapies was 3. A complete response was observed in 26 patients (87%) in the intention-to-treat population. All the patients who had HCL that had been refractory to chemotherapy (10 patients) or rituximab (5) and all those who had previously been treated with BRAF inhibitors (7) had a complete response. Thrombocytopenia resolved after a median of 2 weeks, and neutropenia after a median of 4 weeks. Of the 26 patients with a complete response, 17 (65%) were cleared of minimal residual disease (MRD). Progression-free survival among all 30 patients was 78% at a median follow-up of 37 months; relapse-free survival among the 26 patients with a response was 85% at a median follow-up of 34 months. In post hoc analyses, MRD negativity and no previous BRAF inhibitor treatment correlated with longer relapse-free survival. Toxic effects, mostly of grade 1 or 2, were those that had previously been noted for these agents.

#### Conclusions

In this small study, a short, chemotherapy-free, non-

myelotoxic regimen of vemurafenib plus rituximab was associated with a durable complete response in most patients with refractory or relapsed HCL. (Funded by the European Research Council and others; HCL-PG03 EudraCT number, 2014-003046-27)

### 3. Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

Dorman SE, Nahid P, Kurbatova EV et al., for the AIDS Clinical Trials Group and the Tuberculosis Trials Consortium. N Engl J Med. 2021 May 6; 384(18): 1705-1718.

doi: 10.1056/NEJMoa2033400

**Abstract**

**Background**

Rifapentine-based regimens have potent anti-mycobacterial activity that may allow for a shorter course in patients with drug-susceptible pulmonary tuberculosis.

**Methods**

In an open-label, phase 3, randomized, controlled trial involving persons with newly diagnosed pulmonary tuberculosis from 13 countries, we compared two 4-month rifapentine-based regimens with a standard 6-month regimen consisting of rifampin, isoniazid, pyrazinamide, and ethambutol (control) using a non-inferiority margin of 6.6 percentage points. In one 4-month regimen, rifampin was replaced with rifapentine; in the other, rifampin was replaced with rifapentine and ethambutol with moxifloxacin. The primary efficacy outcome was survival free of tuberculosis at 12 months.

**Results**

Among 2516 participants who had undergone randomization, 2343 had a culture positive for Mycobacterium tuberculosis that was not resistant to isoniazid, rifampin, or fluoroquinolones (microbiologically eligible population; 768 in the control group, 791 in the rifapentine–moxifloxacin group, and 784 in the rifapentine group), of whom 194 were co-infected with human immunodeficiency virus and 1703 had cavitation on chest radiography. A total of 2234 participants could be assessed for the primary outcome (assessable population; 726 in the control group, 756 in the rifapentine–moxifloxacin group, and 752 in the rifapentine group). Rifapentine with moxifloxacin was non-inferior to the control in the microbiologically eligible population (15.5% vs. 14.6% had an unfavorable outcome; difference, 1.0 percentage point; 95% confidence interval [CI], −2.6 to 4.5) and in the assessable population (11.6% vs. 9.6%; difference, 2.0 percentage points; 95% CI, −1.1 to 5.1). Non-inferiority was shown in the secondary and sensitivity analyses. Rifapentine without moxifloxacin was not shown to be non-inferior to the control in either population (17.7% vs. 14.6% with an unfavorable outcome in the microbiologically eligible population; difference, 3.0 percentage points [95% CI, −0.6 to 6.6]; and 14.2% vs. 9.6% in the assessable population; difference, 4.4 percentage points [95% CI, 1.2 to 7.7]). Adverse events of grade 3 or higher occurred during the on-treatment period in 19.3% of participants in the control group, 18.8% in the rifapentine–moxifloxacin group, and 14.3% in the rifapentine group.

**Conclusions**

The efficacy of a 4-month rifapentine-based regimen containing moxifloxacin was non-inferior to the standard 6-month regimen in the treatment of tuberculosis. (Funded by the Centers for Disease Control and Prevention and others; Study 31/A5349 ClinicalTrials.gov number, NCT02410772.)

### 4. Prevalence of symptoms of anxiety and depression in patients with inflammatory bowel disease: a systematic review and meta-analysis

Barberio B, Zamani M, Black CJ et al. Lancet Gastroenterol Hepatol. 2021 May; 6(5): 359-370. doi: 10.1016/S2468-1253(21)00014-5.

**Summary**

**Background**

Inflammatory bowel disease (IBD) is a lifelong condition with no cure. Patients with IBD might experience symptoms of common mental disorders such as anxiety and depression because of bidirectional communication via the gut–brain axis and chronicity of symptoms, and because of impaired quality of life and reduced social functioning. However, uncertainties remain about the magnitude of this problem. We aimed to assess prevalence of symptoms of anxiety or depression in adult patients with IBD.

**Methods**

In this systematic review and meta-analysis, we searched MEDLINE, Embase, Embase Classic, and PsycINFO for papers published from inception to Sept 30, 2020, reporting observational studies that recruited at least 100 adult patients with IBD and that reported prevalence of symptoms of anxiety or depression according to validated screening instruments. We excluded studies that only used a structured interview to assess for these symptoms and studies that did not provide extractable data. We extracted data from published study reports and calculated pooled prevalence of symptoms of anxiety and depression, odds ratios (OR), and 95% CIs.

**Findings**

Of 5544 studies identified, 77 fulfilled the eligibility criteria, including 30 118 patients in total. Overall, pooled prevalence of anxiety symptoms was 32•1% (95% CI 28•3–36•0) in 58 studies (I2=96•9%) and pooled prevalence of depression symptoms was 25•2% (22•0–28•5) in 75 studies (I2=97•6%). In studies that reported prevalence of anxiety or depression in patients with Crohn's disease and ulcerative colitis within the same study population, patients with Crohn's disease had higher odds of anxiety symptoms (OR 1•2, 95% CI 1•1–1•4) and depression symptoms (1•2, 1•1–1•4) than patients with ulcerative colitis. Overall, women with IBD were more likely to have symptoms of anxiety than were men

with IBD (pooled prevalence 33•8% [95% CI 26•5–41•5] for women vs 22•8% [18•7–27•2] for men; OR 1•7 [95% CI 1•2–2•3]). They were also more likely to have symptoms of depression than men were (pooled prevalence 21•2% [95% CI 15•4–27•6] for women vs 16•2% [12•6–20•3] for men; OR 1•3 [95% CI 1•0–1•8]). The prevalence of symptoms of anxiety (57•6% [95% CI 38•6–75•4]) or depression (38•9% [26•2–52•3]) was higher in patients with active IBD than in patients with inactive disease (38•1% [30•9–45•7] for anxiety symptoms and 24•2% [14•7–35•3] for depression symptoms; ORs 2•5 [95% CI 1•5–4•1] for anxiety and 3•1 [1•9–4•9] for depression).

**Interpretation**

There is a high prevalence of symptoms of anxiety and depression in patients with IBD, with up to a third of patients affected by anxiety symptoms and a quarter affected by depression symptoms. Prevalence was also increased in patients with active disease: half of these patients met criteria for anxiety symptoms and a third met criteria for depression symptoms. Encouraging gastroenterologists to screen for and treat these disorders might improve outcomes for patients with IBD.

### 5. Voxelotor in adolescents and adults with sickle cell disease (HOPE): long-term follow-up results of an international, randomized, double-blind, placebo-controlled, phase 3 trial

Howard J, Ataga KI, Brown RC et al Lancet Haematol. 2021 May; 8(5): e323-e333.

doi: 10.1016/S2352-3026(21)00059-4.

**Summary**

**Background**

For decades, patients with sickle cell disease have had only a limited number of therapies available. In 2019, voxelotor (1500 mg), an oral once-daily sickle hemoglobin polymerization inhibitor, was approved in the USA for the treatment of sickle cell disease in patients aged 12 years and older on the basis of HOPE trial data. To further describe the applicability of voxelotor as a treatment for this chronic illness, we report the long-term efficacy and safety of this drug at 72 weeks of treatment; the conclusion of the placebo-controlled HOPE trial.

**Methods**

HOPE is an international, randomized, double-blind, placebo-controlled, phase 3 trial done at 60 clinical sites in Canada, Egypt, France, Italy, Jamaica, Kenya, Lebanon, Netherlands, Oman, Turkey, the USA, and the UK. Patients (aged 12–65 years) with confirmed sickle cell disease, a hemoglobin concentration of 5•5–10•5 g/dL at enrolment, and who had between one and ten vaso-occlusive crisis events in the previous 12 months were enrolled. Patients receiving regularly scheduled transfusion therapy, who had received a transfusion in the previous 60 days, or who had been admitted to hospital for a vaso-occlusive crisis in the previous 14 days were excluded. Patients were randomly assigned (1:1:1) to receive either once-daily oral voxelotor 1500 mg, voxelotor 900 mg, or placebo for 72 weeks. Randomization was done centrally by use of an interactive web response system, stratified by baseline hydroxyurea use (yes vs no), age group (adolescents [12 to <18 years] vs adults [18 to 65 years]), and geographic region (North America vs Europe vs other). The primary endpoint (already reported) was the proportion of patients who achieved a hemoglobin response at week 24. In this final analysis, we report pre-specified long-term efficacy assessments by intention to treat, including changes in hemoglobin concentrations from baseline to week 72, changes in the concentration of hemolysis markers (absolute and percentage reticulocytes, indirect bilirubin concentrations, and lactate dehydrogenase concentrations) from baseline to week 72, the annualized incidence of vaso-occlusive crises, and patient functioning, as assessed with the Clinical Global Impression of Change (CGI-C) scale. Safety was assessed in patients who received at least one dose of treatment (modified intention-to-treat population). This trial is registered with ClinicalTrials.gov, NCT03036813.

**Findings**

Between Dec 5, 2016, and May 3, 2018, 449 patients were screened, of whom 274 were randomly assigned to the voxelotor 1500 mg group (n=90), the voxelotor 900 mg group (n=92), or the placebo group (n=92). At week 72, the adjusted mean change in hemoglobin concentration from baseline was 1•0 g/dL (95% CI 0•7 to −1•3) in the voxelotor 1500 mg group, 0•5 g/dL (0•3 to −0•8) in the voxelotor 900 mg group, and 0•0 g/dL (−0•3 to 0•3) in the placebo group, with a significant difference observed between the voxelotor 1500 mg group and the placebo group (p<0•0001), and between the voxelotor 900 mg group and the placebo group (p=0•014). Significant improvements in markers of hemolysis, as assessed by the difference in adjusted mean percentage change from baseline at week 72 versus placebo, were observed in the voxelotor 1500 mg group in indirect bilirubin concentrations (−26•6% [95% CI −40•2 to −12•9]) and percentage of reticulocytes (−18•6% [−33•9 to −3•3]). The proportion of patients in the voxelotor 1500 mg group who were rated as "moderately improved" or "very much improved" at week 72 with the CGI-C was significantly greater than in the placebo group (39 [74%] of 53 vs 24 [47%] of 51; p=0•0057). Serious adverse events unrelated to sickle cell disease were reported in 25 (28%) of 88 patients in the voxelotor 1500 mg group, 20 (22%) of 92 patients in the voxelotor 900 mg group, and 23 (25%) of 91 patients in the placebo group. Grade 3 or 4 adverse events were infrequent (i.e., occurred in <10% of patients); anemia occurred in five or more patients (two [2%] patients in the voxelotor 1500 mg group, seven [8%] patients in the voxelotor 900 mg group, and three [3%] patients in the placebo group). Of all 274 patients, six (2%) deaths occurred during the study (two deaths in each treatment group), all of which were judged as unrelated to treatment.

**Interpretation**

Voxelotor 1500 mg resulted in rapid and durable improvements in hemoglobin concentrations

maintained over 72 weeks and has potential to address the substantial morbidity associated with hemolytic anemia in sickle cell disease.

### 6. Associations between body-mass index and COVID-19 severity in 6•9 million people in England: a prospective, community-based, cohort study

Gao M, Piernas C, Astbury NM et al. Lancet Diabetes Endocrinol. 2021 Jun; 9(6): 350-359.

doi: 10.1016/S2213-8587(21)00089-9.

#### Background

Obesity is a major risk factor for adverse outcomes after infection with SARS-CoV-2. We aimed to examine this association, including interactions with demographic and behavioral characteristics, type 2 diabetes, and other health conditions.

#### Methods

In this prospective, community-based, cohort study, we used de-identified patient-level data from the QResearch database of general practices in England, UK. We extracted data for patients aged 20 years and older who were registered at a practice eligible for inclusion in the QResearch database between Jan 24, 2020 (date of the first recorded infection in the UK) and April 30, 2020, and with available data on BMI. Data extracted included demographic, clinical, clinical values linked with Public Health England's database of positive SARS-CoV-2 test results, and death certificates from the Office of National Statistics. Outcomes, as a proxy measure of severe COVID-19, were admission to hospital, admission to an intensive care unit (ICU), and death due to COVID-19. We used Cox proportional hazard models to estimate the risk of severe COVID-19, sequentially adjusting for demographic characteristics, behavioral factors, and comorbidities.

#### Findings

Among 6 910 695 eligible individuals (mean BMI 26•78 kg/m2 [SD 5•59]), 13 503 (0•20%) were admitted to hospital, 1601 (0•02%) to an ICU, and 5479 (0•08%) died after a positive test for SARS-CoV-2. We found J-shaped associations between BMI and admission to hospital due to COVID-19 (adjusted hazard ratio [HR] per kg/m2 from the nadir at BMI of 23 kg/m2 of 1•05 [95% CI 1•05–1•05]) and death (1•04 [1•04–1•05]), and a linear association across the whole BMI range with ICU admission (1•10 [1•09–1•10]). We found a significant interaction between BMI and age and ethnicity, with higher HR per kg/m2 above BMI 23 kg/m2 for younger people (adjusted HR per kg/m2 above BMI 23 kg/m2 for hospital admission 1•09 [95% CI 1•08–1•10] in 20–39 years age group vs 80–100 years group 1•01 [1•00–1•02]) and Black people than White people (1•07 [1•06–1•08] vs 1•04 [1•04–1•05]). The risk of admission to hospital and ICU due to COVID-19 associated with unit increase in BMI was slightly lower in people with type 2 diabetes, hypertension, and cardiovascular disease than in those without these morbidities.

#### Interpretation

At a BMI of more than 23 kg/m2, we found a linear increase in risk of severe COVID-19 leading to admission to hospital and death, and a linear increase in admission to an ICU across the whole BMI range, which is not attributable to excess risks of related diseases. The relative risk due to increasing BMI is particularly notable people younger than 40 years and of Black ethnicity.

### 7. Aspirin versus anticoagulation in cervical artery dissection (TREAT-CAD): an open-label, randomized, non-inferiority trial

Engelter ST, Traenka C, Gensicke H et al. Lancet Neurol. 2021 May; 20(5): 341-350.

doi: 10.1016/S1474-4422(21)00044-2.

#### Background

Cervical artery dissection is a major cause of stroke in young people (aged <50 years). Historically, clinicians have preferred using oral anticoagulation with vitamin K antagonists for patients with cervical artery dissection, although some current guidelines—based on available evidence from mostly observational studies—suggest using aspirin. If proven to be non-inferior to vitamin K antagonists, aspirin might be preferable, due to its ease of use and lower cost. We aimed to test the non-inferiority of aspirin to vitamin K antagonists in patients with cervical artery dissection.

#### Methods

We did a multicenter, randomized, open-label, non-inferiority trial in ten stroke centers across Switzerland, Germany, and Denmark. We randomly assigned (1:1) patients aged older than 18 years who had symptomatic, MRI-verified, cervical artery dissection within 2 weeks before enrolment, to receive either aspirin 300 mg once daily or a vitamin K antagonist (phenprocoumon, acenocoumarol, or warfarin; target international normalized ratio [INR] 2•0–3•0) for 90 days. Randomization was computer-generated using an interactive web response system, with stratification according to participating site. Independent imaging core laboratory adjudicators were masked to treatment allocation, but investigators, patients, and clinical event adjudicators were aware of treatment allocation. The primary endpoint was a composite of clinical outcomes (stroke, major hemorrhage, or death) and MRI outcomes (new ischemic or hemorrhagic brain lesions) in the per-protocol population, assessed at 14 days (clinical and MRI outcomes) and 90 days (clinical outcomes only) after commencing treatment. Non-inferiority of aspirin would be shown if the upper limit of the two-sided 95% CI of the absolute risk difference between groups was less than 12% (non-inferiority margin). This trial is registered with ClinicalTrials.gov, NCT02046460.

#### Findings

Between Sept 11, 2013, and Dec 21, 2018, we enrolled 194 patients; 100 (52%) were assigned to the aspirin group and 94 (48%) were assigned to the vitamin K antagonist group. The per-protocol population included 173 patients; 91 (53%) in the aspirin group and 82 (47%) in the vitamin K antagonist group. The primary endpoint occurred in 21 (23%) of 91 patients in the aspirin group and in 12 (15%) of 82 patients in the vitamin K antagonist

group (absolute difference 8% [95% CI −4 to 21], non-inferiority p=0•55). Thus, non-inferiority of aspirin was not shown. Seven patients (8%) in the aspirin group and none in the vitamin K antagonist group had ischaemic strokes. One patient (1%) in the vitamin K antagonist group and none in the aspirin group had major extracranial hemorrhage. There were no deaths. Subclinical MRI outcomes were recorded in 14 patients (15%) in the aspirin group and in 11 patients (13%) in the vitamin K antagonist group. There were 19 adverse events in the aspirin group, and 26 in the vitamin K antagonist group.

**Interpretation**

Our findings did not show that aspirin was non-inferior to vitamin K antagonists in the treatment of cervical artery dissection.

### 8. Peg interferon lambda for the treatment of outpatients with COVID-19: a phase 2, placebo-controlled randomized trial

Feld JJ, Kandel C, Biondi MJ, et al. Lancet Respir Med. 2021 May; 9(5): 498-510.

doi: 10.1016/S2213-2600(20)30566-X.

**Background**

To date, only monoclonal antibodies have been shown to be effective for outpatients with COVID-19. Interferon lambda-1 is a type III interferon involved in innate antiviral responses with activity against respiratory pathogens. We aimed to investigate the safety and efficacy of peg interferon lambda in the treatment of outpatients with mild-to-moderate COVID-19.

**Methods**

In this double-blind, placebo-controlled trial, outpatients with laboratory-confirmed COVID-19 were randomly assigned to a single subcutaneous injection of peg interferon lambda 180 μg or placebo within 7 days of symptom onset or first positive swab if asymptomatic. Participants were randomly assigned (1:1) using a computer-generated randomization list created with a randomization schedule in blocks of four. At the time of administration, study nurses received a sealed opaque envelope with the treatment allocation number. The primary endpoint was the proportion of patients who were negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA on day 7 after the injection, analyzed by a $\chi 2$ test following an intention-to-treat principle. Pre-specified analysis of the primary endpoint, adjusted for baseline viral load, using bivariate logistic regression was done. The trial is now complete. This trial is registered with ClinicalTrials.gov, NCT04354259.

**Findings**

Between May 18, and Sept 4, 2020, we recruited 30 patients per group. The decline in SARS-CoV-2 RNA was greater in those treated with peg interferon lambda than placebo from day 3 onwards, with a difference of 2•42 log copies per mL at day 7 (p=0•0041). By day 7, 24 (80%) participants in the peg interferon lambda group had an undetectable viral load, compared with 19 (63%) in the placebo group (p=0•15). After controlling for baseline viral load, patients in the peg interferon lambda group were more likely to have undetectable virus by day 7 than were those in the placebo group (odds ratio [OR] 4•12 [95% CI 1•15–16•73; p=0•029). Of those with baseline viral load above 106 copies per mL, 15 (79%) of 19 patients in the peg interferon lambda group had undetectable virus on day 7, compared with six (38%) of 16 in the placebo group (OR 6•25 [95% CI 1•49–31•06]; p=0•012). Peg interferon lambda was well tolerated, and adverse events were similar between groups with mild and transient aminotransferase, concentration increases more frequently observed in the peg interferon lambda group. Two individuals met the threshold of grade 3 increase, one in each group, and no other grade 3 or 4 laboratory adverse events were reported.

**Interpretation**

Peg interferon lambda accelerated viral decline in outpatients with COVID-19, increasing the proportion of patients with viral clearance by day 7, particularly in those with high baseline viral load. Peg interferon lambda has potential to prevent clinical deterioration and shorten duration of viral shedding.

### 9. Effect of sodium hyaluronate-arboxycellulose membrane (Seprafilm) on postoperative small bowel obstruction: A meta-analysis

Hajibandeh S, Hajibandeh S. Surgery. 2021 Jun; 169(6): 1333-1339.

doi: 10.1016/j.surg.2020.12.004.

**Background**

This meta-analysis was performed to evaluate the effect of Seprafilm on postoperative small bowel obstruction.

Methods

A literature search was conducted in the PubMed and EMBASE databases through August 2020. The pooled risk ratios as well as the corresponding 95% confidence intervals were calculated using RevMan 5.3 software.

**Results**

A total of 9 clinical control trials involving 4,351 patients (2,123 in the Seprafilm group and 2,228 in the control group) were included. The overall analysis showed that the pooled risk ratio was 0.45 (95% confidence interval = 0.34–0.60; P < .00001), indicating that the risk of postoperative small bowel obstruction can be significantly decreased by the application of Seprafilm. Similarly, an obvious effect of Seprafilm on reducing the rate of postoperative small bowel obstruction was also shown in the subgroup analyses by population (adult participants), study design (randomized control study or nonrandomized control study), region (Japan or Korea), follow-up duration (2 years or 5 years), and sheet number of Seprafilm (1 sheet or >1 sheet).

**Conclusion**

In conclusion, the use of Seprafilm is beneficial for decreasing the rate of postoperative small bowel obstruction.

**10. Functional outcomes & metal ion levels following ceramic on metal total hip arthroplasty: 9 Year follow-up**

Mehta N, Patel D, Leong J, Brown P, Carroll FA. J Orthop. 2021 Feb 23; 24: 131-134.

doi: 10.1016/j.jor.2021.02.030

**Abstract**

In this study, we evaluate the mid-term functional and radiological outcomes of Ceramic on Metal Total Hip Arthroplasty (CoM THA) THA. 66 CoM THAs were performed between 2008 and 2010. These were evaluated and followed up in 2017-18, at a mean follow-up of 9 years to record the Oxford Hip Score [OHS] and whole blood Cobalt and Chrome levels. Our all cause revision rate was 4.5% (3 out of 66). At mid-term follow up, patients with CoM THAs are mostly asymptomatic with reasonable functional outcomes, we have reported similar revision rates in conjunction with raised blood metal ion levels and frequency of radiolucent lines.


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