



National Board of Examination (NBE) Journal of Medical Sciences

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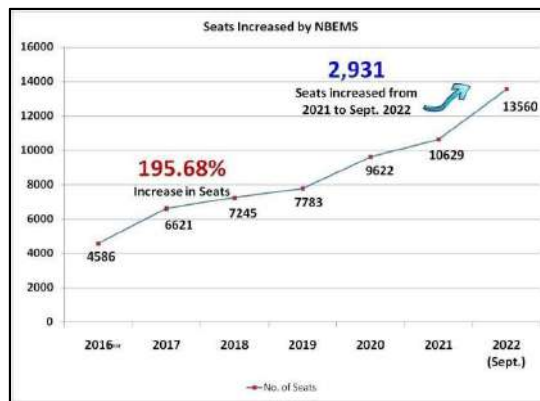
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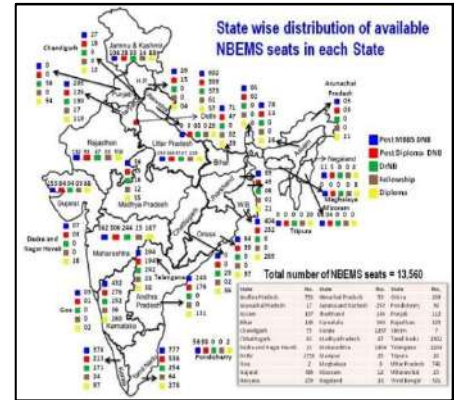
Current and Future Trajectory of NBEMS

Enhancement of PG Seats in NBEMS Accredited Hospitals.

एन. बी. ई. एम. एस. मान्यता प्राप्त हस्पतालो में स्नातकोत्तर सीटों की वृद्धि



Enhancement of PG Seats



State wise distribution of seats

Multimodality Management of Two Pairs of Pyopagus Twins

प्योपेगस जुड़वाँ बच्चों के दो जोड़ो का बहुपद्धतिय प्रबंधन



Pyopagus conjoined twins



Separated twins

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**NATIONAL BOARD OF EXAMINATIONS –
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EDITORIAL

National Board of Examination in Medical Sciences (NBEMS): Current and Future Trajectories — Part-1

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N. Iboyaima Mangang,³ Vinay Gupta,³ Richa Raju,³ N. Rashmi Raj N,³ Devender³ and Sandhya³

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Introduction

NBEMS is registered as an autonomous organization under Ministry of Health & Welfare, Government of India with effect from 01.03.1982 under Societies Registration Act, 1860 and thereafter started its independent functions. Over last 4 decades, NBEMS has been working hard to achieve the objectives mentioned in the Memorandum of Association and Rules and Regulations of NBEMS. The Government of India established the NBEMS with the objective of improving the quality of Medical Education by establishing high and uniform standards of postgraduate examinations in modern medicine on an all-India basis and utilizing existing infrastructure for capacity building. NBEMS at present conducts postgraduate and post-doctoral examination in approved specialities leading to the award of Diplomate of National Board (DNB), Doctorate of National Board (DrNB) Diploma and Fellow of National Board (FNB) respectively. These qualifications awarded by NBEMS in various broad specialities, super specialties and sub-specialties are approved by the Government of India and included in the first schedule of IMC (repealed) Act 1956 / NMC Act 2019. The equivalence of NBEMS qualifications with the corresponding MD/MS or DM/MCh

awarded under the ambit of NMC has also been defined in the above mentioned NMC Act. The examinations conducted by NBEMS provide a common standard mechanism of evaluation of minimum level of attainment of knowledge and competencies of medical specialities. Moreover, intra country and international comparisons are facilitated with availability of common evaluation mechanism.

The dire need of specialists in the country has been long been felt and NBEMS is contributing to a great proportion of this need through its alumni. The NBEMS has accredited more than 1300 hospitals across the country with almost 100 disciplines of modern medicine. NBEMS is contributing more the 13000 DNB/DrNB/FNB seats to the pool of post-graduate, doctoral and post-doctoral seats in the country.

The very basis of creation of NBEMS was to address the issue of uniform standards of medical education across the country. As on date, the NBEMS has successfully established a robust mechanism of uniform accreditation, uniform standardized education and uniform examination in medical disciplines in the country which have been internationally acclaimed (Fig. 1).

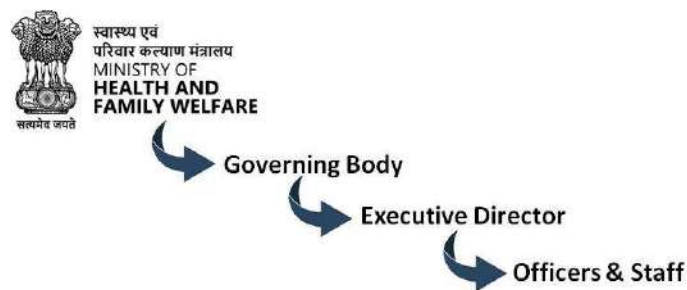


Fig. 1. Organizational Structure of NBEMS

The key objective(s) of NBEMS

- To improve the quality of medical education by elevating the level and standards of postgraduate examinations in modern medicine at the National level.
- To constitute a national resource for assuring quality in evaluation in professional competence in medical disciplines.
- To develop patterns of and to conduct post-graduate examinations ensuring a uniform standard which certifies ability of the candidate thus qualified to practice independently in the specialty.
- To conduct research in methodology of evaluation with a view to designing better methods to evaluate identified areas of professional knowledge, skills and attitudes, and to improve definition of standards of achievement for certification.
- To lay down guidelines and minimum requirements for institutions to be recognised for training of candidates in different specialties.
- To constitute an accreditation committee to evaluate the inspection reports and make appropriate recommendations to the Board (Figs. 2 and 3).

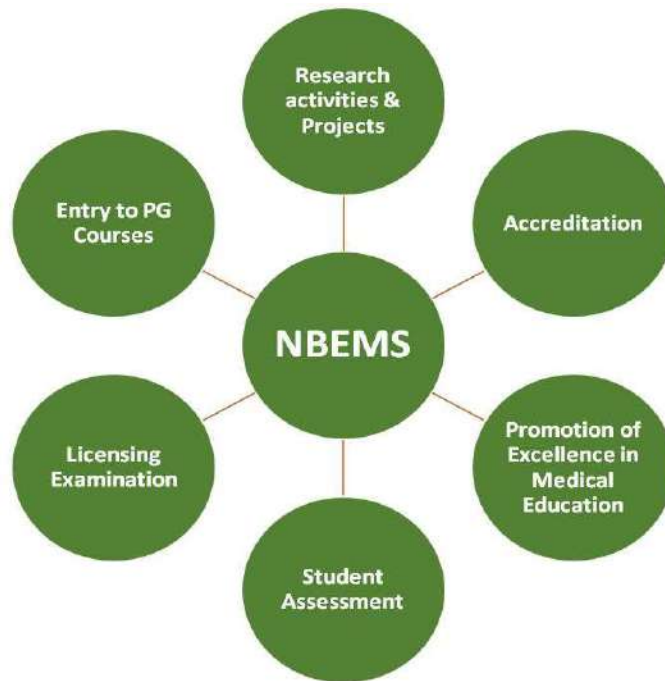


Fig. 2. Scope of functions

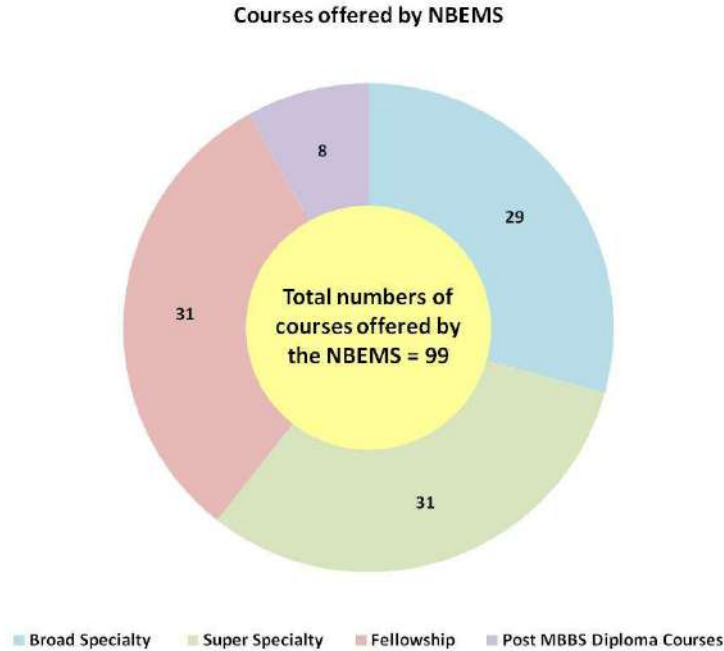


Fig. 3. Courses offered by NBEMS (A total number of courses offered by the NBEMS are 99 which includes 14 courses launched by Hon'ble Union Minister of Health and Family Welfare Dr. Mansukh Mandaviya on the 41st Foundation Function of NBEMS on 14-03-2022).

NBEMS Present Seats Status (Figs. 4-7)

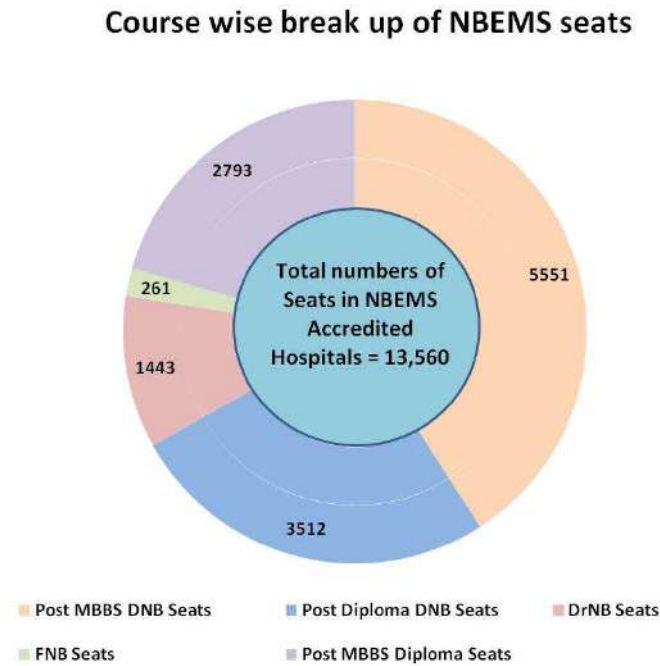


Fig. 4. Course wise break up of Seats in NBEMS Accredited Hospitals (Sept., 2022)

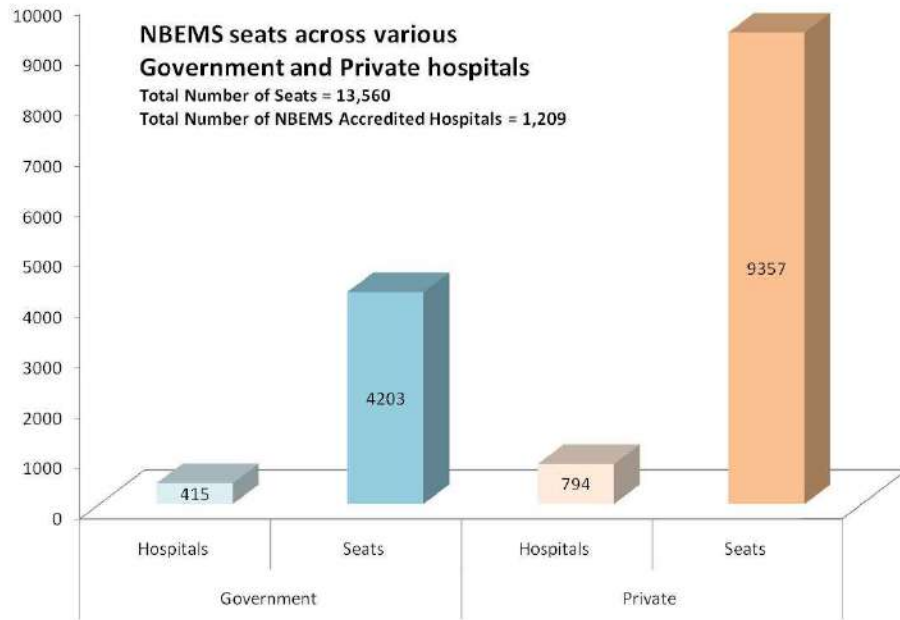


Fig. 5. Break up of NBEMS Seats in Government and Private Hospitals / Institutions

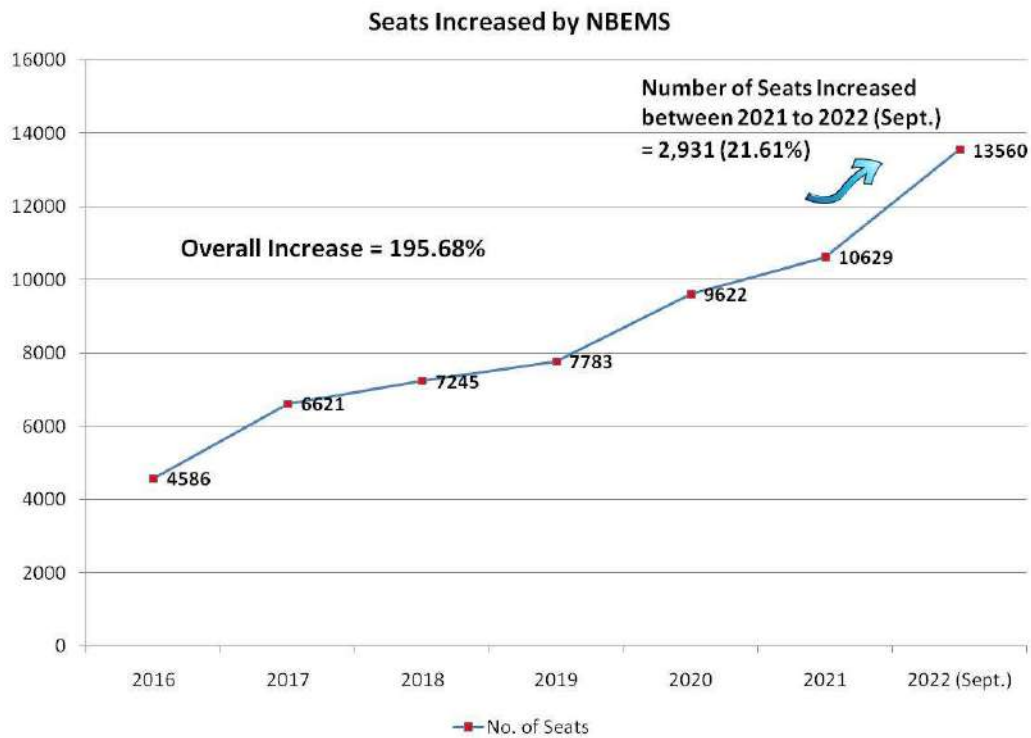


Fig. 6. Enhancement of PG Seats in NBEMS Accredited Hospitals.

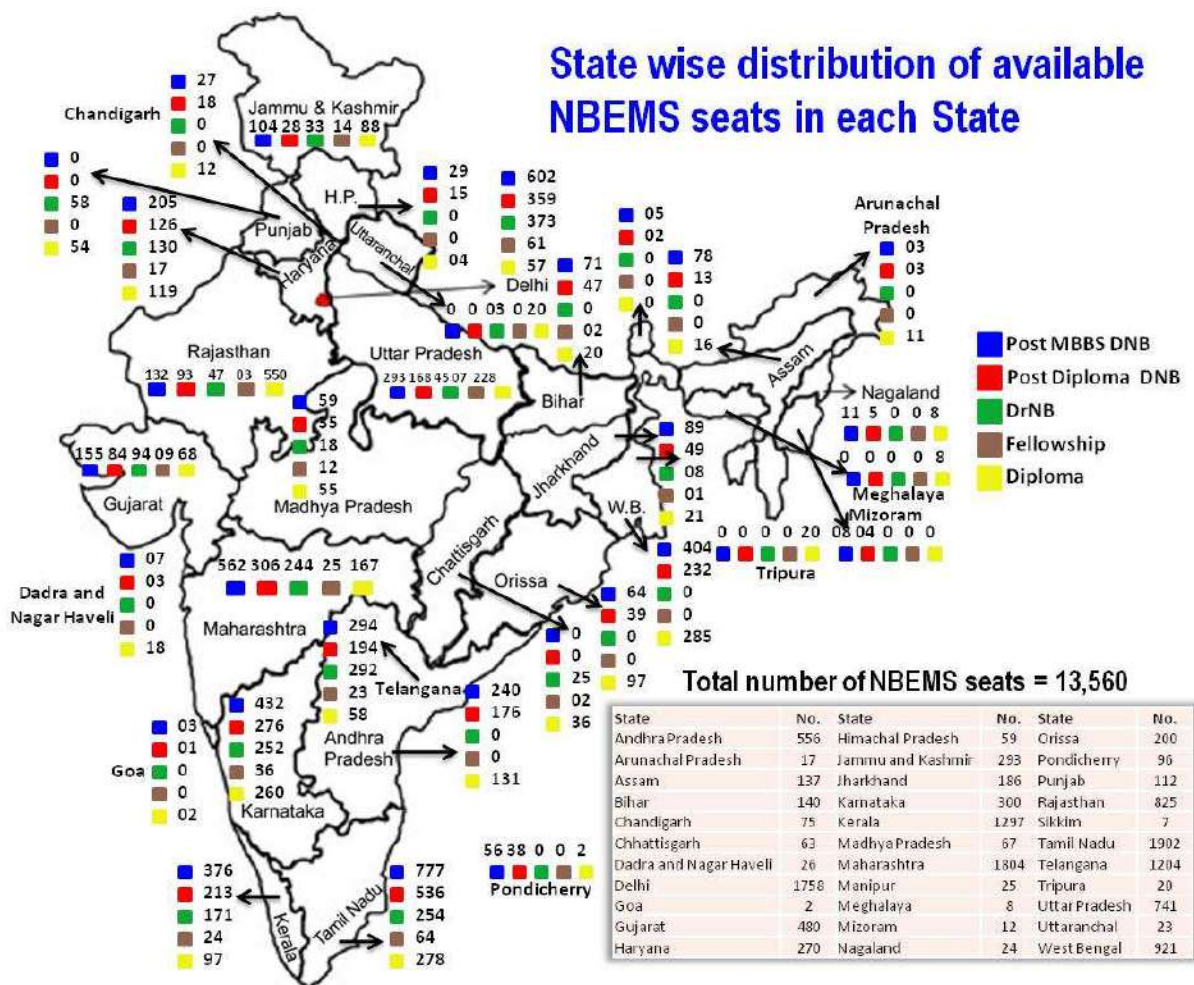


Fig. 7. State wise distribution of available NBEMS seats each Indian state and union territory.

One of the main objectives of NBEMS is to improve the quality of medical education with assurance to quality assessment of capability in medical sciences by establishment of national resource, to ensure a uniform pattern of post-graduate medical examination, research in evaluation methodology, to help and cooperate with the medical institutions with principle evaluation strategy.

Its mission is to use the existing resources and facilitate collaboration of existing medical institutions for the establishment of strong, innovative, low cost post-graduation teaching programme in medical sciences to provide skilled human resources. The vision of NBEMS is to establish the highest standards in medical care and make India a centre of skilled

and specialist doctors with the capability to reduce dissimilarities between urban and rural regions.

Improvement of quality of education

Students are the most important stakeholders. Adequate and relevant training has to be imparted to them in accordance with the curriculum to make them a safe and competent doctor. Some of the measures to be taken by hospitals for improvement of quality of training and education are:

- Allowing adequate hands on experience.
- Availability of adequate education resource material.
- Bedside teaching to be promoted.

- Seminars, lectures and Journal clubs to be held regularly.
- Mock examinations to be undertaken.
- Develop mentor – mentee relationship.
- Promote research and publications; Improvement in quality of thesis.
- Provide an academic atmosphere to attend webinar classes organized by NBEMS.

NBEMS measures for seat enhancement

A. The following steps have been taken by NBEMS for enhancement of NBEMS seats:

- Applications are being invited for all the courses twice a year.
- The application window for submission of applications forms is 2 to 3 months.
- The documentary requirements for the proposed faculty members for DNB courses has been relaxed without compromising on their full-time status. The faculty from the Government Hospitals are being considered for DNB courses on the basis of appointment order. For the faculty in private hospitals, the documentary requirement has been eased and wherever the faculty does not provide Form 26, they have been given an option to submit a Bipartite Agreement / Tripartite Agreement to confirm that they are working in the application hospital on full time basis.

Joint Accreditation

- ***Strengthening of Externship model:*** It was observed that applications from Government Hospitals for accreditation are

sometimes deficient in case mix. For example, in the specialty of Obstetrics & Gynecology there could be a surplus of Obstetrics load in a given hospital but a sub-optimal Gynecological load. It was observed, that, often applications from Private Hospitals had more of Gynecological cases and less Normal Vaginal Deliveries. NBEMS has come up with a scheme of joint accreditation, in which two hospitals could collaborate by way of MoU to complement each other's case mix. This scheme has the potential to allow many hospitals, hitherto, not participating in PG training now becoming eligible for accreditation.

B. NBEMS is giving opportunity to all accredited departments to apply for seat enhancement (at no extra cost).

- The hospital is required to fill and submit a two page application form for seat enhancement, which can be seen at following link:
- Proforma of seat enhancement (https://accr.natboard.edu.in/online_user/frontpage.php?v=6)
- Application forms would be processed as per minimum accreditation criteria and final decision shall be taken by the competent authority.

Significant steps taken by NBEMS in the last 5 years.

1. The NBEMS has taken proactive steps for conducting various post graduate and

post-doctoral courses and to facilitate accreditation of hospitals, ensuring quality in training. The NBEMS has achieved about 200% increase in the number of training seats in the last six years. In the year 2016 we had 4586 seats which increased to 13560 up to September 2022.

2. To compensate for the closure of NMC led diploma programs in 8 specialties (Anaesthesia, Obstetrics, Paediatrics, Family Medicine, ENT, Orthopaedics, Ophthalmology, Radiodiagnosis, Tuberculosis and Chest Diseases), NBEMS has initiated post-MBBS diploma seats in all the eight disciplines. This is a significant initiative taken by the NBEMS after consultations with NITI Aayog, NMC and Ministry of Health and Family Welfare (MOHFW). This has been notified in August 2020 and these courses are approved by the MOHFW and scheduled in the first notification of MCI Act 1956. The NBEMS envisages, that, these courses will form the task force in primary health centre and district hospitals of the country. It will also encourage the doctors working in government medical institutions towards skill development & ultimately strengthening the efforts of Government of India in its healthcare reforms. It is noteworthy that during its first year more than 2000 seats have already been awarded.
3. The Fellowship Programme for International Students (FPIS) has been launched in July 2020. This is the first of its kind programme at National level in which NBEMS provides the opportunity to foreign medical graduates to take fellowship courses in India. The NBEMS also placed this programme as part of Prime Minister's "Neighborhood First"

scheme. The official mechanism of MOHFW will help NBEMS to offer and collaborate with SAARC countries via this programme to strengthen India's relationship with its neighbours.

Fellowship programmes for International Students:

- 1) Hand and Micro Surgery
- 2) Maternal and Foetal Medicine
- 3) Infectious Diseases
- 4) Interventional Cardiology
- 5) Minimal Access Surgery
- 6) Paediatric Haemato-oncology
- 7) Reproductive Medicine
- 8) Spine Surgery
- 9) Sports Medicine
- 10) Trauma and Acute Care Surgery

The eligibility criteria to grant a seat for Fellowship Programme for International Students to an accredited department for a particular Fellowship Course is as under:

“Hospitals already accredited for FNB programme in a specialty for two seats for at least three years and have undergone three admission cycles are eligible to apply for training of International Students for the fellowship course in the concerned specialty.”

4. To create new courses / programmes, modifications or updates in existing teaching programmes and to introduce reforms on teaching/training and all aspects of conducting an examination. The NBEMS considers the suggestions made by the stakeholders. The NBEMS has created boards for all specialties which also make their recommendations from time to time.
5. NBEMS has designed the standardized curricula in all specified subjects and

- ensures that the NBEMS teaching/training programmes are streamlined.
6. The NBEMS has added 4 Fellowships and 3 DrNB/ DNB programme in the last few years in the essential areas of clinical care such as critical care, oncology, pain medicine and palliative care.
 7. By reserving seats for serving doctors, it has increased the capacity of healthcare system in India.
 8. Similar efforts are underway to implement the sponsored seat programme to enable NBEMS to further increase the number of training seats.
 9. DNB in Hospital Administration: Considering, that, few hospitals were accredited for a course hospital administration, efforts have been made to enhance the number of seats in this subject, too (Table 1).

Table 1. Eligibility criteria for DNB Hospital Administration

Specialty	Minimum Eligible Qualification(s)	Minimum Experience after PG in Minimum Eligible Qualification	
		Senior Consultant	Junior Consultant
Hospital Administration	Primary Degree MBBS and DNB(HA)/MD(HA)/MD(CHA) or MHM/MHA from deemed/Government recognized universities (full time course)	8 Years	5 Years

The Health Secretary to the Union Government has also augmented the efforts of the NBEMS from time to time. An online meeting was held with the Principal Secretaries of all the States, informing them about the programme. The Diploma Courses have been very successful. Several district and sub-district hospitals are now participating in the Diploma Courses. This has provided specialist manpower to the semi-urban / rural areas, and the patients do not have to travel to bigger cities for quality treatment. Diploma Courses are a boon for the State Government, medical fraternity, students and patients alike.

10. Some of the other achievements of the National Board include:

- Successful processing of all MCQ based examination on Computerized platform
- Computerized Merit based Counseling
- National Web Learning Programme
- Launch of E-Doc Log Book
- Development of online Thesis Evaluation and Thesis Repository
- Introduction of OSCE system in several specialties for final exit examination to reduce the impact of COVID-19 pandemic on NBEMS evaluation process (Table 2).

Table 2. Courses Launched in 2022

S. No.	Speciality	S. No.	Speciality
1.	Renal Transplant	8.	Onco - Anaesthesia
2.	Andrology	9.	Transplant Anaesthesia
3.	Minimal Access Urology	10.	Trauma Anaesthesia and Critical Care
4.	Paediatric Urology	11.	Head and Neck Oncology
5.	Musculoskeletal Radiology	12.	Bariatric Surgery
6.	Foetal Radiology	13.	Cardiac Electrophysiology
7.	Paediatric Anaesthesia		

- Strengthen the Complaint Redressal Mechanism for its stakeholders (<https://natboard.edu.in/>)
- Preparation of handbooks for trainees of NBEMS in all the courses (<https://natboard.edu.in/>)
- Focus on developing an innovative accreditation system to offer more seats without compromising the quality.
 - In this context, organization of webinar class have been increased further with the help of digital technology
 - With the inclusion of all NBEMS stakeholders and through a consultative mechanism, the NBEMS is committed to its vision and mission through its standard process.
- **NBEMS Reforms, in brief:**
 - Profound trajectory of growth has been witnessed in the last 6 yrs with a quantum enhancement of PG seats from 4000 to 13000 per year
 - Leadership matters & Hon'ble Minister Dr. Mansukh Mandaviya has personally led the pace of current developments.
 - Constant encouragement is received from Advisor health in NITI Ayog Prof. VK Paul & support of officials in the Ministry of Health & Family welfare
 - NITI Ayog expects NBEMS to double up the seats to 25000 in the next 2-3 years.
- Other revolutionary reforms are underway at the time of going to the press.
- **Joint accreditation would be a key scheme in enhancing the PG seats:**
 - Efforts on Skill Laboratory development are at an advanced stage with special emphasis to impart skill-training to NBEMS trainees.
- **Addressing Poor Case mix:**
 1. By Joint accreditation between TWO hospitals, who are independently ineligible to participate in PG training could now collaborate & take candidates for training.
 2. India has 65000 private hospitals & even if 10% of them participate in accreditation through Joint accreditation, it would result in much augmented hospital space for training. Currently we have 1300 hospitals with 13000 PG seats & our conservative estimate is to increase these numbers by 6 times.
- **Constant endeavour:**
 1. To achieve & maintain high standards of training &
 2. To bring uniformity of training across all programmes in each & every speciality

This is being achieved by:

- Live streaming of WEBINARS through NBEMS technology HUB.
- Contribution of course material by 100 specialty boards & 4000 plus specialists' registry of the NBEMS which include:
 - State of the art lectures
 - Seminars
 - COMPLEX Case discussions with interaction with postgraduates & procedural videos in each specialty.

- **Introduction of:**

- Skill enhancing courses through the soon to be commissioned State of the art National Skill Centre.
- Simultaneous, engagement with 25 pre-identified & intensively monitored centres with an equitably distribution across the country.
- Digitally facilitated & App- enabled, Formative Assessment:
- Digitally Enabled Round Books

- **Faculty development programme:**

- **'Training of Trainers'** through Workshops in:
 - Methodology of Teaching & Research through Clinical Trial Units
 - Participation in C.M.Es with credit points
- Performance based incentivization (after approval by G.B.)
- Conferring performance based academic titles of the National Board - at par with the medical colleges
- Regular brain storming sessions, academic & innovative inputs by the recently created Registry of NBEMS faculty

- The NBEMS, has proposed MBBS programmes in private hospitals. On this subject, the Hon'ble Minister held- first round of talk with the CEOs across the country.

Expanding the NBEMS Teachers base:

- **Teacher Eligibility Qualification (TEQ):**
 - NBEMS follows NMC recommendations on TEQ
 - Rapid expansion of PG courses & an increase in number of seats would require a larger pool of experienced teachers

Conclusion

The ultimate aim of the NBEMS is to provide universal access to high-quality health care services. Some proactive steps have been taken by the NBEMS towards universal quality coverage. NBEMS accreditation programme has been successfully implemented in government and private hospital settings. NBEMS is focusing on a strategy to reach all parts of India including rural, urban, sub-urban and remote areas with affordable healthcare system with the security of affordable & quality health care. The main objectives of NBEMS is improve the quality of medical education with an enhanced capacity & by establishing the national resource. Thus, ensuring a uniform pattern of post-graduate medical examination & research in evaluation methodology.



EDITORIAL

Birth Defects, Paediatric Surgeons & The Pyopagus Conjoined Twins during the 2020 Pandemic

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Surgically correctible Birth Defects are also known as Congenital Malformations. The incidence of structural birth defects which are amenable to surgery is 2–3% of all births. Considering the total birth rate in India it amounts to large numbers of children who need corrective surgery.

Birth defect surgery is performed by Paediatric Surgeons. The major surgeries could be carried out in tertiary care centres and require Paediatric Surgeons as well as Paediatric Anesthetists besides skilled Nursing care. While many of these could be treated in medical colleges & even district hospitals, the overall number of these specialists are inadequate in the country.

Paediatric surgery is a specialized field with a cadre of surgeons who perform surgery in children from newborn to up to 18 years of age.

During the Pandemic, published National statistics of treatment received for various conditions in the country, showed an overall decrease in numbers, mostly for routine surgeries during the Pandemic. Birth defect surgery took the biggest hit as it was reduced to 1/3rd of the numbers before COVID-19 Pandemic, viz., 20.9 lakhs in 2019 to 2.6 lakhs with a percentage drop of –87% as per the Ministry of Health's 'Rashtriya Bal Swasthya Karyakram'. (Some statistics are depicted in Figure 1).

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However, despite the Pandemic, irrespective of COVID-19 positivity, lifesaving emergencies continued to receive priority.

During this period, surgeries continued to be offered to newborns. It also included other emergencies involving various organ systems in children, yet, several more elective organ salvage surgeries had to be postponed.

Conjoined twins are a very rare developmental accident of uncertain etiology. Prevalence has been previously estimated to be 1 in 50,000 to 1 in 100,000 births.

Two pairs of Pyopagus, conjoined twins were successfully separated at Department of Paediatric Surgery, All India Institute of Medical Sciences, New Delhi, during the Pandemic. The two-year-old, twin sisters successfully recovered.

While the department of surgery has experience of operating upon conjoined twins in the past, Pyopagus Conjoined twins have been operated for the first time. The challenge in the surgery was the separation of their fused spinal cords without risking neural injury. This part of surgery was accomplished by detailed microdissection with dynamic neurophysiology monitoring and it occupied the major part of the surgical time. Nevertheless, this enabled excellent outcome without inflicting neural injury, thus, restoring the pre-operative status.

The first pair of Pyopagus twins underwent Surgery in May, 2020.

SIDE-EFFECTS OF A PANDEMIC	2019 (Lakhs)	2020 (Lakhs)	Change (%)
Newborns screened for defects at birth (as per RBSK*)	20.9	2.6	-87.6
Outpatient - acute heart disease	7.2	2.0	-72.2
Outpatient - cancers	5.0	1.4	-71.3
Inpatient - typhoid	1.2	0.4	-69.9
Inpatient - asthma, COPD, respiratory infections	4.3	1.5	-65.6
Pregnant women given free medicines under JSSK**	31.9	11.6	-63.7
Minor surgeries	34.2	13.5	-60.6
Major surgeries	11.0	4.4	-60.4
Lab tests done	2,111.7	851.2	-59.7

Source: Health ministry
*Rashtriya Bal Swasthya Karyakram; **Janani Shishu Suraksha Karyakaram

Fig. 1: Times of India. August 31, 2020.

At this juncture our infrastructural facilities were not only over stretched, it required reconfiguring in management strategy almost on a day to day basis.

The baby girls were joined at the hips with complex fusion of their back bones & spinal cords, large intestines at the lower ends with a common rectum and a common passage for passing stools. Also, there were abnormalities of heart & major blood vessels along with lack of adequate skin cover. Both had cardiac anomalies, one baby has encephalomalacia of one side of cerebral hemisphere. They had a single sacrum between them with their Spinal Cords fused at a critical junction in the lower end. Additionally, there was an anomalous crossing of an artery to one leg in one twin with shared supply. Both had single kidneys, each.

Since, the surgery was being carried out during the Pandemic they were first tested

negative for Covid-19. The procedures of separation lasted 24 hours. The total no. of health care manpower involved was 64 people & included several specialist teams: Anesthetists, Paediatric Surgeons, CTVS, Plastic surgery and Neurophysiology, besides Nursing & Paramedics staff. The diagnostic investigations were already completed with the help & participation from other Departments at AIIMS, such as, Radiodiagnosis, Neurophysiology, Nuclear Medicine, Laboratory medicine, Nursing & paramedical staff including C.M.E.T.

The second pair of Pyopagus conjoined twins were separated in January 2021.

Both pairs recovered successfully and were discharged from the hospital. By now they have also made several routine follow up visits to AIIMS.



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EDITORIAL

Pandemic Care and the Post Graduate Residents

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Coronavirus disease (COVID-19) came as a challenge for health care providers in India. The impact of the COVID-19 pandemic continues to pose enormous challenges for medical health care provider especially the resident doctors. The social & economic crisis and saving lives have been a significant issue.

During their training process, residents also contribute to the provision of healthcare services. Given the particular nature of training programs in teaching hospitals, there is an increasing concern regarding the precise effect of medical residency on the performance of these hospitals. In this sense, the productivity of residents has raised interest among economists.

The overall contribution of resident physicians to hospitals' production allows considering them as an input in most cases with their average productivity contributing to around 37% of that corresponding to senior physicians [1].

The National Board of Examination in Medical Sciences (NBEMS) with its 1,182 accredited hospitals (Covid period figures- Government 405 and Private 777) along with its alumni played a crucial role during the pandemic. NBEMS alumni served as frontline warriors for the best patient care and significantly helped to prevent workforce shortages.

Addressing doctors on the occasion of 'National Doctors Day', The Prime Minister of India also recognized the "limitations" of medical infrastructure that were created in the country over several decades and how it was neglected in earlier times. In his statement, the Prime Minister said "In our country, the population pressure makes this challenge even more difficult. But despite this, India's per lakh population rate of infection and death rate has still been manageable compared to more developed countries. Losing even one life is very saddening but India has also saved the lives of lakhs of its people from corona virus. A big credit for it goes to our hardworking doctors, healthcare workers and frontline workers" [2].

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Impact of COVID -19 pandemic on doctors and other support staff

A recent study by Japan International Cooperation Agency – India Office entitled “*Impact of COVID -19 Pandemic on Medical Healthcare Workers in Mumbai City, India*” reported that having 7,37,685 cases and a death toll of 16,048, making Mumbai one of the country’s biggest hotspots. The city has a severe shortage of beds- one per 3000 individuals, well below the WHO guidelines of one per 550. This has exacerbated the stress on medical health workers who have suddenly had to bear a disproportionately large burden of the work. The study also revealed that the risk of getting infection transmission increases by 35% to the doctors and other healthcare providers e.g. Nurses and Technicians. The responsibility of patient care is up to 71% on health care providers (37% Doctors, 23% Nurses and 11% of Technicians). Other 29% staff were engaged to provide administration, security, sanitation services etc. 25% of health care providers experience high or very high burn out levels and 37% experience nervousness or over stressed conditions which showed how our doctors and other support staff fight the pandemic [3].

Telehealth & the residents

The Coronavirus disease 2019 (COVID-19) pandemic has caused a substantial number of deaths worldwide, surpassing a million casualties [4]. However, this number does not even begin to quantify the hidden toll of the pandemic—the collateral damage it has caused. The vulnerabilities of marginalized people were worsened and has pushed them further into poverty and deprivation.

Among these are the excess deaths associated with COVID-19 [5,6] which are at least partly due to disruptions in the healthcare systems, including the discontinuation of emergency and acute care, difficulty accessing routine outpatient services, and difficulties related to accessing essential medications and other therapies such as childhood vaccination programmes contributing to increased mortality and disability [7]. Treatment of chronic diseases requiring regular healthcare has been

particularly affected by the discontinuation and/or reduced capacities of health services and the impact on noncommunicable diseases (NCDs). Students responded to the need of the hour and met standards set at the time monitoring patients with COVID-19 symptoms who did not require hospital admission, via telemedicine & provided teleconsultation under guidance. This would go a long way into adapting to the evolving digital health system & providing teleconsultation for chronic diseases, where necessary.

The roles and responsibilities of NBEMS students during the COVID-19 pandemic

As per the statement of Indian Medical Association (IMA) Around 2,000 doctors died in second wave of COVID-19 and the mortality rate in the country was around 1.5% among the general population and around 2–3% among the healthcare workers. According to this estimate, coronavirus occurred in about 1,00,000 doctors [8,9]. Many global medical associations such as American Association of Medical Colleges (AAMC) framed its guidance by highlighting that “medical students are students, not employees. They are not yet professional doctors” [10]. This is a true statement but it fails to acknowledge that resident doctors or medical students have roles not only as students but also as physician/surgeons-in-training. The primary role of resident doctors is to learn medicine for patient care. They are also the primary health care givers by guiding, providing consultations & responding, communicating, informing and also spreading awareness about the disease to the patients and their families. They are the ones who are taking care of the patient from admission to discharge.

The NBEMS students and alumni have acted as professional health care providers and worked very hard to reduce the viral transmission with limited personal protective equipment (PPE) of which there were serious shortages during the first wave of COVID-19. Allowing the NBEMS students to serve as a corona warriors ultimately benefited patient care, overall, throughout the pandemic. There was precedence for this kind of involvement. During the Spanish flu outbreak of 1918,

medical students at the University of Pennsylvania cared for patients in the capacity of physicians [11]. In the 1952 polio epidemic in Denmark, groups of medical students were tasked with manually ventilating the patients [12]. During the COVID-19 pandemic, all resident doctors including NBEMS students served as frontline corona warriors. The health care system of India and the world had been stretched up to its breaking point. NBEMS students had adapted to many clinical responsibilities, improving patient care long before the health care system reached a personnel crisis, and in some cases even prevented it.

Risks of contracting infections

The medical associations raised concerns about the risks for infection to students, PPE shortages, and associated liability issues. These risks undoubtedly warranted careful consideration & the same were mitigated. The students also performed clinical tasks in specific instances, conferring benefits to patients that outweighed the risks associated with their involvement. From providing assistance with routine emergency services, they provided the necessary boost to the efficiency of lightly staffed clinics. This was in the form taking histories, managing diagnostics, laboratory test results, spreading awareness among patients' family about social distancing, home quarantine etc. Even in a pandemic, patients with chronic conditions needed ongoing care.

Collaborative efforts between National authorities and NBEMS accredited private sector

At the beginning of the pandemic, most of the initial Covid-19 testing and treatment had been done in public facilities. In India, the authorities responded decisively with a strong whole-of-government approach even after the enormity of the economic challenge. According to the World Health Organization, a critical lesson from the 2014-16 West African Ebola crisis is, that, both the public and private sectors need to work in tandem in responding to large-scale epidemics. As the epidemic progressed,

both these services have been expanded several-fold, and the private sector has stepped in as a major partner and stakeholder. In the Covid-19 response, the private sector in the country (for-profit and not-for-profit segments) has played an even more important role, as it is the dominant provider of health services in the country. The National Sample Survey Office's 71st round data demonstrated that the private hospitals, clinics and nursing homes provided over 70% of health care. Data on the nearly 10 million treatments received under the Ayushman Bharat Pradhan Mantri Jan Arogya Yojana (AB PM-JAY) corroborate with this finding [13].

The creation of a large and accessible testing infrastructure was the key weapon to control the infection transmission. Countries such as South Korea, Singapore, Germany and Japan have been successful in controlling its spread and reducing mortality through early detection and quick containment. This had been possible only through widespread testing. India had opened testing up to private labs and payment for testing covered under the ABPM-JAY as well. Testing capacity was substantially expanded which was something not possible without the active participation of the private sector.

Conclusion

Medical students and physicians undeniably played a critical role in dealing with COVID-19 pandemic. The adequacy of their knowledge, training, dedication toward patient care was commendable in dealing with the COVID-19 pandemic. The senior doctors with higher clinical experience have used their experience to guide young medical students particularly towards pre-clinical medical students. NBEMS students and its alumni are a valued group within our health care system. They are well qualified & have received or pursuing their DNB, DrNB and FNB degrees with additional training for being able to be specialists and receive their certification. Their training usually takes three to six years before becoming an independent practitioner. They are on the frontline as COVID-19 corona warriors. They have presence in the Clinics, OPD, IPD, wards, ICU, managing ventilators, screening

patients and sometimes they are the ones that are with the patients alone in their final moments.

Conflict of Interest

The authors declares that they do not have conflict of interest.

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ORIGINAL ARTICLE

Multimodality Management of Two Pairs of Pyopagus Twins

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Abstract:

Background and Aim: Conjoined twins, due to their rarity and complex anatomy, pose not only a technical, but also a physiological challenge for their separation, with each case being uniquely distinct. The aim of the present article is to describe the surgical approach and management strategy for two cases of pyopagus conjoined twins operated at our center.

Case Report:

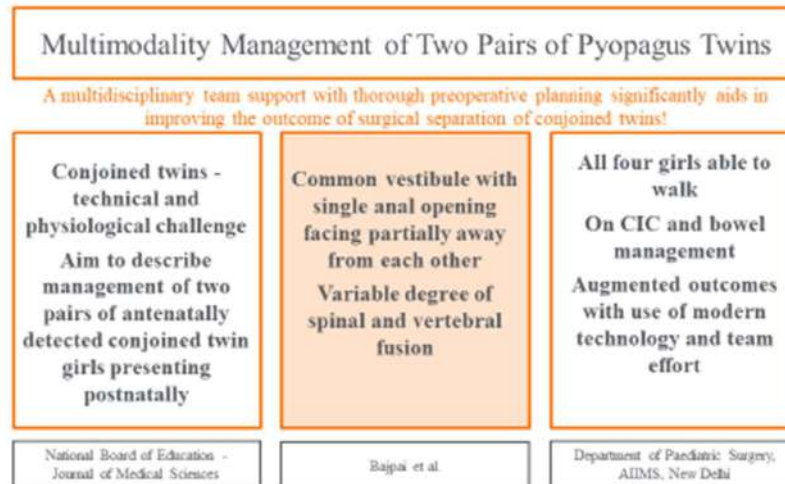
Case 1: Antenatally detected conjoined twin girls presented postnatally to our centre. They were found to have a common vestibule with single anal opening facing partially away from each other. On evaluation they were found to have a single sacrum and fused conus and filum terminale. They were taken up for separation at 2 years of age & the 24-hour long surgery, culminated in successful separation. The children had good post-operative outcome at 10 months post separation.

Case 2: Conjoined pyopagus twin girls presented postnatally, and were found to have fused cords, having a terminal syrinx and partially separate sacrum. They were separated at 2.5 years of age, with a multi-departmental effort and coordination. They are doing well 2 months post-operatively.

Conclusion: A multidisciplinary team support with thorough preoperative planning significantly aids in improving the outcome of surgical separation. This has been possible by using modern technology. Each reported case contributes significantly to literature.

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Graphical Abstract

**Introduction**

Twinning is an embryopathy and the spectrum varies, just as the constellation of anomalies, based upon the insults at different stages of embryogenesis [1]. Conjoined twins, due to their rarity and complex anatomy, have always been the source of academic and social fascination. [2,3].

The incidence is 1:50,000–100,000 pregnancies but as 60% are still-born or die soon after birth being incompatible with life [5], the true incidence is 1:200,000 live births with female predominance [4]. These same sex twins develop from a single fertilized ovum with a single placenta, however no well-defined etiological factors are known. Of the different types of conjoint twins, approximately 15–20% are pyopagus, their fusion is thought to occur at the region of the caudal neuropore, and the structures derived from the cloacal membrane in them are said to be normally developed [5].

We are describing two cases of pyopagus twins with complex sacral and spinal cord anatomy, involving detailed work-up of individual organ systems, along with the multidisciplinary approach to management and the final outcome.

Case Reports:**Case 1:**

Conjoined twin girls, joined at the sacrum, with fused spinal cords, were diagnosed antenatally through a standard screening ultrasound to a 28 years old mother.

The twins were delivered via Caesarean section at 36 weeks of gestation with

a combined birth weight of 5000 g. The twin on the right in anatomical position was designated as Twin A and the one on the left as Twin B.

Initial examination revealed the twins to be fused at the lower spinal region, sharing a perineum with a single anus, so that they faced away from one another in a partially oblique fashion [Fig. 1]. Although both were moving their lower limbs, they had associated neuro-orthopaedic deformities. They eventually developed a degree of deformational plagiocephaly.

A series of investigations were performed to clearly delineate the anatomy, while assessing their growth and neurological milestones. Imaging revealed spina bifida of L3 to L5 vertebra, fusion of the sacral vertebrae (S2 - S5) with common coccygeal vertebrae. [Fig. 2a] The rectum from both the twins was seen to open into a single anal opening. Both had crossed fused ectopic kidneys to their shared side. Twin B had a prior right MCA territory infarct with cystic encephalomalacic changes with dilatation of the ipsilateral lateral ventricle and atrophy seen in right half of brainstem. Magnetic resonance imaging of lower spine revealed two separate conus medullaris with a common fused filum terminale [Fig.2b]. Arterial supply and venous drainage of the right leg of twin B was found to be from the left internal iliac vessels of twin A [Fig.2c].

One of the most useful imaging adjuncts, was the development of a three-dimensional acrylic model of the ilia, sacrum and lumbar spines using a 3D printer, which allowed a thorough appreciation of the skeletal

anatomy, site of fusion and orientation, aiding the operative planning [Fig.3].

A management team was organized that consisted of paediatric surgery, plastic surgery, cardiothoracic and vascular surgery, anaesthesiology, radiology and neurophysiology.

Prior to the separation surgery, neuronal mapping was done of the lower limbs and anal sphincter which revealed some weakness in myotomes of twin B. The anal sphincter was predominantly controlled by twin A. There were some cross over fibres between

twin A and B, MEP to twin B stimulated lumbar myotomes of twin A [Fig.4].

Six months prior to separation, the plastic surgery team inserted tissue expanders however they had to be removed due to resulting infection, leading to slight delay in the final separation.

The operation was performed at our facility at a date accommodating all surgical specialties, which corresponded to the twins' age of 24 months when the preoperative combined weight was 15kg.

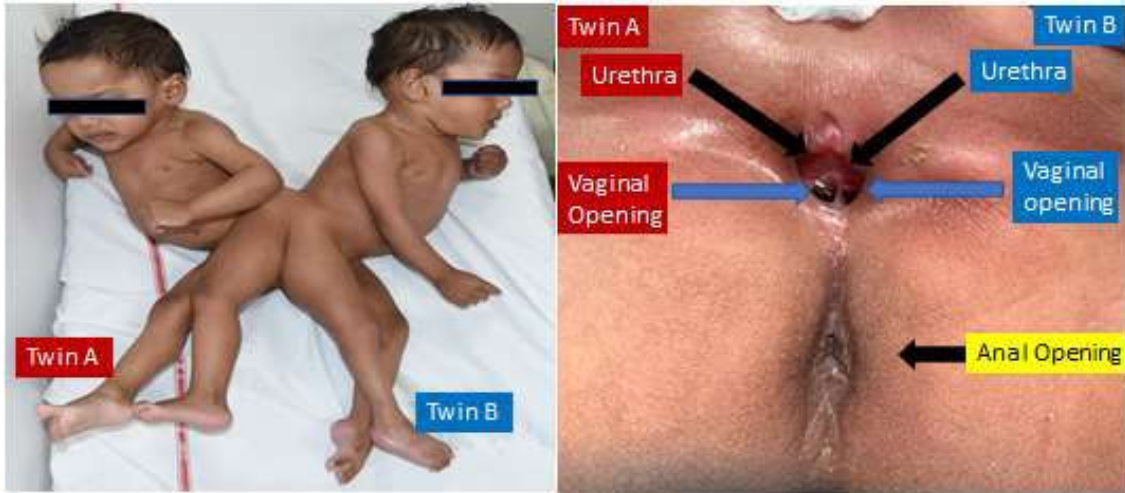


Fig. 1. a. Presentation of the pyopagus conjoined twins, joined at the hip, facing partly away from each other, b. Common perineum with two urethral and vaginal openings and single anal opening.

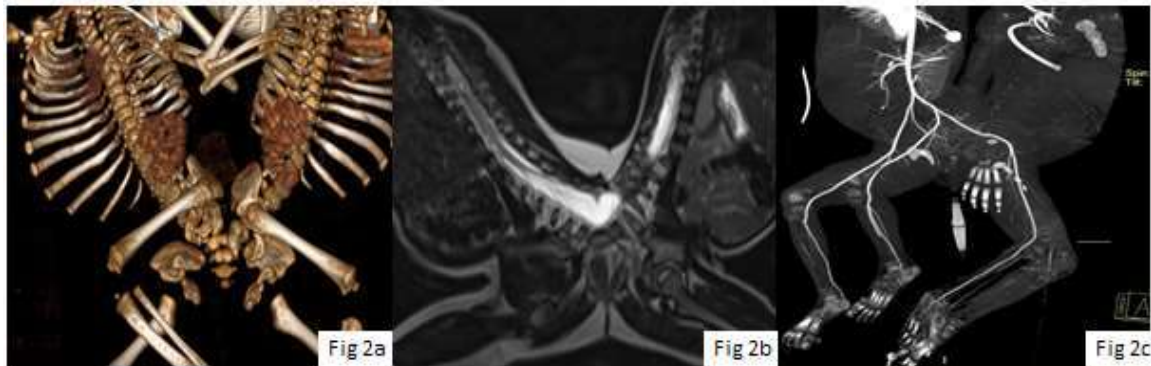


Fig. 2a. CT reconstruction demonstrating spina bifida of L3 to L5 vertebra, fusion of the sacral vertebrae (S2 - S5) with common coccygeal vertebrae;

Fig. 2b. Magnetic resonance imaging of lower spine showing two separate conus medullaris with a common fused filum terminale;

Fig. 2c. CT Angiography demonstrating the arterial supply and venous drainage of the right leg of twin B to be from the left internal iliac vessels of twin A.



Fig. 3. A three-dimensional reconstruction model of the shared bony anatomy.

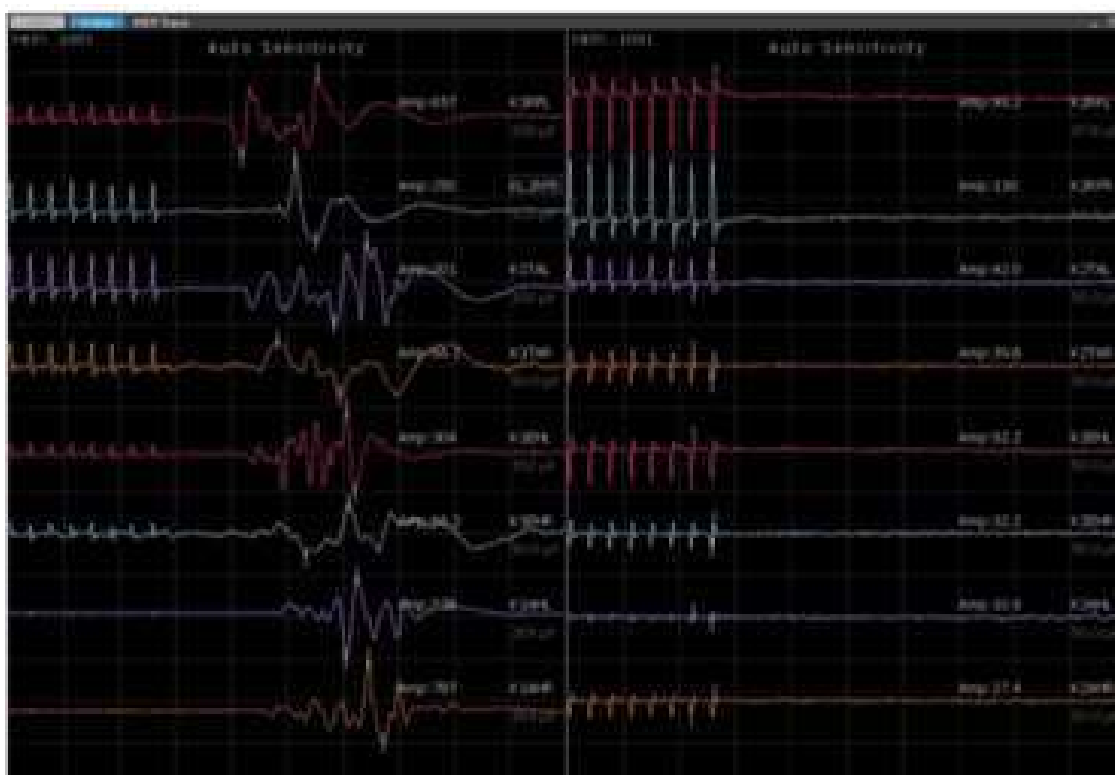


Fig. 4. Neuromonitoring done under anaesthesia showing MEP to twin B stimulated lumbar myotomes of twin A indicating crossover of neural fibers from B to A.

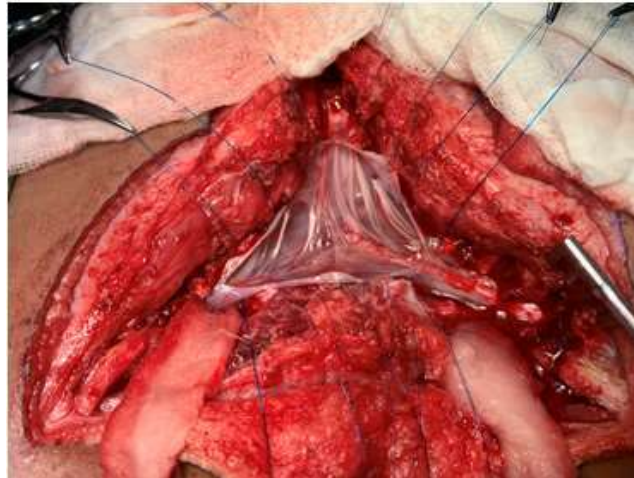


Fig. 5. Laminectomy in first set of conjoined twins revealing a U- shaped spinal cord and fused filum terminale.

An important anaesthetic consideration was restrictive small perimembranous VSD with left to right shunt in twin B. Anaesthetic workflow for the separation surgery had been well rehearsed by the anaesthesia team with models and a mock drill. The lines and drugs for the twins had been colour coded. The patients were then each intubated, with central, arterial and peripheral lines placed. Initially, the patients were positioned in supine position, bladders were catheterized, marking of flaps was done followed by electrode placement by neurophysiology team. The twins were then placed prone, following which surgery was commenced by the paediatric surgery team with exposure of the lower lumbar spine and sacrum by raising subcutaneous flaps as pre-decided for closure in consultation with plastic surgery team.

Spine of twin I identified after diving the paraspinal muscles, ligamenta flava and longitudinal ligaments. Laminectomy was performed in both twins, dura was found to be complete and durotomy was done under the effect of mannitol, the incision was carried down to expose a U-shaped spinal cord with asymmetric and complex cauda equina and fused filum terminale [Fig.5]. Once detethered, neurophysiological monitoring was used to identify nerve roots of individual twin. Bipolar lead used to identify response in twins, if absent confirmed with monopolar lead, keeping in mind the high rate of false positive responses. The main concern were the nerve rootlets arising at the distal and lateral aspects of the fused cord, some of which passed distally and contralaterally. The fibres passing

contralaterally were found to be cross over fibres from twin B to A. The nerve roots were separated to the side of individual twins as per the neurophysiological response. Cordotomy done as per the plane of demarcation supplemented by neurophysiological response. Primary dural closure was possible in both twins using 6'0 prolene continuous sutures after inserting a thecoperitoneal shunt (Chabra Lumboperitoneal shunt).

After clearing the tissue caudally in the midline, the complex anatomy of the sacrum identified was suggestive of fusion of 2 sacrum with a preserved lateral sacral foramina to each twin which were juxtaposed to each other and crowding of the cauda equina in a paramedian fashion leaving a very thin strip of bone in the median position. This fused sacrum was divided in midline, preserving neural outflow with the help of responses to neuronal stimulation.

On dissection of the presacral space, peritoneum opened to further visualize pelvic structures. Using Hegar's dilator, the rectum of both twins were identified, which were fused in a Y configuration, leading into a common anal canal [Fig. 6]. This common anal canal and sphincter with adjacent levator ani fibres were kept to the side of Twin A. The rectum of twin 2 was disconnected from the common rectum with the help of a linear stapler and pull through was done by hanging bowel technique [6]. The perineal skin incision completed in as per the previously designed flaps to separate the vagina and urethra.

Continuing the rest of the surgery in supine position, the aberrant supply to left

lower limb of twin B was restored primarily, perineum and soft tissue separated and skin closure done by flaps and cadaveric grafts. The total anaesthesia duration was 24 hours.

The post-operative course was prolonged and constituted intensive critical care management with the help of the pediatrics team. The cadaveric grafts were eventually rejected and replaced by autograft harvested from Twin A. Twin B suffered from perineal wound dehiscence for which she was re-operated and an enterostomy was created. Once the perineal flaps had healed, bowel trimming was performed. Children were then started on clean intermittent catheterisation and bowel management programme for Twin A. Physiotherapy and mobilisation started using splits and walkers. At 1 year of follow up, the twins are doing well [Fig.9a].

Case 2:

Antenatally detected conjoined twin girls, were delivered at term with a combined weight of 5500gms and presented to us postnatally. As in the first case, they were also pyopagus twins, joined at the sacral region, facing partially away from each other. They had a common perineum with separate urethral and vaginal openings but

a single anal opening [Fig.7]. The twins also had associated neuro-orthopedic deformities and deformational plagiocephaly.

Complete investigational panel was done showed multiple lumbar vertebral defects in both twins with fused lower sacral vertebra, S2 of twin A and S3 on twin B onwards, with open posterior elements. Magnetic resonance imaging revealed that the conus was low lying and fused at L5 level. There was a syrinx in the cord, which over 1 year increased in size to reach the conus, as a result there was a 1.3 mm of neural tissue separating the fused conus with terminal syrinx and dysplastic neural tissue. Hyperintensity seen in the bilateral deep white matter in the occipital lobe of Twin B due to suspected metabolic insult. There was a small branch arising from left external iliac artery of twin A, seen to cross midline anteriorly to supply the antero-lateral part of right upper thigh of twin B, which had its own vascular supply. Bilateral kidneys were normally located, echocardiography was essentially normal except for dextroposition of Twin A. On contrast enema, there was a common channel length of 2.1cm which bifurcated into the respective rectum of the twins.



Fig. 6. A Y-shaped configuration of the rectum of both twins were identified leading into a common anal canal.



Fig. 7. Second set of pyopagus twins showing nearly identical anatomy, with a single perineum, separate urethral and vaginal opening and single anal opening.



Fig. 8. Lower shared part of spinal cord in second set of twins showing a terminal syrinx.



Fig. 9. Separated twins prior to discharge with intact motor functions.

The preoperative planning and management progressed in a similar manner as previous set of twins; however, tissue expanders were not used and neurophysiological monitoring was conducted after induction during the separation surgery.

The separation surgery progressed in a similar manner as in the first case. The dura was

common in the lower aspect enclosing a U-shaped spinal cord, terminal part of which had a syrinx [Fig. 8]. Intra-operative neurophysiological monitoring showed no cross over and equal control of the anal sphincter, which was given to the neurologically better twin A. Enterostomy was not required in either twin. The crossing vessel

could not be separately identified and was ligated in the cleavage plane during the separation. The total anesthesia duration was 13 hours.

Subsequently in the post-operative period, twin B underwent trimming of the hung bowel and both twins underwent autologous skin grafting harvested from Twin A, after rejection of their cadaveric grafts. There was no evidence of lower limb weakness.

Currently both twins are doing well at 4 months follow up and have been started on bowel training program and clean intermittent catheterization. They are being mobilized with the help of splints and walkers [Fig.9b].

Discussion

Conjoined twins, joined at homologous sites are clinically classified based on the most prominent site of union [7]. Pyopagus conjoint twins represent a group in which separation of the embryonic axis in the caudal region was incomplete during 3rd-4th week of gestation, with resultant fusion of the sacral and neural elements to varying degrees. The first successful separation of conjoined twins was performed in 1689 by Johannes Fatio [8]. To our knowledge 37 cases of pyopagus conjoined twins have been described in detail in literature, and ours is the first report of two cases managed successively with all 4 surviving twins.

A thorough planning and preoperative evaluation is needed prior to separation in view of a very complex anatomy and high incidence of associated anomalies [9], surgery should be planned on an elective basis at a time when the twins gain weight and are stable to handle the surgical stress of major reconstruction. The survival rate correlates with age at separation being less than 50% if attempted in the neonatal period but increased to 90% if separation was delayed until 6 months of age or later [10].

Majority of these cases have bony fusion and 68% have sharing of dural sac [11]. Conjoinment of the distal cord and cauda equina forming a U-shaped spinal cord is not uncommon. A spectrum of anomalous, intraspinal variations exist involving the spinal cord & this group of anomalies possesses unique challenges in separation [12,13].

Functional and anatomical midline may not coincide. In our case, use of preoperative neurophysiological monitoring along with its intraoperative use helped to divide the spinal cord in the functional rather

than anatomical midline, preserving the outflow to each twin, mitigating post-operative neural deficits, including neurogenic bladder [14].

It also helped to allocate the anal sphincter to the twin in better control of it. Role of preoperative neuromonitoring cannot be over emphasized, as it helped in preemptive planning and saved prolonged general anesthesia time during the final separation [12]. The anatomy of the common sacrum was further complicated by the apparent fusion of 1st sacral vertebra which led to the medial sacral outflows of both twins being crowded and exiting through a fused common foramen, where surgical separation was immensely benefited by neuronal monitoring. The benefit was self-evident during the immediate post-operative period when the children were able to move their lower limbs.

Placement of a lumbo-peritoneal shunt helps in preventing CSF leak which enables the flaps and grafts placed to heal adequately. A thorough mechanical bowel preparation and performing neurosurgical separation and dura closure first helps in preventing ascending CNS infection in these children, also requiring concomitant gastrointestinal surgery.

Some of the pyopagus conjoined twins have significant cross-circulation, and in up to 25 %, large anastomotic vessels including transverse veins may be observed intraoperatively leading to unexpected blood loss by damaging unidentified vascular structures [11].

The outcome of separation is highly dependent on the use of modern technology by an expert multidisciplinary team at a tertiary care center. Exhaustive parental counselling is mandated prior to surgery, explaining the possible complications, and expected outcomes resulting from an extensive and prolonged surgery.

Conclusion

Outcomes of surgical separation of conjoint twins have drastically improved over the years. Surgical separation, however, continues to be very challenging involving multiple organ systems, needing support from a multidisciplinary and dedicated team. Due to the rarity of cases and complexity of anatomy, every successfully separated case adds immensely to the literature to help guide and improve subsequent outcomes.

Statements and Declarations

Conflicts of interest

The authors have no competing interests to declare that are relevant to the content of this article

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ORIGINAL ARTICLE

Renin Angiotensin System (RAS) Pathways in COVID Pathogenesis

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Abstract

Background – Covid-19 pandemic has posed some rare diagnostic & therapeutic challenges. Recurrent waves of varying severity are caused by ongoing mutations in the virus. It is vital to understand the fundamentals of Renin Angiotensin System (RAS) pathway which has been incriminated in the Covid-19 pathogenesis.

Aim – We aim to understand the basic pathological and molecular basis of the disease and thereby understanding the basis of treatment options and possible outcomes of the disease.

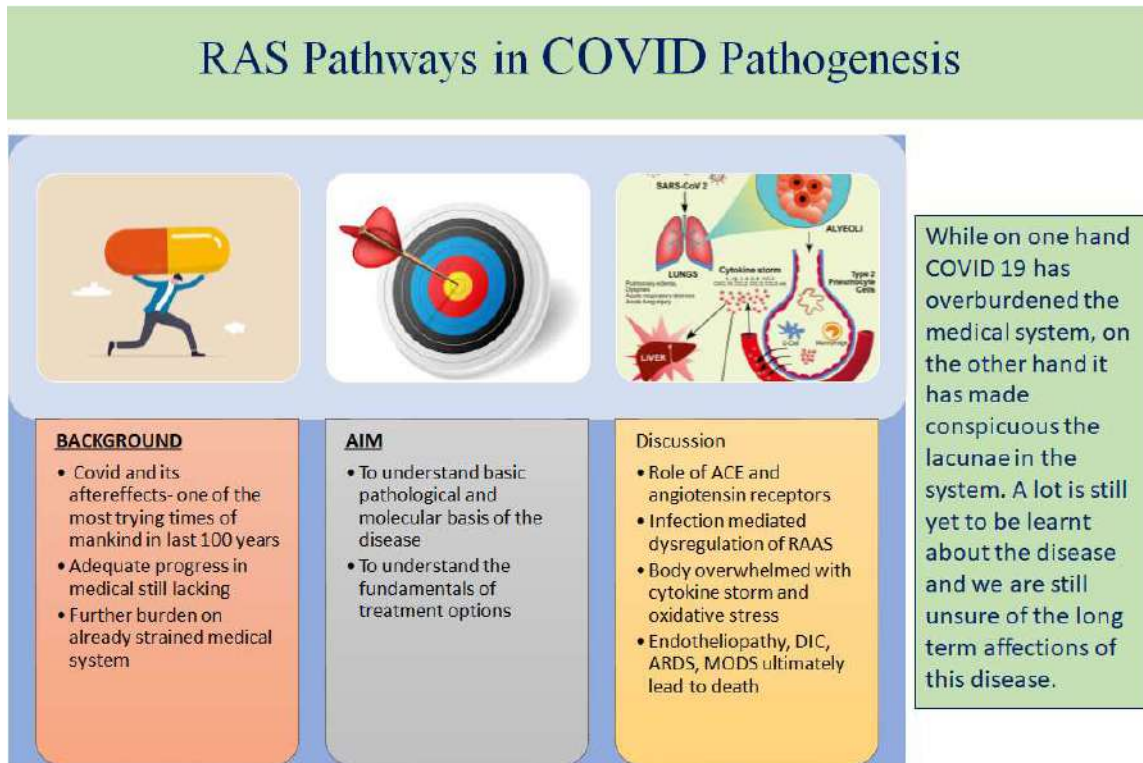
Discussion- The role of ACE and angiotensin receptors take the center stage in COVID pathogenesis. The crux of the disease process lies in the infection mediated dysregulation of the renin angiotensin aldosterone system which further leads to an oxidative stress that overwhelms the body's protective mechanisms. Children, on account of having a more robust immune system, tend to get less affected by the disease process. Various therapeutic options can be explained by understanding the pathogenesis and biology of the disease.

Conclusion- Children have an abundance of AT₂ receptors which have a predominantly anti-inflammatory effect and less of AT₁ receptors which are proinflammatory. Furthermore, children tend to have a more robust and active innate immunity due to repeated viral and bacterial infections in the childhood. Ongoing research on RAS pathways may unravel the, hitherto, unsurmountable challenges in the understanding of COVID-19 pathogenesis.

Keywords: COVID, ACE, Angiotensin, Paediatrics

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Graphical Abstract



Introduction

After having witnessed one of the most horrifying events of the century, those of us who came out safely to the other side of the tunnel are still reeling from the effects and aftereffects of the COVID Pandemic. Each person across the globe has lost something or someone to this disease. The disease acted as a mirror in ways, where all the inadequacies and defects of the medical system were suddenly exposed and made very conspicuous to the entire world. Thus, it becomes imperative to thoroughly understand the core and functioning of the disease so that we are prepared to tackle any future shock waves and long term or delayed complications or repercussions of COVID 19. This we will do by going back to the basics and understanding the molecular and cellular working of COVID 19, which is the main aim of this article.

The basic biology of Angiotensin converting enzyme (ACE) and Angiotensin receptors (AT)

The role of ACE2 and AT receptors came to center force in the pathogenesis of COVID 19, interestingly the same ACE 2 receptor and RAS pathway is also a key player in CAKUT pathogenesis in children. Thus, this article will mainly focus on RAS pathways and ACE in COVID pathogenesis.

Angiotensin converting enzyme (ACE) converts angiotensin I to angiotensin II (AT II). AT II is further acted upon by ACE 2 into Angiotensin 1-7 (Ang 1-7). Furthermore, AT II acts via AT1 receptors and Ang 1-7 act via AT2 receptors. The human body maintains homeostasis by a fine coordination and regulation between ACE and ACE 2, which have counter regulatory effects. Disturbance of this delicately balanced relationship is the cornerstone in pathogenesis of COVID.

In the mid-1950s, ACE was discovered after an observation that dialysis of plasma and kidney extract with saline and water before incubation had produced two distinct pressor substances namely Angiotensin 1 and 2. ACE was rediscovered in 1966 when a bradykinin

degrading enzyme was found in the kidney namely ACE [1]. The ACE 2 enzyme was discovered much later in 2000, when homologous ACE was cloned by two independent research groups, which would convert Angiotensin I to Ang 1-9, but also was captopril insensitive [2].

The ACE gene and ACE 2 genes are located on chromosome 17q22 and Xp22. The somatic ACE contains N and C domains which as two catalytic domains and a C-terminal transmembrane stalk. Both the catalytic domains are zinc metallopeptidases wherein the zinc ion coordinates with two histidine residues. The transmembrane stalk has a dual function. It anchors the enzyme on the membrane and also helps in its release into plasma after cleavage by shedding enzymes. The ACE 2 is a chimera protein with only one catalytic domain and a C-terminal resembling collectrin, which acts to deliver other proteins to brush border membrane like a chaperone protein. ACE 2 is regulated at multiple levels including transcriptional, post transcriptional (miRNA and epigenetic) and post translational levels. While the ACE via (angiotensin II) AT1 receptors acts via Gi 2/3 mechanism, the ACE2 via (ang 1-7) AT2 receptor acts via Go/11, Gi/o mechanism [3-4].

ACE 2 receptors are widely distributed in the body in endothelial cells, smooth muscle cells, podocytes, cardiomyocytes, proximal tubules of kidneys, hepatocytes, lymphatic system, goblet and ciliary cells of upper airway and type II alveolar epithelial cells to name a few. There are wide variations in ACE2 expression both in the body and in the population.(3)(5) The expression of this ACE2 receptor is hypothesized to be induced by cellular or environmental stimuli, in the intestinal epithelial cells and apical zone of respiratory epithelium. Thus forms an integral part of the innate immune system [5].

Likewise, the AT 1 receptors are located in heart, blood vessels, kidney, adrenal cortex, lung, basal ganglia and brain stem. It is stimulated by Angiotensin II and acts via G protein mediated decrease in cyclic AMP (cAMP), which causes vascular smooth muscle contraction due to increased calcium inside the cells. It also increases aldosterone thereby increasing proximal and distal tubule sodium reabsorption. It also causes vasoconstriction by stimulating endothelin production. It is overall effective in

increasing blood pressure, anti-natriuresis, stimulating cyclooxygenase release, inhibiting renin release, anti-apoptotic, and pro-growth and proliferation. It is also known to stimulate renal growth in fetuses [6,7].

AT 2 receptors are located in large numbers in fetus and neonate and found in cerebellum in adults. It has the opposite effect of AT 1 mediated actions. It gets stimulated by binding of Ang 1-7 and increases bradykinin, nitric oxide and cyclic GMP (cGMP). This leads to vasodilation, natriuresis, low blood pressure, stimulation of cytochrome P-450, pro apoptotic, anti-growth and anti-proliferative by inhibition of fibrosis and collagen deposition. It has been known to cause inhibition of cell growth and tissue development in fetuses [8,9]

AT3 and AT4 are two other receptors of angiotensin II but are very poorly characterized. AT 4 is activated by angiotensin II metabolite angiotensin IV and may play a role in central nervous system extracellular matrix regulation and modulation of oxygen release [10,11]

Thus, to summarize, ACE acts on angiotensin I and converts it into AT II which acts via AT1 receptors and has vasoconstricting, pro inflammatory, pro apoptotic, pro fibrogenic action and it increases oxidative stress, whereas, in contrast, ACE 2 via Ang 1-7 is a potent vasodilator, anti- apoptotic, anti-proliferative agent which reduces oxidative stress (as shown in Figure 1). Therefore ACE 2 functions as a negative regulator of classical ACE in the RAS pathway [9].

SARS Cov-2 infection and entry into a cell

Severe acute respiratory syndrome coronavirus 2 (SARS – Co-V-2) uses membrane bound ACE-2 to gain cell entry. The SARS – CoV-2 spike protein has structural homology to the spike protein of SARS-CoV, however, the former binds to ACE2 with much higher affinity than the latter. The membrane fusion of the virus with the cell via ACE 2 leads to down regulation of ACE2 and therefore an imbalance in ACE/ACE2 ratio which tips the body's homeostasis to pro inflammatory and apoptotic state. The spike protein for both the SARS viruses require priming by TMPRSS2 (a serine protease) for optimal entry of the virus into the cell [1]. This is utilized in the fact that camostatmesylate- an

inhibitor of TMPRSS2- can be used in treatment strategies [12].

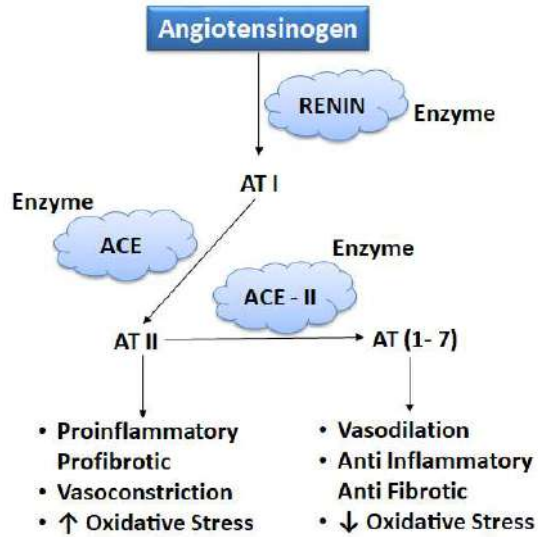


Fig. 1. Role of ACE and ACE-II in the body.

The primary target of SARS Cov2 are the epithelial cells in the tracheal and bronchial epithelium and the gastrointestinal tract. The spread of the virus into blood and alveoli is

further facilitated from there on. The virus enters the epithelial cell from the apical pole in the initial stage of infection and exits the cell from basolateral pole in the late stage of infection and begets infection to subsequently more cells [13]. Endogenous serine proteases such as furin, cathepsin, human airway trypsin like protease and transmembrane serine protease (TMPRSS2 and 4) separate the S- spike of the virus into two pincers- S1 which binds to the ACE2 receptor, and S2 which anchors to the cell membrane thereby gaining cell entry. S1 and ACE binding triggers the cleavage of ACE2 by a disintegrin and metalloproteinase domain 17 (ADAM 17) and tumour necrosis factor converting enzyme (TACE) at the ectodomain sites. This process leads to shedding of host ACE2 receptor and systemic release of S1/ACE2 complex (as shown in Figures 2a, 2b, 2c, 2d, 2e). This causes inflammation, oxidative stress (direct stimulation of polymorphonuclear cells and production of superoxide dismutase), reduced innate immunity, pulmonary endothelial vasoconstriction and microthrombi formation leading to ARDS [1].

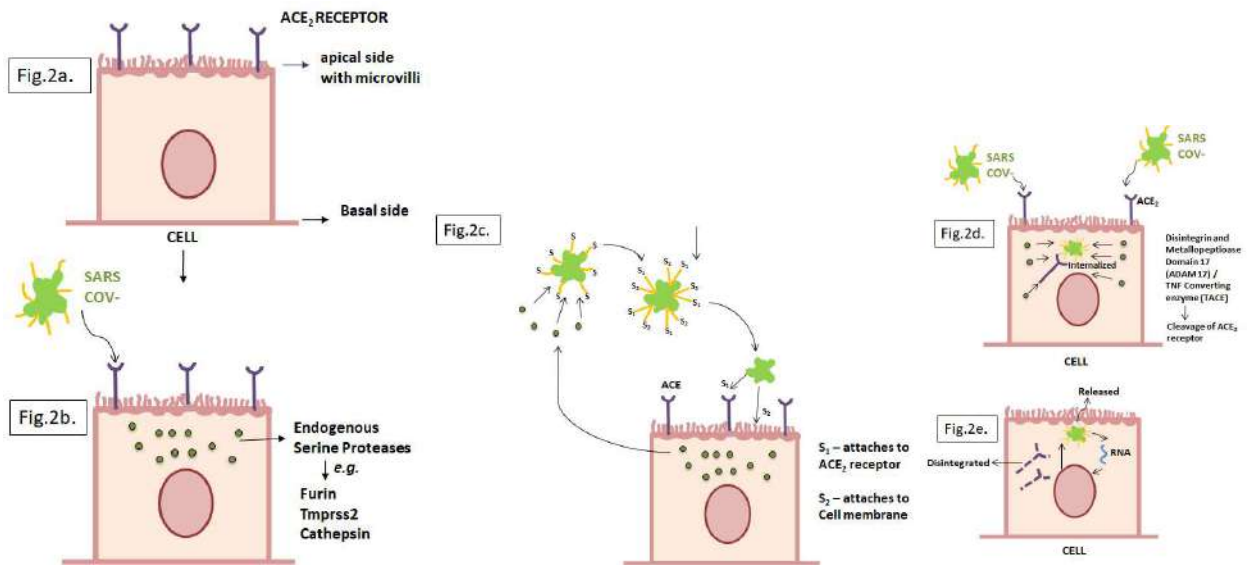


Fig. 2: Pathogenesis of SARS Cov 2 entry in cells: 2a- Normal cell. 2b- Infection with SARS Cov-2. 2c- attachment of SARS Cov virus to ACE receptor. 2d, 2e- Cleavage of ACE 2 receptor.

Systemic involvement of SARS Cov-2 virus

The vasoconstriction caused by ACE 2 inhibition causing turbulent blood flow in addition to the oxidative stress causes extensive and widespread endothelial damage. This is

called endotheliopathy [14] Damage of endothelium exposed the subendothelial von Willebrand factor inside the blood vessels to factor VIII which is freely present in blood [15] (as shown in Figure 3a, 3b, 3c).

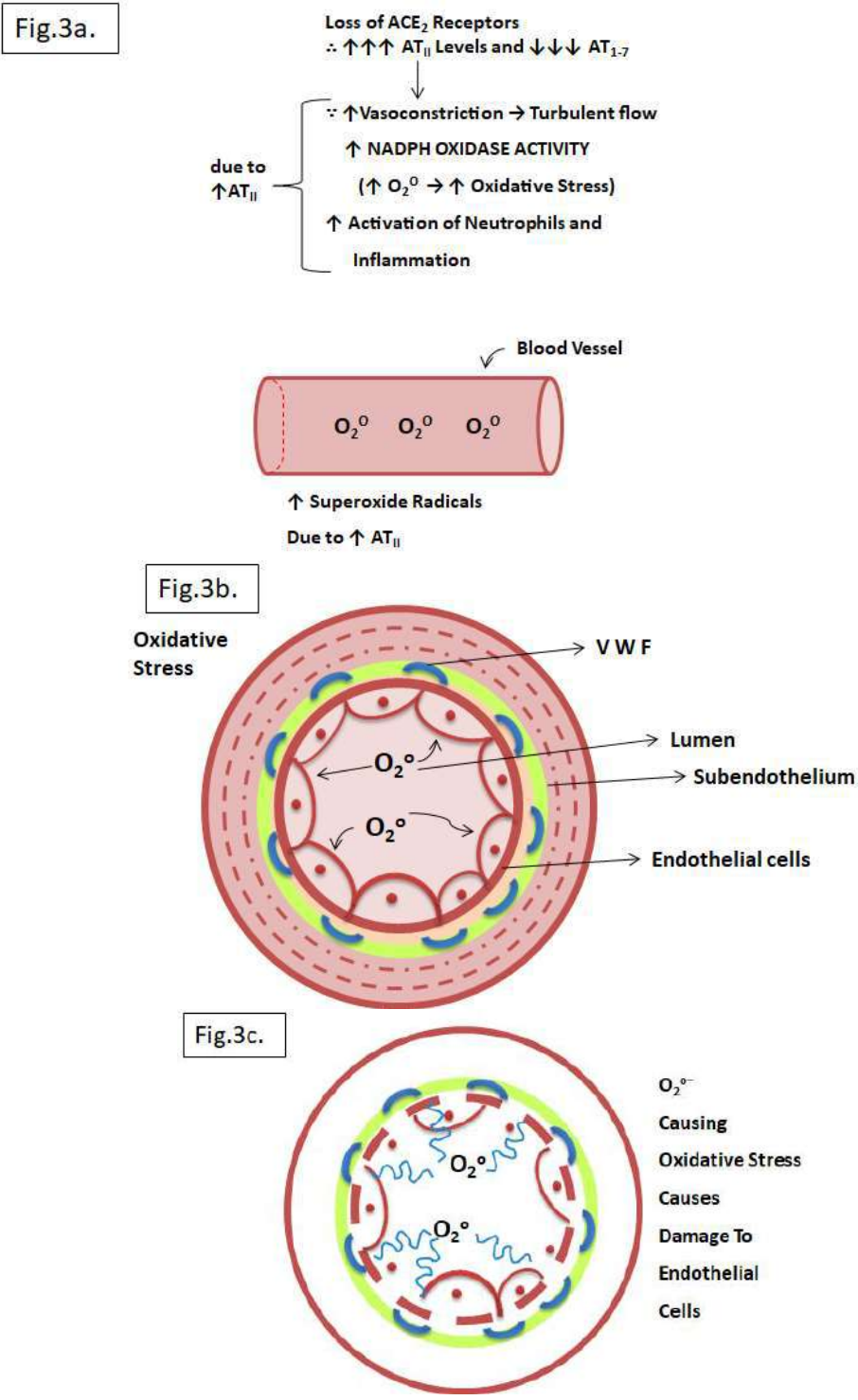


Fig. 3a, b, c: Oxidative stress, endothelial damage and release of Von Willebrand factor from subendothelial layer.

Binding of these two factors causes platelet activation, aggregation, and activation of the coagulation cascade thus production thrombosis (as shown in Figure 4a, 4b). Higher

levels of serum vWF indicate a more extensive thrombosis and associated with a worse outcome [15].

Fig.4a.

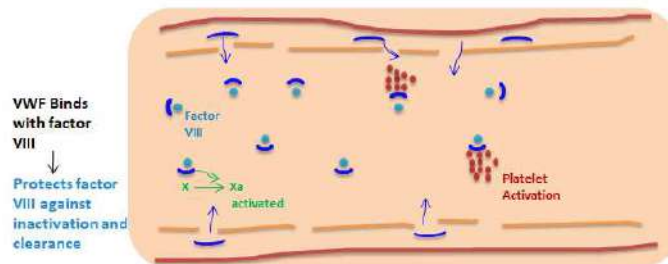
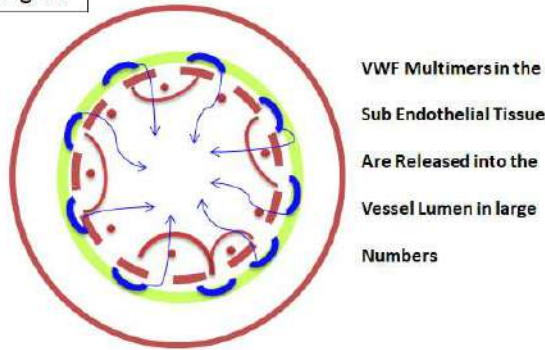


Fig.4b.

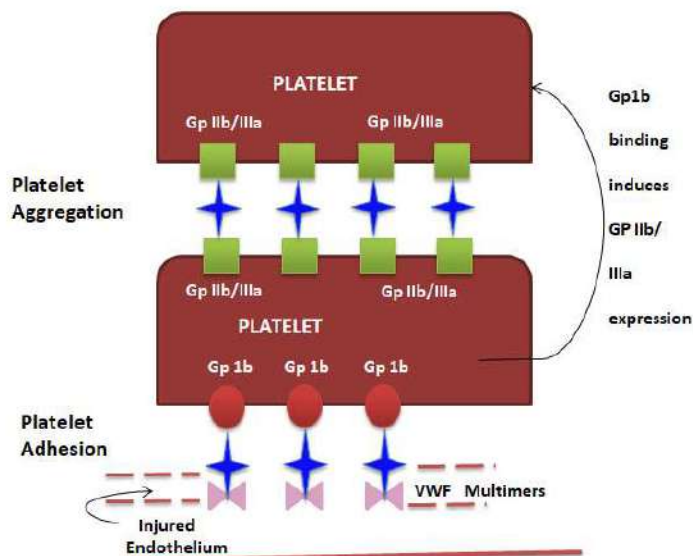


Fig. 4: 4a: Release of subendothelial von Willebrand factor. 4b. Platelet adhesion by attachment of Gp 1b with vWF multimers and platelet aggregation by interlinking of Gp IIB/IIIA between platelets. This further leads to formation of widespread microthrombi and DIC.

Thus, Virchow's triad of thrombus formations is favored i.e., altered blood flow, endothelial damage, and hypercoagulable state.

In addition, extensive endotheliopathy causes widespread thrombus production in the body which overwhelms the plasmin mediated

thrombolytic system thus leading to the formation of widespread microthrombi which eventually leads to cytokine storm- DIC (disseminated intravascular coagulopathy)- MODS (multiorgan dysfunction) and ARDS finally leading to death. The factors favoring this extensive endotheliopathy is directly related to the load of viral infection, collateral; damage to tissues because of immune infiltration and activation, compliment activation and release of large number of inflammatory cytokines all at once [16]. It is also higher in patients with preexisting oxidative stress. This sudden load of cytokines on the body also known as the cytokine storm is way too much to tackle especially in adults who are already dealing with an ongoing oxidative stress and have a dysregulated renin angiotensin system to start with such as in people with obesity, diabetes, hypertension or any cardiovascular or any other such morbid disease [16].

Pathogenesis of COVID pneumonia

Inhalation of the SARS virus leads to primary assault of the respiratory system which is essentially the principal target of the virus. As discussed, the virus enters the cell from the apical surface and the virions exit the cell from the basal surface of the alveoli. Inactivation of ACE2 and endotheliopathy leads to pulmonary endothelial vasoconstriction and microthrombi which causes

ARDS. This results in high elastance of the lung and a right to left shunt due to pulmonary vasoconstriction. Increased exodus of fluid into the alveoli from the high-pressure vessels cause increase in lung weight and increase in recruitment of lung alveoli to counter hypoxia (type H lung problem). Patients present with gradual onset progressive dyspnea, bilateral lung infiltrates and co2 retention, eventually requiring mechanical ventilation. The picture is that of a full-blown ARDS. Prone positioning and low tidal volume and high PEEP ventilation may help tide over this state. However, this process takes some time and occurs slowly [17, 18].

The virions after release from alveoli also enter the systemic circulation. It then causes widespread endotheliopathy, vasoconstriction and microthrombi which leads to occlusion of blood supply to all the organs in the body leading to sudden acute multi organ failure. This type causes a L type of lung with low ventilation: perfusion ratio, low elastance and low recruitability. Such patients present early on in the disease process. Vasoplegia due to modest local subpleural interstitial edema contributes to severe hypoxemia [17-19]. However, some recent studies postulate that both these types describe the early and late stages of COVID pneumonia and both benefit from the same type of treatment [20].

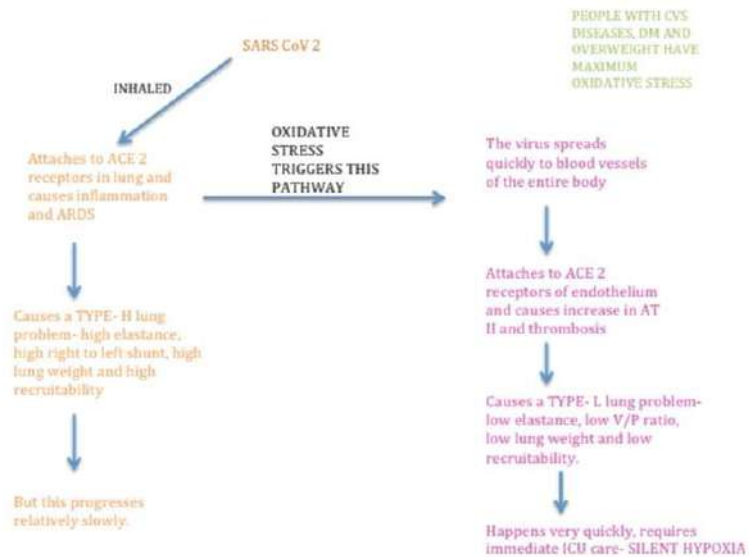


Fig. 5: Flowchart depicting an overview of the SARS CoV 2 pathogenesis.

Treatment options

The possible treatment modalities include usage of ACE inhibitors or ACE receptor blockers (ARBs) which downregulate the ACE pathway by putting a block to this vicious cycle at an early stage and preventing an uncontrolled oxidative stress and cytokine storm (as shown in Figure 6). There are a multitude of other treatment modalities that have been tried with some success including use of N-acetylcysteine (NAC), eculizumab, tocilizumab, dipyridamole, defibrotide, zinc, vitamin D etc. NAC in addition of being an antioxidant also works by cleaving vWF multimers inside occlusive thrombi, thus, causing recanalization of vessels [21]. Eculizumab and Tocilizumab are monoclonal antibodies against C5 complement and IL6 respectively thereby regulating cytokine storm [22,23]. Dipyridamole is under clinical

trials for usage in severe covid infection. It is an antiplatelet agent that prevents platelet aggregation and thus, prevents formation of microthrombi [24]. Similarly, defibrotide is an antithrombotic agent that is under trials for usage in severe pneumonia in COVID [25]. Zinc has been widely studied for their prophylactic and preventive role in COVID infection. It enhances antiviral immunity of the body by a multitude of actions on the innate and humoral immunity [26]. Vitamin D has a conflicting role, while correct body levels of vitamin D favours a milder disease course; vitamin D itself as a does not act as a treatment modality for COVID [27,28]. Other possible drugs that can be used in treatment and act as possible area of future research include TMPSSR inhibitor- camostat mesylate- which works by inhibiting viral entry into the cell.

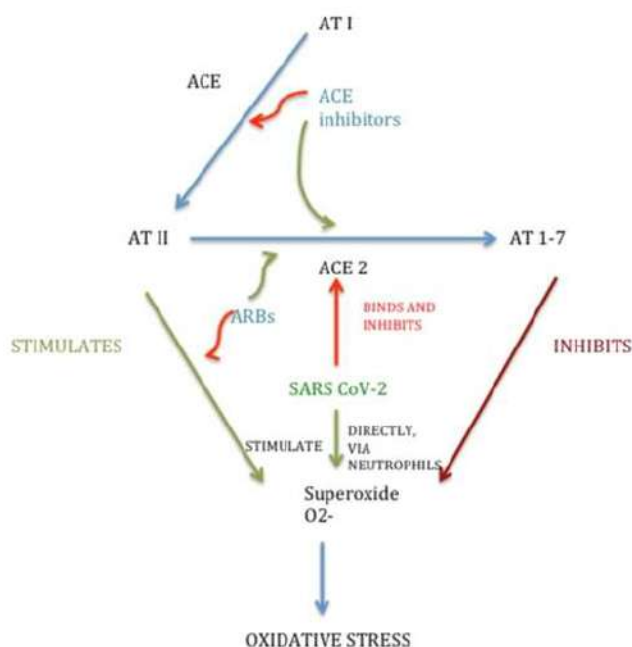


Fig. 6: Role of ACE inhibitors and ARBs in COVID.

COVID infection in paediatrics

It is now well understood that children and infants have some sort of inherent immunity against COVID infection and older people are increasingly susceptible to the infection. Children even after being infected tend to show milder symptoms with very quick recovery. This may be explained by a physiological elevation of lymphocytes and reduction in pro inflammatory cytokines and higher production of anti-

inflammatory in children as compared to adults. Also, children have an abundance of AT 2 receptors which have a predominantly anti-inflammatory effect and less of AT1 receptors which are proinflammatory. Furthermore, children tend to have a more robust and active innate immunity due to repeated viral and bacterial infections in the childhood. In addition, the endothelium is less pre-damaged in children on account of less age [29].

Conclusion

COVID pathogenesis is still not fully understood. Children have an abundance of AT 2 receptors which have a predominantly anti-inflammatory effect and less of AT1 receptors which are proinflammatory. Furthermore, children tend to have a more robust and active innate immunity due to repeated viral and bacterial infections in the childhood. Ongoing research on RAS pathways may unravel the, hitherto, unsurmountable challenges in

the understanding of COVID-19 pathogenesis. Ongoing studies on Renin Angiotensin System pathways have the potential to unravel the pathogenesis of COVID-19.

Conflicts of interest

The authors have no competing interests to declare that are relevant to the content of this article

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REVIEW ARTICLE

Competency Based Assessment in Paediatric Surgery: Strengths, Challenges, Limitations

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Competency based education (CBE) is a criterion-referenced, outcomes-based framework used for curriculum design and assessment in medical education [1].

The goals of CBE are:

- ❑ To define and assess-
 - Provider competence along a trajectory
 - From novice to expert
 - Using objective performance measures
- ❑ There is a general realization of the need to improvise training directly by engaging with residents, in a certain section of their curriculum-
 - Assessment methods profoundly influence student motivation and effort, it is critical to measure all desired aspects of performance throughout an individual's medical training.

- The proficiencies and aptitudes of professionalism and professional practice in postgraduate education are best taught through direct clinical care as well as simulation and technology enhanced learning (TEL).
- Simulation can allow residents to be put in uncomfortable, high-risk, or difficult environments and give them the ability to act out what they might do in a real situation. They are able to get direct feedback, and re-enact to some of the situations if needed.

- ❑ In the current times, KNOWLEDGE is exploding. The challenge is how to impart meaningful knowledge-

- The twentieth century witnessed the emergence of medical education as a recognized medical discipline, if not a profession. Medicine owes this transformation to a handful of pioneers who dared to challenge the conventional medical education. The initiatives of these individuals were based upon new thinking about education in general that was voiced during the second half of the century and

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- On better understanding of the neuropsychological basis of the learning process. These, together with growing dissatisfaction with contemporary medical education, brought about the efforts to change.
- In sync with the recommendations made by national and international organizations such as-
 - The American Association of Medical Colleges (AAMC),
 - The World Health Organization(WHO), and
 - The World Federation for Medical Education. All of them proposed somewhat similar lines along which medical education should develop

These guidelines have universal application.

□ What the Residents require:

- Residents learn by analysis and synthesis.
- What is going on, and why, are the questions that arise first.
- As the diagnosis develops through clinical and diagnostic implementation the process of synthesis occurs and the picture is put together.
- But, within this paradigm are the features of dealing with complexity and uncertainty:
 - There is not always one correct answer.
 - How do we challenge our trainees who are brought up with their assessments to assume that one answer is correct and the other four are wrong?
- To achieve this, there is a shift towards COMPETENCY- BASED MEDICAL EDUCATION. This is by:
 - Tracking their achievements
 - Making curricula more flexible & relevant
 - Faculty development by more training & support for supervisors.

- Instead of reliance on HIGH STAKE EXIT EXAMINATIONS to constant assessment
- LONGITUDINAL ASSESSMENT relevant to day to day practice
- Essentially, OUTCOMES-BASED training programmes

- The National Board of Examinations in Medical Sciences (NBEMS) recognizes, that, attainment of competence is rarely a linear path for a resident, just as developmental progression is not the same for children:

- Residents learn at different rates,
- Have different strengths, and
- Different areas for improvement.
- These areas for improvement are rarely stable throughout three or four years of residency training.

The lack of inter-rater consistency among faculty is normal and expected.

□ Strengths:

- The NBEMS set up its purposes. A centrally administered, curriculum oriented, outcomes-based approach adopted by the National Board of Examinations in Medical Sciences (NBEMS). These guidelines included, among other recommendations, the following:
 - To set institutional objectives
 - To centralize the administration of resources, including curricular time and content
 - To refocus the orientation from teachers to students
 - NBEMS-App-Enabled guidance, monitoring & assessment

□ Formative Assessment

- Includes various formal and informal assessment procedures by which

evaluation of student's learning, comprehension, and academic progress is done by the teachers/ faculty to improve student attainment.

- Formative assessment test (FAT) is called as "Formative" as it informs the in process teaching and learning modifications.
- FAT is an integral part of the effective teaching.
- The goal of the FAT is to collect information which can be used to improve the student learning process.
- Formative assessment is essentially positive in intent, directed towards promoting learning; it is therefore part of teaching.
- Validity and usefulness are paramount in formative assessment and should take precedence over concerns for reliability.

□ **Competency-based assessment**

- Seeks to align measures of performance directly with desired learning outcomes based upon the needs of patients and the healthcare system:
- Its assessment does not seek to ensure only minimal competence, but rather promotes each learner's trajectory toward excellence across multiple domains of performance.
- It is advantageous to introduce students to the competency domains and milestones early in training and to emphasize the need for continual development throughout one's medical career.

□ **Practice based curriculum: Its advantages are-**

- Students benefit from practice because **they are able to apply knowledge through interaction**

- Students connect with the material when they work with texts and concepts beyond a one-time exposure
- For quality development in post graduate training
- It is a dynamic process
- It engages with the individual to calibrate his performance with the expected outcomes
- Milestone-based assessment has significant potential to guide the development of medical students.

□ **Formative Assessment has Six Domains of core competencies. These are:**

1. Patient Care
2. Medical Knowledge
3. Professionalism
4. Interpersonal and Communication Skills
5. Practice-Based Learning and Improvement
6. Systems-Based Practice

□ **Milestones: The performance levels in each domain is reflected by 3 milestones in each:**

1. Skills,
2. Knowledge &
3. Behaviour

□ **Performance levels in each milestone could be graded as follows:**

1. For Undergraduates:
 - i) novice performance and
 - ii) performance expected of a graduating MD.
2. For Postgraduates:
 - i) novice,
 - ii) advanced beginner,
 - iii) competent individual,
 - iv) proficient individual, and v) expert physician.

□ **The original Pediatric Surgery Milestones** (hereafter referred to as Milestones 1.0) was unveiled in July 2015. Over time, experience using the Milestones 1.0 revealed some of its weaknesses and limitations.

- Five key criticisms were raised
 1. There were too many sub-competencies in many specialties.

2. The Milestones were written in overly complex language.
3. There were too many individual milestones within each subcompetency.
4. Few junior and mid-level faculty were involved in the creation of Milestones 1.0.
5. There was considerable variability across specialties with regard to the non-patient care and non- medical knowledge sub-competencies (interpersonal and communication skills, practice-based learning and improvement, professionalism and systems-based practice).

These differences were thought to interfere with, rather than facilitate, collaboration in assessment and faculty development activities across specialties.

□ **Pediatric Surgery Milestones 2.0**, summarizes key changes from Pediatric Surgery Milestones 1.0 and highlights implications for important stakeholders, viz.:

- Pediatric surgical trainees,
- Faculty at training programs and
- Subsequent employers
-

□ **The working group for Milestones 2.0 created eleven Patient Care sub-competencies.** There are Seven intraoperative sub-competencies:

- 1) Endoscopy Procedural Skills,
- 2) Procedural Skills for Minimally Invasive Surgical Procedures,
- 3) Procedural Skills for Thoracic Cases,
- 4) Procedural Skills for Abdominal Procedures,
- 5) Procedural Skills for Oncologic Cases,
- 6) Procedural Skills for Other Operations and Tissue Handling of Delicate and Neonatal Tissue
- 7) Separate sub-competencies were created for Patient Evaluation &
- 8) Clinical Decision-making
- 9) Postoperative Care
- 10) Critical Care and
- 11) Trauma Management.

□ **Challenges:**

- Variability in national educational provisions have constantly been observed.
- There remain major differences in the training, including years of training, exposure to pediatrics & other non-surgical areas during training.
- Exposure to pediatric trauma & pediatric neurosurgery are available only in some institutions.
- These wide variations in pediatric surgical training hinder a more standardized criteria for training and evaluating pediatric surgeons on a global level.

While the National Board imparts its curriculum through its central IT-Hub, the same uniformity could not be found in other programmes in India.

This is the singular feature of the NBEMS.

□ **Limitations:**

- The programmes have fixed period- 3 or 6 yrs.
- If the anticipated level is not achieved within the stipulated time then residency will need to be extended.
- While experience continues to be gained after the degree, the dilemma for course directors to allow appear in EXIT exam will be there.
- Alternatively, desirable and permissible OR independent vs partially dependent grading would be needed.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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REVIEW ARTICLE

Neurosurgery Simulation-based Skills Training: From Mannequins and Cadavers to Virtual Reality and Artificial Intelligence

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Abstract

Simulation in the neurosurgical context broadly refers to systems that either create or enhance the perceivable and sometimes interactable environment of the user. Adequate resident training requires hands-on experience, but operative neurosurgery affords few such chances. Moreover, the pressure of performing well, time constraints and fear of mistakes hinder adequate learning. It may also lead to an erroneous evaluation of the residents' surgical aptitude on the part of the supervisor. Simulation systems offer a unique solution for resident training in a safe environment as well as unbiased evaluation. Simulation-related technologies can also be used to better counsel patients, pre-operative planning and development of newer techniques and devices. Various modalities of simulation training available at present include physical (PR), virtual (VR), augmented (AR), and mixed (MR) reality. Though we have achieved significant advances in all forms of simulation models, largely we are dependent on human experts for the evaluation of the performance of trainees. Artificial Intelligence (AI) algorithms may offer an alternative to human experts with several advantages including the removal of human bias, and preserving human resources. In this manuscript, we have summarized our innovations and lessons learned from our neuro-engineering collaboration at the Neurosurgery Education and Training School (NETS): Neurosurgery Skills Training Facility (NSTF), All India Institute of Medical Sciences (AIIMS), New Delhi that will help in pushing the boundaries of the role of simulation in neurosurgery.

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Graphical Abstract

**Background of Neurosurgery Training**

There has been a paradigm shift from the old Halstedian apprenticeship-based teaching model being practiced in the past. There are several reasons for this, including reduced teacher: student ratio, reduced working hours of residents, financial and medico-legal constraints in the operating rooms. Along with this, supervised training by expert neurosurgeons although essential, as the sole training modality could induce anxiety, subjectivity and unquantified learning. Neurosurgery being a challenging specialty with morbidity can be intimidating for both teachers to teach and students to learn. Iatrogenic injuries are being increasingly recognized, with a need for additional training post formal neurosurgical certification [1,2]. In Low and Low Middle Income countries (LMICs), there is a dearth of trained neurosurgeons to cater to the need of the large population [3]. Majority of institutions providing training in neurosurgery lack the infrastructure for holistic skills training such as cadaver lab, animal facility and simulation training. This is compounded by lack of a standardized training curriculum. Although, creating and grooming a neurosurgeon is rigorous, resource intensive and time consuming as it is a long road, there is a severe need felt for neurosurgery skills training facilities in India. There is approximately one neurosurgeon for every 250,000 population in

India with close to 230-250 neurosurgeons being trained each year. Nearly 31% of the institutes with neurosurgery training programs in India have not published peer-reviewed papers in the last 5 years [4-5].

Origin of the Neurosurgery Skills Training Facility

The Experimental Micro-Neurosurgery Laboratory at the Department of Neurosurgery, All India Institute of Medical Sciences (AIIMS), New Delhi was started in 1971 through the efforts of the stalwarts of Indian Neurosurgery - Prof. P. N. Tandon and Prof. A. K. Banerji. It was intended to be a nexus of neurosurgery skills training and imparting of practical knowledge to future trainees. It has since evolved into a state-of-the-art multifaceted Neurosurgery Skills Training Facility (NSTF) with crucial roles in skills training, cutting edge research and evolution of biomedical engineering in neurosurgical simulation (Figure 1).

Pioneering work is being done in the fields of developing and standardizing an objective structured modular neurosurgical skills training curriculum, virtual reality (VR) application in training, artificial intelligence (AI) usage in evaluation of training, developing physical models for task-based training and creation of virtual repository of computer assisted design (CAD) models of neurosurgical devices [6,7]. Objective assessment of skills

and standardization of curriculum is evolving across neurosurgery [8] and the role of simulation in neurosurgical education and training is expanding constantly [9-15] and our facility is contributing to it as one of the pioneers.

A unique and indispensable arm of the NSTF at AIIMS, New Delhi is the Neurosurgery Education and Training School (NETS); a holistic training effort undertaken by intramural inter-departmental collaboration between the departments of neurosurgery, anatomy, forensic medicine and central animal facility with extramural experience injected by national and international dignitaries in the field of neurosurgery. Its workshops provide in-depth skills training, along with refinement of neurosurgical understanding in a holistic context.

The quality of training being imparted at our skills training facility is showcased by the large number of trainees from outside AIIMS who apply for short term training (STT). The far-reaching impact of the research work being done within and beyond neurosurgery is evident by the collaboration of the NETS with the departments of Biomedical Engineering and Computer Science Engineering at the Indian Institute of Technology (IIT), New Delhi.

Simulation training and research are intricately tied up in the NETS-NSTF with training sessions providing background and data for research activities which in turn are applied for betterment of the training modules. There are multiple carefully designed modules with physical and/or virtual simulators for task and procedure-based simulation training in various facets of Neurosurgery.



Figure 1. Overview of neurosurgery simulation-based training at NETS-NSTF.

Simulation in Neurosurgery

Simulation based training in neurosurgery comprises of the different modalities of simulation viz physical, virtual and mixed reality low and high-fidelity simulators. Human and animal cadaveric models, live small experimental lab animal models, custom designed mannequins, bench trainer models and state-of-the-art virtual reality simulators with task and procedure-based simulation are available and routinely utilized in our lab. The performance of subjects is assessed objectively with expert feedback and automation to improve ability to generalize and eliminate bias. Computerized AI based automated, objective assessment coupled with sensor based kinematic assessment of skills leads to holistic assessment causing the learning curve to flatten. The various simulation modalities available at our lab are summarized in Table 1.

Microneurosurgery Module

Microsuturing: Three levels of complexity are used to provide structured task-based microsuturing physical simulator training with expert feedback and AI based evaluation. The 'Basic' level entails introduction to microsuturing ergonomics and proper technique with meticulous expert intervention to teach novices the basic tenets of microsuturing. It involves supervised 4-0 and 5-0 suture size microsuturing. The 'Intermediate' level is where the trainees expand their horizons by working with finer suture sizes – 7-0, 8-0, 10-0, and where the requirements and evaluation of the task-based training exercise are more stringent. The 'Advanced' level is where the trainees start training in physical simulator task-based exercises on micro-anastomosis of nerve and vessel models. It starts with orientation and expert feedback

provided on physical simulator models such as silastic tubes followed by progression onto animal models such as chicken wing arteries and finally live animal models such as live anesthetized rat/guinea pig nerve and vessels (Figure 2A). At all levels of training, constant expert feedback and supervision is provided to help trainees develop the proper technique and learn from their performance. This is supplemented with AI based objective, unbiased and instant performance scoring for standardizing training for all trainees. We have developed a Deep Learning-based automated performance scoring system with ranking which can automatically and accurately segment the suture line from a provided picture of the final sutural construct and give overall and parametric scores. This AI-based system has been trained on expert feedback-based ground truth evaluation of thousands of sutural constructs, thus making it very close to accurate.

Microneurosurgery: Physical simulators have been created emulating various neurosurgical procedures for procedure-based and task-based training with expert supervision and feedback supplemented by automated AI segmentation and assessment. Various simulators available are for aneurysm dissection and clipping, and cadaveric skull base approaches. State-of-the-art VR modules with multiple training exercises with in-built evaluation and feedback augment the training provided in our lab- NeuroVR for brain tumor surgery eg. glioma and meningioma excision, laminectomy, etc. and ImmersiveTouch for ventricular catheterization and pedicle screw fixation. (Figure 2B). The trainees are also exposed to finer microneurosurgical nuances on cadavers especially for skull base approaches (Figure 2C).

Table 1. Summary of various simulation modalities available at NETS-NSTF

S. No.	Name of the Skill Lab	State	Management	Courses and Duration
1.	Neurosurgery Education and Training School (NETS), Neurosurgery Skills Training Facility (NSTF), Department of Neurosurgery, AIIMS New Delhi.	New Delhi	Government	<p>Neurosurgery 2 weeks & 4 weeks short-term simulation based skills training. (Recommended 3 sessions of two weeks or 2 sessions of four weeks in MCh/DNB Neurosurgery)</p> <p>Microneurosurgery Module</p> <ol style="list-style-type: none"> <u>Microsuturing</u> <ul style="list-style-type: none"> Basic: 4-0, 5-0 Intermediate: 7-0/8-0, 9-0/10-0 Advanced: Silastic tube, Chicken wings artery, live anesthetized rat/ guinea pig vessel/nerve anastomosis <u>Microneurosurgery</u> <ul style="list-style-type: none"> Aneurysm Clipping Cadaveric Skullbase Approaches Physical Simulator with AI-based Skills Evaluation Virtual Reality <p>High-Speed Drilling Module</p> <ul style="list-style-type: none"> Basic: Sheep head, Scapula Intermediate: Microscopic/Endoscopic Drilling Advanced: Neurosurgery Craniotomy Physical Simulator with AI-based Skills Evaluation Virtual Reality <p>Neuroendoscopy Module</p> <ul style="list-style-type: none"> Basic: Natural Simulation, Mannequin Intermediate: Neuroendoscope Box Trainer Advanced: Cadaveric Endonasal Approaches Physical Simulator with AI-based Skills Evaluation Virtual Reality <p>Spine Instrumentation Module</p> <ul style="list-style-type: none"> Saw bone Virtual Reality <p>Clinical Observership</p> <ul style="list-style-type: none"> Ward/ICU rounds Operative room (OR) Observership <p>Case Scenarios</p> <ul style="list-style-type: none"> Video-based training

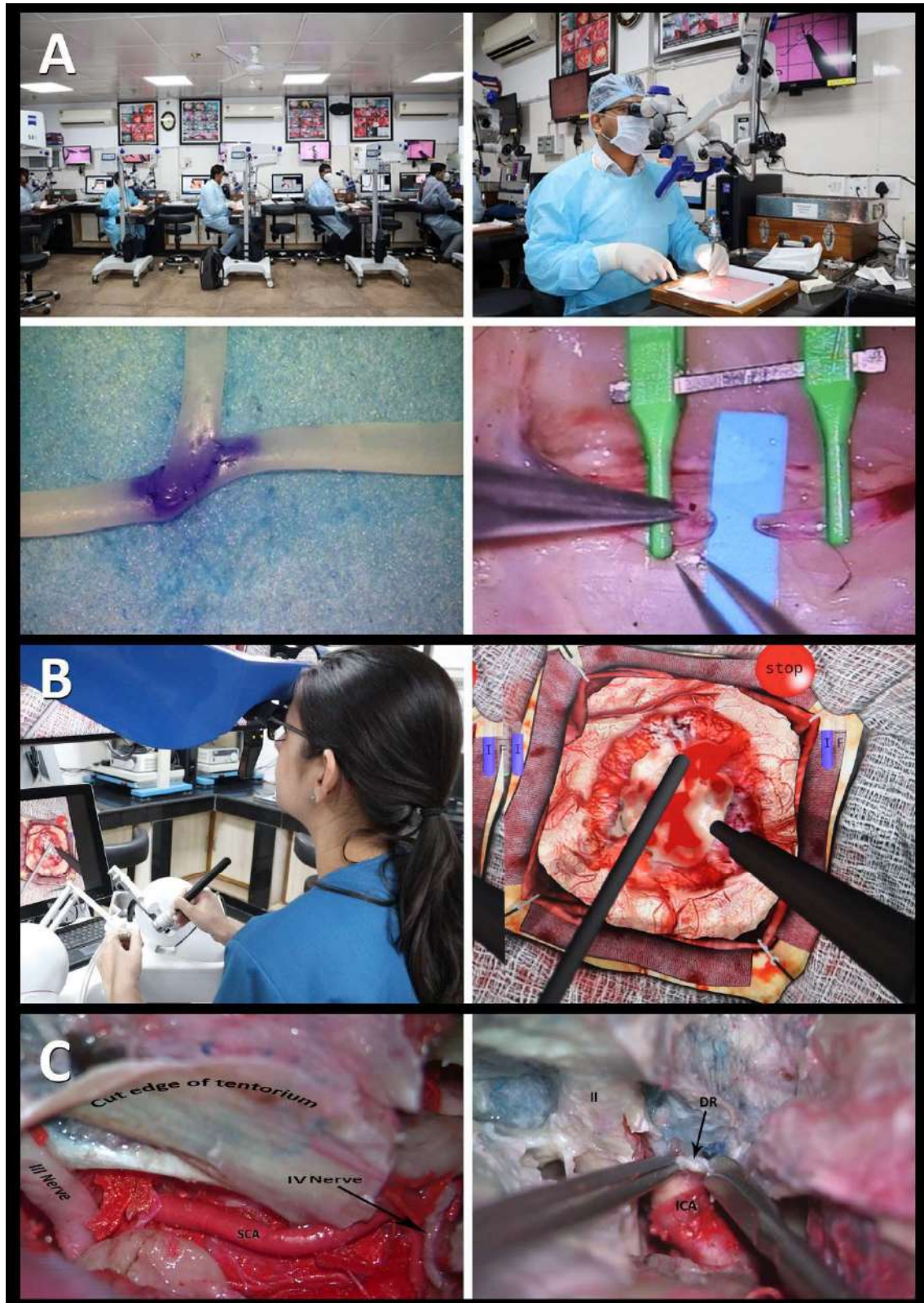


Figure 2. Various microscopic simulation modules- A. Microsuturing, B. Virtual reality based microneurosurgery, C- Cadaver-based microneurosurgery.

High Speed Drilling Module

Neurosurgical drilling is an integral part of cranial as well as spinal surgical procedures. The NETS-NSTF provides cutting edge and world class physical and virtual reality simulators for accurately emulating and assessing microscopic and endoscopic drilling. Three levels of drilling training are provided to trainees; 'Basic' entails orientation to drill handling and ergonomics with constant expert supervision and feedback followed by macroscopic task-based training on cadaver sheep head and scapula specimens; 'Intermediate' level incorporates microscopic and endoscopic drilling with familiarity and ease of handling being a focus with the change in visualization methods. The 'Advanced' level emulates real world application of drilling with neurosurgical craniotomy simulation with expert feedback on the adequacy, speed and safety of the craniotomy (Figure 3A). This is augmented with AI based automated, objective skills evaluation and ranking which has been trained on hundreds of expert ground truth evaluations. The NeuroVR haptic feedback simulator also has a module for microdrilling hemilaminectomy. (Figure 3B) The 'Advanced' level neurodrilling training exposure is further enhanced by supervised cadaveric workshops conducted at our lab (Figure 3C).

Neuroendoscopy Module

When endoscopic interventions were introduced in neurosurgery, they initiated a revolution of minimally invasive neurosurgical procedures. As these procedures require a different skill set in terms of orientation and planning as compared to traditional microneurosurgery- NETS-NSTF has developed original, custom-designed and open-source training modules with a structured training regime incorporating self, expert and AI based feedback. As with microsuturing and drilling, endoscopic simulator training is also structured into different levels with trainees perfecting the learning objective of one level to incorporate all the skills required to benefit maximally from the subsequent level. This provides them with self-feedback and a smoother learning curve. The 'Basic' level

teaches safe and ergonomic endoscope handling, assembly and disassembly along with orientation to the 2-dimensional screen space-enabling trainees to recreate a 3-dimensional projection of the same. This is followed by task-based training with expert supervision and feedback in natural and mannequin physical models for endonasal as well as intraventricular procedures. In the 'Intermediate' level, trainees are introduced to and familiarized with our cutting-edge in-house physical simulator for neuro endoscopy training- the Neuro-Endo-Trainer [19–22]. (Figure 4A) It enables evaluation of the ease and ergonomics of bimanual endoscope and instrument handling. It also has a movable platform thus simulating the various angles at which anatomic structures present themselves during actual procedures. It entails a task-based structured training regime amenable to AI auto-segmentation and objective automated scoring with different levels of difficulty to enable the trainee to learn through self-feedback on a continually improving pace. Automated evaluation of Neuro-Endo-Trainer performance with AI based segmentation of instrument tip and auto tracking of task completion and steps taken has been developed in our lab. Electromyography based assessment of tremors and correlation with neurosurgical skills has also been undertaken at our lab. The systems for tracking the tip of the endoscopic operating tool in 3D space by exploiting the rigid body properties of the tool and dry bone have also been developed which enable precise endoscopic skull base interventions. NETS-NSTF also provides NeuroVR based endoscopic third ventriculostomy (ETV) virtual reality simulation training with haptic feedback. (Figure 4B) After adapting to bimanual handling, variable angles and 3D projection of the 2D space, trainees progress to the 'Advanced' level where cadaveric endonasal approaches are taught under constant expert supervision. (Figure 4C).

Spine Instrumentation Module: Both physical saw-bone and virtual reality simulators with expert feedback are provided in our lab for task and procedure based spinal instrumentation training.

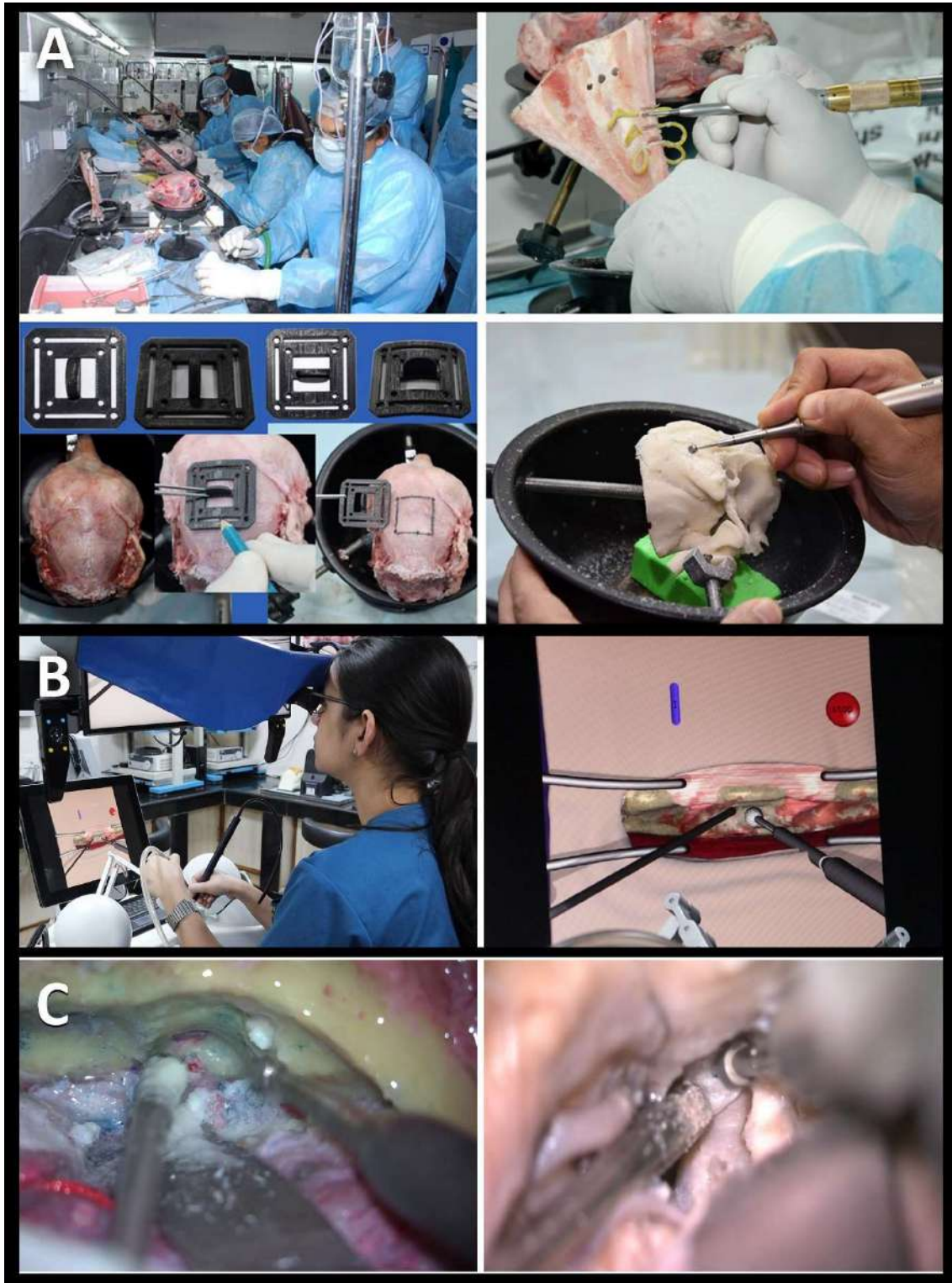


Figure 3. Various high-speed neurodrilling simulation modules- A. Microdrilling, B. Virtual reality-based microdrilling, C- Cadaver-based microdrilling.

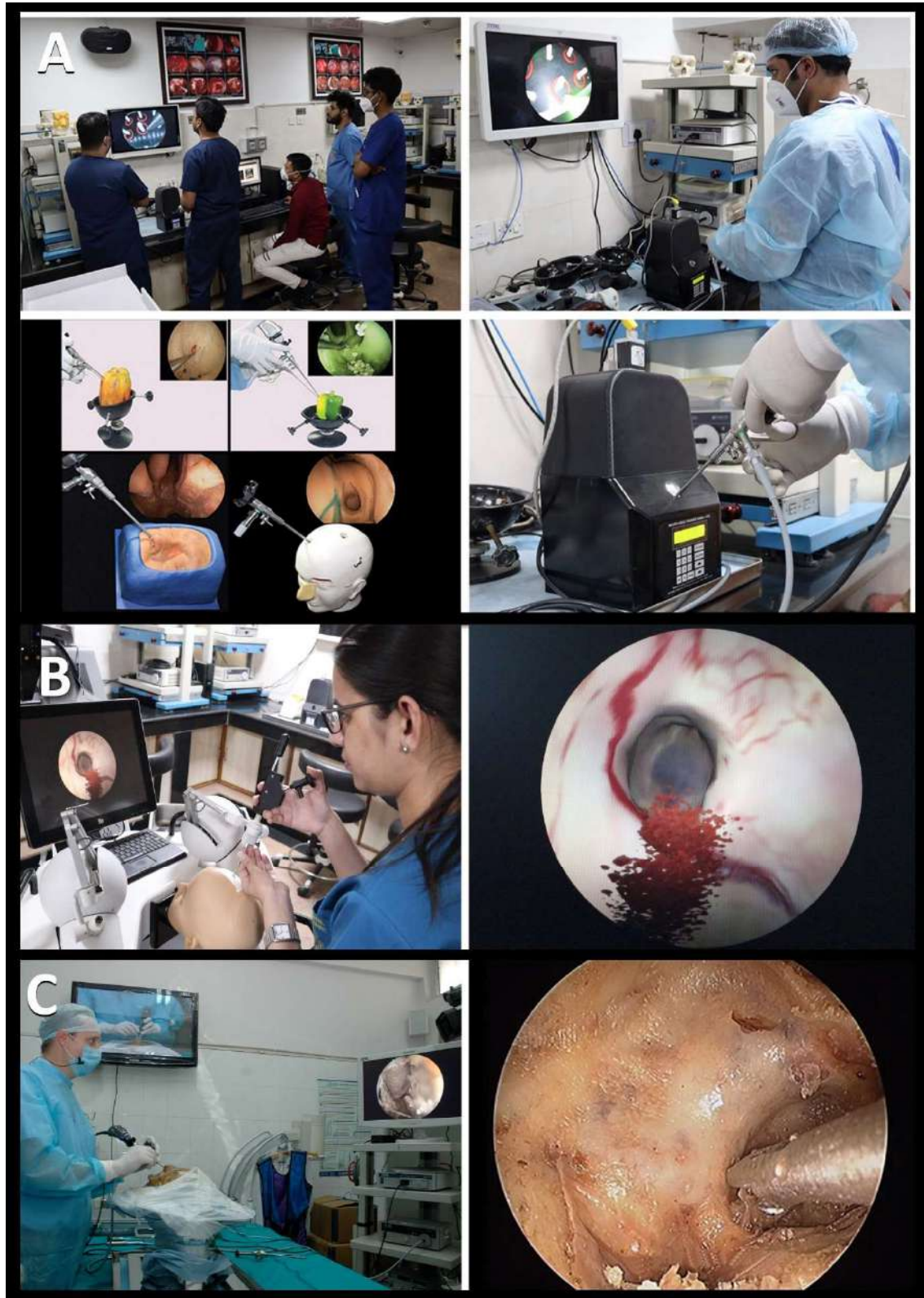


Figure 4. Various neuroendoscopic simulation modules- A. Neuroendoscopy , B. Virtual reality based neuroendoscopy, C- Cadaver-based endoscopic approaches.

Table 2. Various Components of AIIMS-NETS-SAS

S. No.	Criteria	Evaluation parameter	1	2	3	4
1	Eye hand coordination	-Handling of instruments (Needle holder, forceps, endoscope, grasper) -Depth perception (under magnification)	Continuous struggle throughout the activity	Frequent loss of coordination	Grossly smooth coordination	Perfect coordination
2	Instrument tissue manipulation	-Tissue handling under magnification with various instruments -Appropriate pressure and force -Confrontation with neighboring objects (Repeated puncture)	Grossly unacceptable	Frequent difficulty	Smooth handling	Perfect manipulation
3	Dexterity	-Tremors/ jitteriness -Therblig (intraoperative elemental motion)	Irregular therblig/ tremors/ jitteriness throughout the activity	Frequent difficulty	Grossly smooth	Perfect dexterity
4	Flow of procedure	-Time management during activity -Total duration in task completion -Unnecessary delays in inter or intra therblig	Grossly unacceptable	Frequent lapses	Grossly smooth	Perfect flow
5	Effectualness	Evaluation of end result on predefined criteria* for: -Microsuturing -Neuroendoscopy	Grossly unacceptable	Partially acceptable	Grossly acceptable	Perfect end result
*Criteria for effectualness						
Microsuturing <ul style="list-style-type: none"> • Margins (overlapped/loose/apposed) • Inter-sutural distance (equal/unequal) • Sutural distance on both sides of the incision (equal/unequal) • Angulation between suture and knot (Near perpendicular- Yes/No) 			Neuroendoscopy <ul style="list-style-type: none"> • Final position of rings <ol style="list-style-type: none"> 1. ≥ 3 rings slipped 2. 2 rings slipped 3. 1 ring slipped 4. All rings in place 			

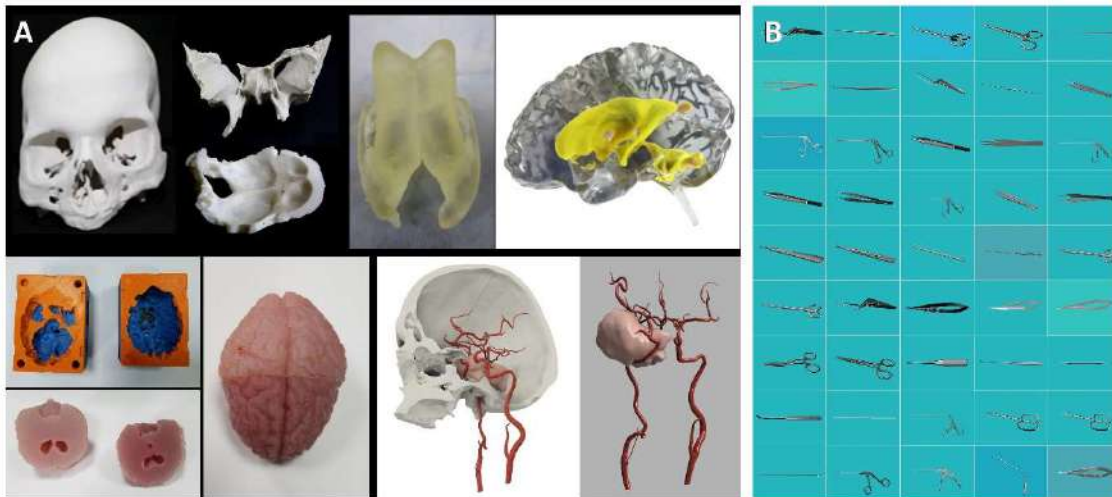


Figure 5. A. CAD based 3D-printed models, B- Virtual surgical instrumentation repository.

Development of scoring system NETS-SAS

We have developed an in-house expert objective scoring system for a holistic and objective evaluation of neurosurgical skills. Their development has been tested with AI for automation which provides multi-dimensional assessment and avenues for feedback. The Neurosurgery Education & Training School – Skills Assessment Score (NETS-SAS) has been summarized in Table 2 and it has been validated in previous studies [6,14].

Development of unique physical simulators

NETS-NSTF has developed, tested and compared unique synthetic physical simulator material simulating skin and dura mater using silicones. The hardness of our various in-house silicone mixtures was measured and neurosurgical opinion after practicing micro suturing on the material was used to determine the best mixture, which was haptically closest to simulating skin and dura mater.

The NETS-NSTF has a 3-D printing facility for developing various in-house 3D CT/MRI segmented biomechanical and anatomically accurate physical models for various procedure-based training such as aneurysm clipping and skull base models [16]. We have also developed scanned CAD models of various neurosurgical instruments for 3D space manipulation, which also enables creation of more elaborate simulations [17,18] (Figure 5A-B).

International Collaboration

International workshops and conferences:

Collaborative training with multi-departmental and multifaceted workshops are being continually held and facilitated by our lab. Since 2006, there have been 101 NETS collaborative workshops with 1119 total delegates. Multiple professional neurosurgical bodies such as the World Federation of Neurosurgical Societies (WFNS) and International Society of Pediatric Neurosurgeons (ISPN) have held their benchmark workshops at our facility. Short term training (STT) 2 weeks and 4 weeks courses for participants working and training in neurosurgery outside AIIMS, New Delhi are being constantly chosen by many trainees from all over the country. There have been 296 total short-term trainees and 14377 total STT sessions. (Figure 6).

Indo-German Collaboration:

NETS-NSTF was instrumental in Indo-German collaboration neurosurgical training workshops involving the Ministry of Science & Technology, Govt. of India and the University of Mainz with dignitaries and stalwarts such as Prof. Martin Bettag. From 2009-2015, there were 16 workshops and 231 delegates trained with special emphasis on neuroendoscopic and spine physical simulator training.

NETS Short-Term Neurosurgery Skills Training (2002-2022)	
2 Weeks short-term trainees: 151	
4 Weeks short-term trainees: 145	
Total no. of short-term trainees: 296	
AllIMS residents (Neurosurgery, ENT, General surgery, GI surgery, Maxillo facial surgery, Orthopedics, Plastic surgery): 460	
Total no. of training sessions: 14377	
NETS Workshops (2006-2022)	Indo-Japan Workshops (2017-2018)
Total no. of workshops: 101	Total no. of workshops: 3
Total no. of delegates: 1119	Total no. of delegates: 167
WFNS Neuroanatomy Workshop (2018)	NESI Workshop (2016)
Total no. of delegates: 75	Total no. of delegates: 28
Indo-German Workshops (2010-2015)	WFNS Neuroendoscopy Workshop (2015)
Total no. of workshops: 16	Total no. of delegates: 112
Total no. of delegates: 248	
MIT-HARVARD-IITD Workshop (2013)	ISPN Craniofacial Workshop (2012)
Total no. of delegates: 34	Total no. of delegates: 15
Int. Neurovascon Workshop (2011)	WFNS Skull Base Workshop (2007)
Total no. of delegates: 38	Total no. of delegates: 41

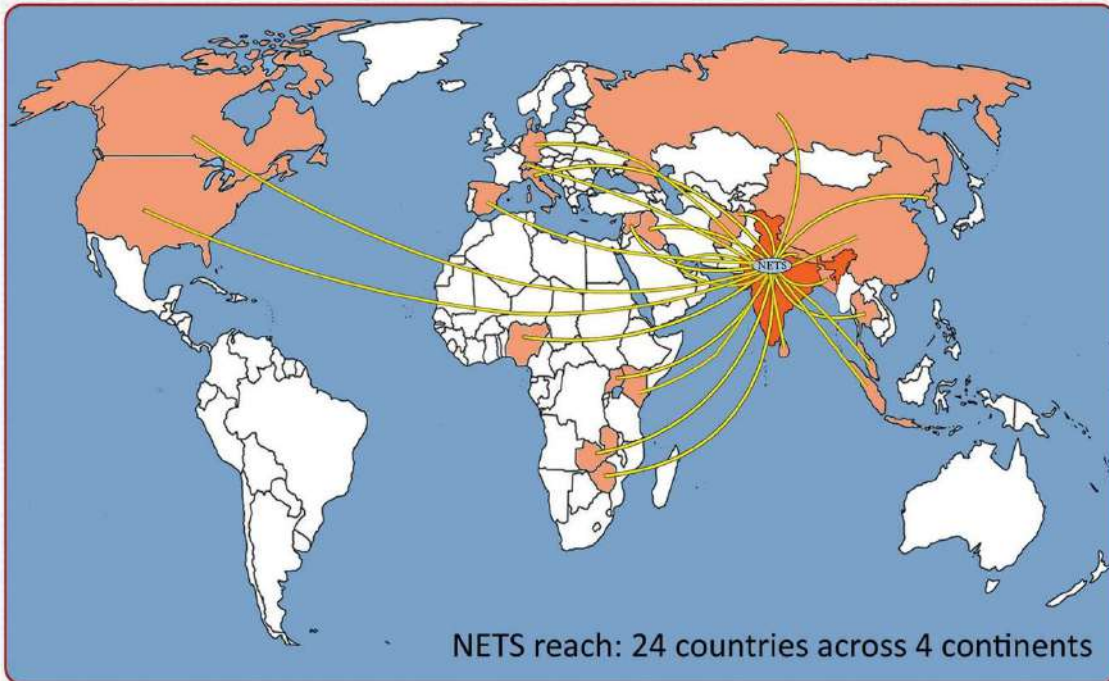


Figure 6. Impact and outreach of NETS-NSTF short-term training program.

Indo-US Collaboration:

NETS-NSTF was central to 3 Indo-US collaboration workshops held at Coimbatore, Hyderabad and Chennai involving American and Indian Professional Neurosurgery Societies-Congress of Neurological Surgeons (CNS) and Neurological Society of India (NSI)

respectively with dignitaries from all around the world. The workshops involved virtual reality and physical simulator-based training and evaluation.

Indo-Japan Collaboration:

Three Indo-Japan collaboration workshops were held at our lab with luminaries such as Prof. Kenji Ohata from the University of Osaka, Japan and involving the Ministry of Economy, Trade & Industry, Govt. of Japan. The workshops had special focus on 3D neuroendoscopic anatomy, cadaveric skull base demonstrations, neurovascular simulator training and assessment with 3 modules, 10 stations, 40 delegates, and 4 Japanese faculty.

Philosophy of NETS-NSTF

The development and practice of any skill evolves the subject as a whole and converts what was perceived as an innate God given Art to a meticulous science with a structured modality of practice. This practice is difficult in medicine and neurosurgery in particular as patients cannot be treated as experimental specimens for practice without any previous training. Hands-on, open-source, low-cost, validated, structured training modules such as the ones developed and employed in the NETS-NSTF, AIIMS, New Delhi, if made widespread shall reduce the number of cadaver and animal models needed for training. Furthermore, automated, objective AI based evaluation with expert oversight will ensure to flatten the learning curve and help rapidly develop anatomic orientation and operative intelligence. Ad-hoc training at centers of excellence such as ours with formative and summative assessment shall provide a boost to the development of acumen and skills. This philosophy if integrated in neurosurgical curriculum worldwide with national and international collaborations shall bolster future neurosurgical training.

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Conflicts of interest

The authors declares that they do not have conflict of interest.

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Ethics Approval

Institute Ethics Committee Approval:
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REVIEW ARTICLE

COVID-19 Pandemic – Nephrologist’s Perspective

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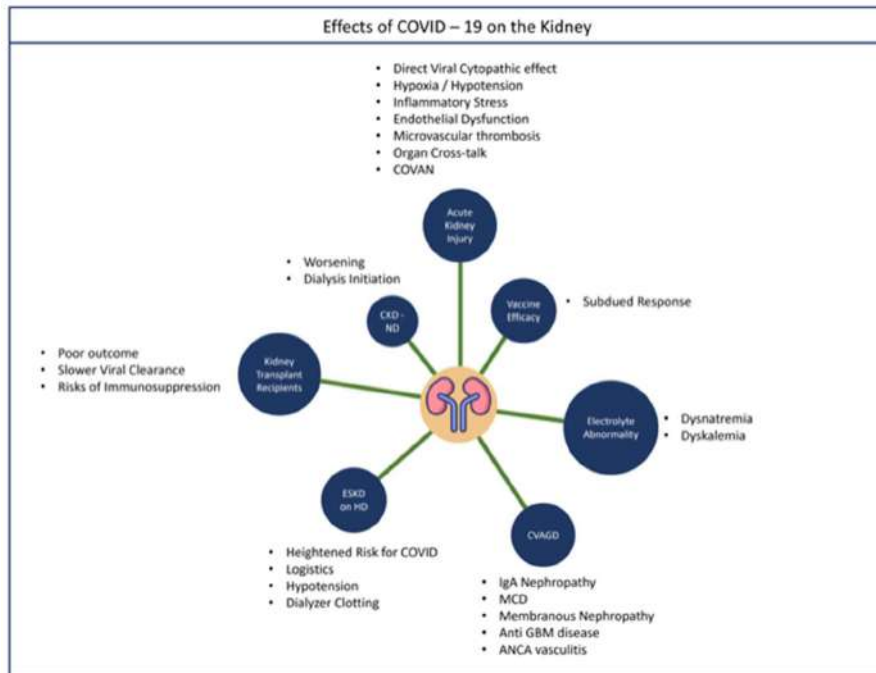
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Abstract

Nephrology services across the world, already struggling to cope up with chronic kidney disease (CKD) of epidemic proportions, faced enormous challenges during the COVID pandemic. SARS CoV -2 virus affects kidney directly and indirectly through systemic effects. Also, the pandemic impacted almost all aspects of renal care services in several ways. This review article aims to discuss the impact of COVID on kidney and renal care services under the following headings.

Keywords: COVID 19, Coronavirus pandemic, Kidney

Graphical Abstract



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Introduction

Coronavirus pandemic, has in fact, proved to be a 'war in disguise'. The hither-to unexperienced medical, administrative, financial and emotional challenges posed by the pandemic provided an opportunity for introspection on the adequacy of health care delivery system and on the resilience of health sector to face unexpected challenges.

Though lung is the primary organ affected by the coronavirus, other organ systems including kidney also are affected in several ways.

Acute Kidney Injury

There has been a wide discrepancy in the incidence of acute kidney injury (AKI) in patients with COVID, ranging from 5% to 60%. The reasons for the wide variations in AKI incidence could be the different definitions of AKI used and the varying degrees of severity of COVID in the study population. Incidence of AKI increases with increasing severity of COVID. Patients requiring mechanical ventilation are at higher risk for AKI. In a study of 154 patients with COVID associated AKI, the mortality was 38% and old age, severe CT severity, higher CRP and requirements of inotropes were independent predictors of mortality [1].

The patho-mechanisms of COVID-related AKI are multi-factorial, including systemic effects, possible direct viral cytopathic effect and the host's immune responses to COVID. Renal tubular epithelial cells and podocytes express ACE II receptors. Hence, it is possible that there can be direct viral cytopathic effect. Following factors, in varying degrees and combination contribute for AKI (Table 1).

Table 1. Mechanism of Acute Kidney Injury

1	Hypoxia
2	Hypotension
3	Macrophage activation
4	Inflammatory stress (Hyper-ferritinemia is a surrogate)
5	Activation of coagulation
6	Microvascular thrombosis
7	Endothelial dysfunction
8	Cytokine storm – IL-1, IL-6, TNF alpha
9	Oxidative stress
10	Complement activation
11	Organ 'cross-talk'
12	Rhabdomyolysis

1. COVID – related acute kidney injury (AKI)
2. Impact of COVID on patients with non-dialysis requiring CKD
3. COVID in patients on maintenance hemodialysis
4. COVID in kidney transplant recipients (KTR)
5. COVID vaccination in patients on Renal Replacement Therapy
6. COVID vaccine – associated glomerular diseases (CVAGD)
7. Dyselectrolytemia in CCOVID
8. Kidney in Long-COVID

Kidney Pathology in COVID

Acute tubular necrosis and acute interstitial nephritis are the commonly reported pathological lesions. Rhabdomyolysis induced by COVID may result in myoglobin pigment cast nephropathy. Severe endothelial dysfunction/injury ensues in thrombotic microangiopathy (TMA). Renal artery occlusion resulting in renal infarction has been reported.

An exciting pathology, 'collapsing glomerulopathy' has been encountered in COVID. Collapsing glomerulopathy is characterised by glomerular tuft collapse and proliferation of visceral epithelial cells. This pathology is referred to as COVAN (COVID – Associated Nephropathy). It is debated whether COVAN is induced by direct viral invasion of the glomerular epithelial cells or mediated by heightened gamma interferon activity in COVID. Collapsing glomerulopathy was classically described in patients with Human immunodeficiency virus, of African ancestry, and referred to as HIVAN – HIV-Associated Nephropathy. Most of the patients with HIVAN possess specific APOL 1 (apolipoprotein 1) gene polymorphisms which confer protection against trypanosomiasis. The same phenomenon of presence of nephropathic APOL 1 gene alleles has been observed in most of the patients with COVAN also [2].

Management

Milder forms of AKI can be managed conservatively. Renal replacement therapy is required for severe AKI. Mode and form of dialysis have to be decided by the

hemodynamic status of the patient. For hypotensive and hypoxemic patients, acute peritoneal dialysis, continuous renal replacement therapy (CRRT) or sustained low-efficiency dialysis (SLED) would be preferable. In critically-ill ICU patients who are hemodynamically unstable to tolerate hemodialysis, acute intermittent peritoneal dialysis was shown to be effective in resource-limited settings in a retrospective cohort of 91 patients [3]. A meta-analysis of 6 studies done in pre-COVID era, showed no difference in mortality and rate of complications in patients with acute kidney injury who underwent acute intermittent peritoneal dialysis to those who received extra-corporeal dialysis therapy [4]. The mortality risk in such sick patients was governed by the presence of comorbidities and severity of COVID pneumonia and not the modality of renal replacement therapy. There is evidence that peritoneal dialysis has added advantage of clearance of inflammatory cytokines like TNF- α and IL-6 [5,6].

In a South Indian study of COVID patients with AKI age above 70 years and the need for mechanical ventilation were associated with increased mortality [7].

It is commonly observed that AKI worsens prognosis in COVID patients. Collapsing glomerulopathy has a poor renal outcome.

It is a matter of concern that COVID-related AKI may predispose to progression to chronic kidney disease. In an observational study of 313 patients with severe COVID warranting intensive care unit admission, 240 patients developed AKI. There was a mortality of 34% and among the survivors, 16% of patients progressed to CKD at 3 months [8].

Impact of COVID on patients with non-dialysis requiring Chronic Kidney Disease (CKD-ND) (Figure 1)

Patients with CKD-ND are at a higher risk for contracting COVID as compared to general population. Most of the patients with CKD-ND experience worsening of kidney function, even necessitating initiation of dialysis in some patients. Inflammation, microvascular thrombosis and oxidative stress are the possible mechanisms. COVID induces a hypercoagulable state. Macrophage activation,

release of 'death-associated molecular patterns' and 'pathogen-associated molecular patterns' result in release of tissue factor resulting in activation of coagulation. There is evidence for complement activation in severe COVID. Complement activation and hypercoagulable state mutually enhance each other [9].

COVID in patients End Stage Kidney Disease (ESKD) on maintenance dialysis

Patients with ESKD undergoing maintenance haemodialysis are a heightened risk for getting COVID in view of the compromised immunological status and the frequent visits to hospital for getting dialysis. These patients and the health care delivery system faced several challenges

- a) Reaching the dialysis centre was difficult during complete lockdown for many patients. A survey was conducted to study the impact of complete lockdown on haemodialysis services after 3 weeks of lockdown implementation [10]. The survey included 19 major hospitals across the country (8 public and 11 private hospitals). There was a decrease in the number of patients from 2517 to 2,404. 28.2 % patients had missed one or more dialysis sessions, 2.74% required emergency dialysis session and 4.13% patients stopped reporting for dialysis.
- b) Need for establishing a dedicated dialysis facility for COVID patients with dedicated medical and paramedical staff
- c) Higher incidence of hypotension during haemodialysis due to hypoxemia
- d) Increased incidence of clotting of dialyzers due to hypercoagulability.

Patients on continuous ambulatory peritoneal dialysis (CAPD) did not encounter significant challenges. This advantage realised during COVID pandemic has prompted policy makers to promote CAPD in some parts of the country. There was also resurgence of urgent start CAPD during the pandemic [11,12].

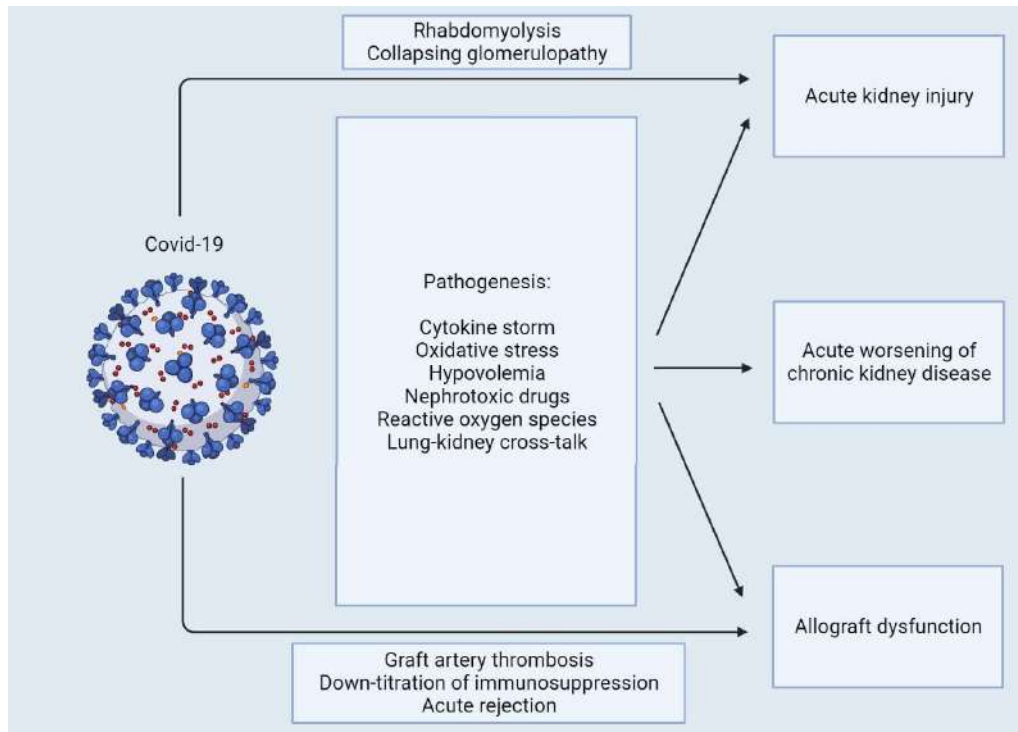


Fig. 1. Impact of COVID on Kidney - Pathomechanisms

The subset of patients requiring initiation of renal replacement therapy due to worsening of their kidney function during COVID infection had worse prognosis than those already on maintenance hemodialysis. A study of 109 patients who required initiation of hemodialysis during COVID infection showed a higher mortality rate of 44% with older age and presence of diabetes as independent predictors of poor outcome [13].

Initially, there was hesitancy to use remdesivir in patients with kidney failure due to uncertainty on safety and tolerance. Aiswarya et al. [2], in a prospective, observational study of 48 COVID patients with ESKD and on regular haemodialysis, administered remdesivir in a modified dose (100 mg intravenous infusion on alternate days, four hours prior to haemodialysis session) and found to be safe and well tolerated. Though remdesivir did not confer mortality benefit, early administration (<48 hours of hospitalisation) of remdesivir resulted in a significant decrease in duration of hospitalisation.

Nithya et al. [3], in an observational study of 483 COVID patients who required dialysis, noted a mortality of 18.8%. Old age and acute -on-chronic kidney failure were the

significant predictors of mortality. Report from another cohort of patients from South India reported a higher mortality rate of 27.5% in patients with end-stage renal disease. Patients with comorbidities like hypertension, diabetes and pre-existing pulmonary disease had a poor prognosis [16].

Patients with end-stage kidney failure on maintenance hemodialysis are less likely to mount an adequate immune response against SARS CoV due to low immune status. Hence, it was hypothesised that passive immunisation with convalescent plasma (CP) would be beneficial. But, in an Indian study on the safety and efficacy of CP, there was no mortality benefit in 37 patients who received CP, as compared to 31 patients in the control group [4].

COVID in Kidney transplant recipients

COVID in kidney transplant recipients (KTRs) poses additional challenges. Being on anti-rejection immunosuppressive drugs, KTRs, are at a higher risk for contracting COVID and a poor outcome. A higher mortality has been documented among KTRs afflicted

with COVID. As per a study based on United Network for Organ Sharing (UNOS) database [18], direct COVID death and all-cause mortality were seen in 28.7% KTRs.

Another study using data of ERACODA [19] (European Renal Association Covid 19 Database) reported a 28-day probability of death of 21.3% in 305 KTRs. Advanced age was significant determinant of mortality in KTRs.

An Indian study of 129 KTRs affected with COVID, reported mortality of 20.1% and graft dysfunction in 68.9% [20]. It was also observed that the mortality rate and severity if COVID infection were the highest during the second wave (delta variant) of COVID-19 infection compared to other waves. Kidney pathology in those who survived COVID infection and had acute allograft dysfunction showed varied pathologies like acute cellular rejection, antibody mediated rejection and graft pyelonephritis, although evidence for COVID per se as a risk factor for acute rejection is lacking [21]. The possible reason for acute rejection could be down-titration of immunosuppression. It is rather a difficult decision to down-titrate immune suppressants to facilitate recovery since it would increase risk of allograft rejection. The situation was more complicated during the second wave by the concurrent/succeeding occurrence of invasive mucormycosis in some patients [22].

Though there are no definite guidelines, it is a widely accepted practice to discontinue anti-metabolites (mycophenolate mofetil / azathioprine) and reduce the dose of calcineurin inhibitors (tacrolimus / cyclosporine) in the hospitalised patients with COVID. It remains uncertain as to when to restore original dosage of immune suppressives, whether only after complete recovery or early in the recovery phase itself. KTRs are particularly vulnerable to secondary bacterial infections with a significant negative impact on the outcome.

There is no evidence for COVID per se, being a trigger for acute rejection.

In general, viral clearance takes a longer time in KTRs and patients with end stage kidney failure.

Kidney Transplantation services during COVID pandemic

Kidney transplantation services were suspended in most centres across the globe

during COVID pandemic, since the KTRs have to be on intensive immunosuppression during the initial post-transplant period, making them more susceptible to COVID.

Guidelines were subsequently issued by NOTTO (National Organ and Tissue Transplantation Organisation), governing kidney transplantation. It is mandatory to rule out Covid infection in recipients and donors. Failure to identify asymptomatic COVID infection in either the recipient or the donor would result in disastrous consequences for the recipient.

1. COVID Vaccination in patients on Renal Replacement Therapy

There has been subdued response to vaccination in patients with end stage kidney failure on dialysis and in KTRs due to the impaired immunity.

The possible causes for impaired immune response include, reduced expression of co-stimulatory molecules and Toll-like receptors on immune -reactive cells, decreased production of T cell cytokines with resultant impaired activation and proliferation of T cells and reduced number of naïve and memory B cells [23].

KTRs, being on triple immune suppressants (steroids, calcineurin inhibitor and mycophenolate mofetil) are particularly vulnerable for failure of seroconversion following vaccination.

In a meta-analysis of 27 studies [24] involving 4,264 patients on renal replacement therapy (dialysis or KTRs), humoral response after two doses of vaccination for SARS CoV was 44% lower than in the general population. Seropositivity rates among KTRs, patients on peritoneal dialysis and haemodialysis were 26.1%, 92.4% and 84.3% respectively. Compared to general population, KTRs were 80% less likely to mount humoral response after COVID vaccination. Use of mycophenolate mofetil (MMF) has been found to be a significant contributory factor for blunted immune response.

Strategies to improve seroconversion rates include administration of additional doses of vaccine, heterologous additional dose, intradermal administration and use of adjuvants.

Kamar et al. [25], observed an increase in seropositivity rate from 40% to 68% in KTRs after a third dose of vaccine.

A study involving infection-naïve KTRs, showed lack of humoral response to 3rd and 4th doses of vaccine in 24% and 19% respectively [26]. The authors concluded that there was no additional benefit of fourth dose of vaccine due to poor T cell responses..

COVID Vaccine – Associated Glomerular Disease (CVAGD)

Glomerular diseases have been reported [27] in close temporal association with administration of COVID vaccination. The most common glomerular diseases associated with COVID vaccine are IgA nephropathy and minimal change disease. Other reported glomerulopathies include membranous nephropathy, anti-glomerular basement membrane disease and anti-neutrophil cytoplasmic antibody vasculitis.

Also, there have been anecdotal reports of recurrence of IgA Nephropathy, minimal change disease and membranous nephropathy following COVID vaccination.

Both mRNA and adenoviral vaccines have been associated with CVAGD.

The putative patho-mechanisms of CVAGD include molecular mimicry of the spike protein with host peptides.

Dyselectrolytemia

Dysnatremia and dyskalemia are common in patients with COVID. Dyselectrolytemias contribute for added morbidity and mortality. Hyponatremia is the most common dyselectrolytemia observed. The most common cause for hyponatremia is hypovolemia. There are anecdotal reports of 'syndrome of inappropriate anti-diuresis' associated with COVID resulting in severe hyponatremia [28,29].

Hypernatremia due to poor intake of water, particularly in the elderly is common in the severely ill patients. Hypernatremia has to be managed with administration of water and hypotonic solutions viz., 0.45% saline and 5% Dextrose solution.

Causes for hypokalemia include poor oral intake, insulin administered for hyperglycemia and diarrhoeal illness observed in about 10% of patients with COVID.

Hyperkalemia was observed in COVID patients who developed rhabdomyolysis as a rare complication of the disease and in those who developed renal failure.

Kidney in 'Long COVID'

There is emerging evidence that some COVID survivors develop post-acute phase sequelae involving pulmonary and extra-pulmonary organ systems including the kidneys. A cohort study [30] involving 1,81,384 COVID survivors treated at Veterans Health Administration Healthcare system revealed a higher risk for AKI, eGFR decline, end-stage kidney failure and major adverse kidney outcomes (MAKE). The kidney disease risk correlated with severity of COVID illness. This study has highlighted the potential long-term adverse renal consequences of COVID. It is imperative that post-COVID follow-up care should include kidney care component also.

Conclusion

The clinical spectrum of COVID includes kidney also. Kidney disease and COVID exert a mutually negative impact on each other. Management of Kidney disease in COVID is fraught with challenges.

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Conflicts of interest

The authors declares that they do not have conflict of interest.

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