Open Neural Tube Defects in COVID-19 Pandemic: An Analysis of 26 Neonatal Patients in a Tertiary Care Center

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Coronavirus disease-2019 (COVID-19) pandemic has severely affected and disrupted medical practice all over the world since December 2019 till date. This has affected the pediatric surgical practice in general and neurosurgical practice in particular. An analysis of 26 neonatal patients with open neural tube defects who underwent surgery in the neurosurgery department at the King Edward VII Memorial Hospital (KEM), Mumbai during the period of March 2020 till December 2020 is presented. The cumulative experience and challenges encountered in the comprehensive management of these cohort of patients in the difficult period of the pandemic is discussed in accordance with relevant literature on the subject.

**Keywords:** COVID-19, open neural tube defect, surgery

**INTRODUCTION**

Coronavirus disease-2019 (COVID-19) pandemic has gripped the entire world disrupting lives and livelihoods of people at large. There have been multiple waves of this dreadful disease and the lockdown imposed to control the spread has impacted the surgical practice as well. The pediatric surgery practice has also been severely affected by the COVID-19 pandemic, including elective and outpatient services. The most common birth defect in India is neural tube defects (NTDs).[1,2] Open NTDs usually are preventive if adequate folic acid supplementation is done from preconception period.[3-5] If detected early, a decision can be taken for termination of pregnancy based on its merit. In the postnatal period, early corrective measures including surgery and rehabilitation can be done. During the pandemic, all these measures were affected resulting in distress to the patient and the family. In view of the above fact, an institutional analysis of surgically treated NTDs at a tertiary center are presented. The challenges encountered during their management in the hospital is discussed and the relevant literature on the subject is reviewed accordingly.

**MATERIALS AND METHODS**

An analysis of 26 cases of open NTDs referred to the Department of Neurosurgery, KEM Hospital, Mumbai during the period March 2020 to November 2020 are presented. The available birth history, clinical profile, diagnostic investigations, COVID status, and surgical intervention were retrieved and analyzed. The period of study was divided from March 2020 to June 2020 (national lockdown period) and July 2020 till November 2020 (relaxation of lockdown restrictions).

**RESULTS**

A total of 26 cases of open NTDs were admitted to the neonatology and pediatric services of KEM Hospital, Mumbai during the period March 2020 till November 2020. During the national strict total lockdown period of 4 months—March till May 2020, only four patients of open NTDs underwent surgery, whereas 22 patients were operated on following easing (unlocking) of lockdown restrictions from June 2020.
till November 2020 [Table 1]. About two-thirds of the patients \((n = 13)\) during unlocking period were operated in the month of October and November 2020. The male-to-female ratio was 0.9:1. The maximum patients were in the age group of 1–7 days followed by 3 months or older [Table 2]. The details of antenatal ultrasonography (USG) were available in 13 patients only [Table 3]. The antenatal USG was not done in six patients. In seven patients, the antenatal USG data could not be obtained as there was no verified information available for documentation. Only three patients had USG done in all three trimesters. In six patients, the first antenatal USG was done beyond 22 weeks. Ruptured myelomeningocele was seen in five patients. Fetal distress at birth was seen in two patients who had occipital encephalocele and the anomalies were detected at 32 and 33 weeks on antenatal USG, respectively. All patients underwent repair of the open NTD after appropriate COVID testing protocol. The mother of one patient aged day 5 tested positive for COVID and hence surgery was deferred for 1 month. 23 patients recovered well following surgery. Three patients died in the postoperative period which included two cases of ruptured lumbar myelomeningocele and one patient of occipital encephalocele with severe hydrocephalus and upper cervical anteriorly placed cystic lesion compressing the cord posteriorly.

### DISCUSSION
Open NTDs are the most common birth defect in India.\(^{[1,2,6]}\) It could vary from anencephaly to spina bifida aperta.\(^{[6]}\) They are a major source of morbidity and mortality. They are known to occur more often among female neonates and stillbirths than among males. It has been shown that the increased risk of open NTDs in the female fetus is due to relatively more deficiency of human chorionic gonadotropin than in the male fetus.\(^{[7]}\)

They are detected in about 300,000 neonates worldwide. In India, as there is no national registry for birth defects, the estimation of prevalence of birth defects is difficult. Geographical or hospital-based studies or survey remain the predominant source of information.\(^{[1,2]}\) It is highest in the Northern India at 7.7 cases per 1000 births, whereas prevalence in the Eastern region was 1.1 cases per 1000 births. The prevalence of NTDs is 11.5/1000 total in children born to consanguineous parents, whereas it is 4.3/1000 total births in children of nonconsanguineous parents.\(^{[1,2,6]}\) The risk of occurrence of NTDs is directly dependent on the adequate consumption of folic acid prior to conception and in early pregnancy.\(^{[3-5]}\) It can be decreased by 60%–70% if maternal intake of folic acid can be increased around the time of conception. The Food Safety and Standards Authority of India (FSSAI) reports that the cost fortification of 1 kg of wheat flour with iron, folic acid, and vitamin B\(_12\) is approximately 3–15 paisa.\(^{[3-5]}\) It has been shown conclusively that folic acid fortification in the diet has reduced the incidence of NTDs in Canada, Chile, South Africa, and the United States of America (USA).\(^{[8-11]}\) In India, the compliance is lower due to socioeconomic factors and variation in diet. In addition, simple gene mutations and chromosomal abnormalities as well as maternal factors such as age, ethnicity, obesity, and the use of antiepileptic drugs are of concern.\(^{[12,13]}\)

The elective and outpatient services in pediatric surgery have been severely affected by the COVID-19 pandemic. The most frequently performed surgeries were ventriculoperitoneal shunts and supratentorial tumor. There was a significant reduction in subspecialized surgeries like NTDs and craniosynostoses.\(^{[14]}\) Hence, a

| Table 1: Neural tube defect | Patients \((n = 26)\) |
|-----------------------------|-------------------|
| Myelomeningocele            |                   |
| Thoracic                    | 2                 |
| Lumbosacral                 | 21                |
| Occipito cervical encephalocele | 3               |

| Table 2: Age demographics |
|---------------------------|
| Age of patient at presentation | Number of patients |
| 0–7 days                   | 9                 |
| 7–15 days                  | 5                 |
| 15 days–1 month            | 3                 |
| 1–2 months                 | 3                 |
| 2–3 months                 | 1                 |
| More than 3 months         | 5                 |

| Table 3: Antenatal ultrasonography | Patients \((n = 13)\) | Percentage |
|-----------------------------------|----------------------|------------|
| One USG                           | 3                    | 22         |
| Two USG                           | 4                    | 14         |
| Three USG                         | 3                    | 12         |
| Not done                          | 6                    | 22         |
| Unverified data                   | 7                    | 30         |
A comprehensive strategy is needed to avoid morbidity from the neglected elective surgeries during the pandemic. There is a need for a proper risk estimation between COVID-19 cross-infection and the benefits of elective procedures.

The average number of open NTDs performed in the neurosurgery department range from 25 to 35 patients per year. There is usually a consistency in the incidence pattern throughout the year. The pandemic had posed a dramatic twist since early 2020. The strict national lockdown measures caused an abrupt halt in the transport vehicles, movement of people, and even smooth access to the emergency services. The open NTDs observed during the course of study were interesting. During the period of total national lockdown period March 2020 to May 2020, there were only four cases of ruptured lumbar myelomeningoceles and in the unlocking period from June 2020 to November 2020 there were 22 cases of open NTDs. This trend suggests that the restrictions during the lockdown period could have possibly raised concerns regarding folic acid fortification, antenatal care, difficulties in obtaining fetal anomaly USG as

Figure 1: Neonate presenting with gross hydrocephalus, Chiari II malformation, Ventral CSF cyst extending from C4-D1, and low-lying tethered cord. The ventral CSF cyst is compressing the cord. (A) Clinical photograph: frontal view showing gross hydrocephalus and sunsetting sign. (B) Chiari III malformation. (C) Sagittal T₂-weighted MR image showing the ventral CSF cyst-C4-D1 compressing the upper cervical cord, Chiari II malformation, and occipitocervical encephalocele. (D) Sagittal T₂-weighted MR image showing low-lying cord with tethering.
well as elective medical termination of pregnancy. The restrictions on transport as well as movement of people might have resulted in hindrance for timely medical consultation and hospitalization. Approximately 22% of patients had no antenatal care and no details could be obtained regarding antenatal care in 30% of patients. Only 11% of patients were able to complete the scheduled antenatal USG in all three trimesters.

The anomalies seen were complex and severe in intensity [Figures 1-4]. These patients were largely diagnosed antenatally at 27 weeks or beyond. They had higher incidence of rupture of myelomeningoceles, Chiari II malformation, and gross hydrocephalus. They had multiorgan anomalies as well. Amongst them, two patients with lumbar myelomeningocele expired following birth. Two patients who were diagnosed prenatally at 32 and 33 weeks of gestation had large occipitocervical meningoencephaloceles, had fetal distress at birth and required interim ventilatory assistance.

**Logistic issues**

During the total national lockdown, the rural and urban areas were affected uniformly but the impact in these regions was different. The strict regulations and restrictions on individuals and family during this period brought the society to a standstill. It compromised the access to child and maternity services to a significant extent. As a consequence, the follow-up services and surveillance were also compromised and inconsistent. The folic acid fortification of women in childbearing age and expectant mothers, maternal counseling, scheduling of antenatal USG services, and access to medical termination of pregnancy were hampered as a consequence due to poor availability of manpower and resources. As a result, the expectant mothers either remained ignorant about appropriate antenatal care or had difficulty in access to delivery of health care and timely intervention, medical, or surgical.

**Figure 2:** Lateral Clinical photograph showing a large occipitocervical meningoencephalocele in a 1-week-old neonate

**Figure 3:** A 1-month-old child with spondylocostal dysostosis (Jarcho-Levin syndrome), single kidney, and atrial septal defect. (A) Upper lumbar limited dorsal myeloschisis. (B) Diplomyelia with dorsal lipoma tethered to both hemicords. (C) X-ray chest PA showing absent left-sided second to sixth ribs
Neonatal intensive care unit challenges
The neonates born with open NTDs with complex anomalies were in compromised neurological condition. The raised intracranial pressure had to be stabilized. Patients with ruptured myelomeningoceles were monitored for impending infection, meningitis/ventriculitis/hydrocephalus, fluid and electrolyte disturbances. Other contributing factors like low birth weight, nutrition, coagulopathies, and visceral anomalies also needed attention. The COVID testing of the mother and the neonate needed to be done at regular intervals as per protocol. The mother suffering from symptomatic COVID needed to be isolated from the child for few days till she recovers completely. The positive COVID status of the patient delayed the neuroimaging study and also increased the waiting time for surgery. Sometimes intermittent or long-term ventilatory assistance is required in case of compromised airway or lung function.

Neurosurgical issues
There was a significant reduction in emergency surgeries during the COVID-19 pandemic across centers all over the world. It has affected surgical procedures, scheduling, and staffing. The COVID pandemic had affected the smooth functioning of the neurosurgical cases due to a shortage of resident, anesthesia, nursing, and ancillary support operation theatre staff during the total lockdown period. The other service departments were working in compromised conditions and hence multidisciplinary involvement including pediatric medicine, neonatology, intensive care, plastic, and pediatric surgery was a daunting task. Special precautions need to be taken before, during, or after surgeries. The availability of fresh blood and blood products was also an issue in absence of any planned blood donation drives. Hence the timing of surgery required to be rescheduled after few days till all the logistics were sorted. Psychological support and training platforms were necessary for the surgical team. However, new treatment and teaching modalities emerged in response to the pandemic.

Postoperative course
The need for frequent evaluation of the neonatal patients, close neurological observation, and monitoring for hydrocephalus, wound infection, and CSF leak was challenging during total lockdown period. An optimal minimum scheduling of manpower and allied resources had to be arranged to prevent frequent visits to the neonatal intensive care unit (NICU) and thereby avoid additional burden on the health system.

Conclusion
There was a definite upsurge of open NTDs seen as a collateral sequel of COVID-19 pandemic following the lockdown period. A comprehensive collaborative effort was paramount for optimal use of resources and personnel during this period. Family counseling is crucial and needed attention on priority. Heightened awareness and social responsibility about this unprecedented condition need to be highlighted and emphasized.

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Conflicts of interest
There are no conflicts of interest.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/
her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

REFERENCES

1. Allagh KP, Shamanna BR, Murthy GV, Ness AR, Doyle P, Neogi SB, et al.; Wellcome Trust- PHFI Folic Acid project team. Birth prevalence of neural tube defects and orofacial clefts in India: A systematic review and meta-analysis. PLOS One 2015;10:e0118961.

2. Bhide P, Sagoo GS, Moorthie S, Burton H, Kar A. Systematic review for birth prevalence of Neural tube defects in India. Birth Defects Res A 2013;97:437-43.

3. Hoddinott J. The investment case for folic acid fortification in developing countries. Ann N Y Acad Sci 2018;1414:72-81.

4. Laurence KM, James N, Miller MH, Tennant GB, Campbell H. Double-blind randomised controlled trial of folate treatment before conception to prevent recurrence of neural-tube defects. Br Med J (Clin Res Ed) 1981;282:1509-11.

5. Honein MA, Paulozzi LJ, Matthews TJ, Erickson JD, Wong LY. Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects. JAMA 2001;285:2981-6.

6. Botto LD, Moore CA, Khoury MJ, Erickson JD. Neural-tube defects. N Engl J Med 1999;341:1509-19.

7. Santos LM, Lecca RC, Cortez-Escalante JJ, Sanchez MN, Rodrigues HG. Prevention of neural tube defects by the fortification of flour with folic acid: A population-based retrospective study in Brazil. Bull World Health Organ 2016;94:22-9.

8. Castillo J, Castillo H, Brei TJ. Guidelines and scientifically-based spina bifida care: Guidance across the lifespan in a global health context. J Pediatr Rehabil Med 2020;13:453-5.

9. De Wals P, Taïrou F, Van Allen MI, Uh SH, Lowry RB, Sibbald B, et al. Reduction in neural-tube defects after folic acid fortification in Canada. N Engl J Med 2007;357:135-42.

10. Hertrampf E, Cortés F. Folic acid fortification of wheat flour: Chile. Nutr Rev 2004;62:S44-8; discussion S49.

11. Sayed AR, Bourne D, Pattinson R, Nixon J, Henderson B. Decline in the prevalence of neural tube defects following folic acid fortification and its cost-benefit in South Africa. Birth Defects Res A Clin Mol Teratol 2008;82:211-6.

12. World Health Organization, Regional Office for South-East Asia. Prevention and control of birth defects in south-east Asia region: Strategic framework (2013–2017). New Delhi: WHO, Regional Office for South-East Asia; 2013.

13. Gupta S, Arora S, Trivedi SS, Singh R. Dyslipidemia in pregnancy may contribute to increased risk of neural tube defects—a pilot study in North Indian Population. Indian J Biochem 2009;24:150-54.

14. Soltany A, Hamouda M, Ghzawi A, Sharaqi A, Negida A, Soliman S, et al. A scoping review of the impact of COVID-19 pandemic on surgical practice. Ann Med Surg (Lond) 2020;57:24-36.

15. D’Urbano F, Fabbri N, Koleva Radica M, Rossin E, Carcoforo P. Emergency surgery in COVID-19 outbreak: Has anything changed? Single center experience. World J Clin Cases 2020;8:3691-6.