Pattern of malformations in central nervous system and its association with other congenital anomalies in perinates

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Abstract
Introduction: The congenital malformations of the central nervous system is one of the leading causes of perinatal mortality in this region of the country. It may present as an isolated defect or may be associated with other organ system malformations.

Aims and Objectives: Aim of the present study was to find out the pattern of congenital malformations in the central nervous system both in live and still born perinates. Our main objective was to ascertain its association with other organ systems most commonly involved.

Materials and Methods: The prospective study was carried out on 76 perinates having congenital anomalies out of 15,970 births (15,614 live born and 356 stillborn) ranging from 28th weeks of gestation to 7 days after birth. Twenty, out of 76 were born with central nervous system malformations.

Results and Observations: The congenital malformations of central nervous system were found to be 26.31%. Anencephaly was the most common malformation (50%) observed amongst the central nervous system in the study with a female preponderance 1:5:1, followed by spina bifida with meningo(myelo)cele (35%), hydrocephalus (10%) and holoprosencephaly (5%). Anencephaly was associated with occipital meningoencephalocele in 10% cases.

Conclusion: Anencephaly is the most common malformations in the study, followed by spina bifida and meningo(myelo)cele. The other malformations found in the central nervous system are hydrocephalus, meningoencephalocele and holoprosencephaly. The incidence of congenital malformations in present study is comparatively lower than in other parts of India and abroad.

Keywords: Congenital malformation, Perinates, Anencephaly, Spina bifida, Meningomyelocele.

Introduction
The malformations of the central nervous system result from alterations in the morphogenesis or histogenesis of the nervous tissue itself. Some of the aberrations, however are extrinsic in that they result from developmental failure or abnormalities in the mesodermal structure related to the early nervous system. Proper differentiation of these mesodermal derivatives such as notochord, somite, vertebrae and mesenchyme are essential for normal development of the brain and spinal cord.¹ Congenital anomalies of the central nervous system are major causes of mortality during perinatal period and results from failure of the closure of the neural tube between third and fourth week of embryonic life. Major neural tube defects are spina bifida, meningocele, meningo(myelo)cele, anencephaly and meningoencephalocele.²³ Anencephaly occurs if the rostral part of neural tube fails to close, associated with degeneration of the exposed neural plate tissue¹ resulting in failure to develop major parts of the brain. In place of the normal neural tissue, there are thin-walled vascular channels resembling the choroid plexus and masses of neural tissue.⁴ Anencephaly is the most severe form of neural tube defect and is not compatible with life. Most of these cases are diagnosed during pregnancy by ultrasonography or amniocentesis and after delivery of the babies in neonates.³ Anencephalic infants are mostly stillborn or die shortly after birth. Spina bifida is midline defect of vertebral arches without protrusion of the spinal cord or meninges. The most common site of spina bifida is in the lumbosacral region. Meningocele occurs when the meninges protrude through the defect in the posterior arches of vertebrae. Spina bifida with meningo(myelo)cele is a more common and severe defect than spina bifida with meningocele. Hydrocephalus results from blockage of cerebrospinal fluid in the ventricular system or subarachnoid space. Meningoencephalocele results from defective closure of the rostral neuropore during the fourth week and affects skull with protrusion of meninges and cerebellum, cerebrum or portions of the brainstem.⁶

Aims and Objectives
Aim of the present study was to find out the frequency of the pattern of major congenital malformations in central nervous system both in live and still born perinates. Our objective was to ascertain its association with anomalies of other organ systems most commonly involved.

Materials and Methods
The prospective study was carried out on 76 perinates having congenital anomalies out of 15,970 births (8,312 male and 7,682 female) in the Department of Anatomy, Assam Medical College & Hospital, Dibrugarh. The specimens (15,614 live born & 356 stillborn) were obtained during 28th weeks of gestation to 7 days after birth. In the present study, the congenital malformations of the central nervous system were studied in 76 perinates. The malformations of the central nervous system were divided into two major parts: (a) malformations of cranioencephaly and (b) malformations of spinal system. The cranioencephalic malformations were assessed with special reference to holoprosencephaly, anencephaly, encephalocele, meningocele, hydrocephalus, meningomyelocele, meningo(myelo)cele and myelomeningocele. The spinal system malformations were assessed with reference to spina bifida, encephalocele, meningocele, hydrocephalus, meningomyelocele, meningo(myelo)cele and myelomeningocele.
stillborn babies) were procured from the Department of Obstetrics & Gynaecology, Assam Medical College & Hospital, Dibrugarh. Twenty, out of 76 were born with central nervous system malformations.

**Study Population:** Live and still born perinates ranging from 28th weeks of gestation to 7 days after birth. Foetuses born before 28 weeks of gestation, terminated pregnancy and macerated babies were excluded from the present study.

The still born foetuses were examined in the Department of Anatomy after fulfillment of a proforma and in figure. The written consent from the parents was taken before examination and dissection of perinates. The result and observations were presented in tabular form and in figure. Statistical calculations were done in percentage and in per thousand live birth.

**Results and Observations**

In the present study, total 76 (62 stillbirth, 17.41% & 14 live birth, 0.09%) cases of congenital malformations were found in 15,970 births (Table 1). Total percentage of congenital malformation was found to be 0.47%. Out of 76 congenital malformations, 20 cases (26.31%) were found to be of central nervous system with male female ratio 1.5:1 (Table 1).

Anencephaly was the most common (50%) malformation observed in the central nervous system with male female ratio 1:1.5 (table 2, chart 1, Fig. 1 & 5). Incidence of anencephaly was 0.62 per 1000 birth. Spina bifida with meningocele was observed in 35% cases of central nervous system malformation with an incidence rate of 0.438 per 1000 birth (table 2, chart 1 & Fig. 2). Hydrocephalus was noted in 10% cases with an incidence of 0.125 per 1000 birth (Table 2, Chart 1 & Fig. 3). Holoprosencephaly was recorded in 5% cases with an incidence of 0.063 per 1000 birth (Table 2).

Association with other organ system:

In the present study of central nervous system malformations, anencephaly showed association with occipital meningoencephalocele (10%) (Table 2, Chart 2, Fig. 1 & 5), craniorachischisis (5%) (Fig. 4), spina bifida (20%), with CTEV and syndactyly (10%) and with omphalocele major, single umbilical artery and contracture right wrist (5%) (Table 2 & Chart 2). Spina bifida and meningocele showed association with CTEV and polydactyly (10%) and omphalocele major, CDH, imperforate anus (5%) cases (table 2 & chart 2). Hydrocephalus showed association with syndactyly, CTEV (10%), spina bifida and low set ear (5%) (Table 2 & Chart 2, Fig. 3). 5% cases of CNS malformations showed association of holoprosencephaly with cleft lip, cleft palate, proboscis, syndactyly and amputated digit. (Table 2 & Chart 2)

**Table 1:** Showing frequency distribution of congenital malformations. (n=76)

| No of cases | Male | Female | Total | Central nervous system malformation (n=20) |
|-------------|------|--------|-------|-------------------------------------------|
| Congenital malformations | 62   | 14     | 76    | 12 | 08 | 20 | 1.5:1 | 1.25 |
| Percentage % | 17.41% | 0.09% | 0.47% | 15.79% | 10.52% | 26.31% |

**Table 2:** Frequency distribution of malformation in CNS & its association with other organ system (n=20)

| Malformations in central nervous system | No. of cases | Percentage | Incidence per 1000 birth | Malformations with other organ system | Percentage | Incidence per 1000 birth |
|----------------------------------------|--------------|------------|--------------------------|--------------------------------------|------------|--------------------------|
| Anencephaly                            | 10           | 50%        | 0.62                     | Occipital meningoencephalocele       | 10%        | 0.125                    |
|                                        |              |            |                          | Spina bifida                         | 20%        | 0.250                    |
|                                        |              |            |                          | Craniorachischisis                   | 5%         | 0.063                    |
|                                        |              |            |                          | CTEV, syndactyly                     | 10%        | 0.125                    |
|                                        |              |            |                          | Omphalocele major, Single umbilical artery, Contracture right wrist | 5%         | 0.063                    |
| Spina bifida & meningo-myelocoele      | 07           | 35%        | 0.438                    | CTEV, polydactyly                    | 10%        | 0.125                    |
|                                        |              |            |                          | Omphalocele major, CDH, imperforate anus | 5%         | 0.063                    |
Table 3: Comparative data showing incidence of neural tube defects by various researchers

| Study group          | Year | Anencephaly | Spina bifida | Meningo-myeolocele | Hydrocephalus | Holoprosencephaly |
|----------------------|------|-------------|--------------|--------------------|---------------|------------------|
| Laurence et al       | 1968 | 3.54/1000   | 4.13/1000    | -                  | 0.45/1000     | -                |
| Tibrewala & Pai      | 1974 | 0.49/1000   | 0.65/1000    | -                  | 0.16/1000     | -                |
| Mathur et al         | 1975 | 3.8/1000    | 0.3/1000     | 0.9/1000           | 1.9/1000      | -                |
| Choudhury et al      | 1984 | 0.52/1000   | -            | 0.24/1000          | 0.43/1000     | -                |
| Swain et al          | 1994 | 1.52/1000   | -            | 0.76/1000          | 2.03/1000     | -                |
| Rajab et al          | 1998 | 0.69/1000   | -            | 0.45/1000          | 0.44/1000     | -                |
| Hendricks et al      | 1999 | 4.9/10,000  | 6.7/10,000   | -                  | -             | -                |
| Datta & Chaturvedi   | 2000 | 0.69/1000   | -            | 0.34/1000          | 0.34/1000     | -                |
| CDC                  | 2000 | 6.1/10,000  | 6.3/10,000   | -                  | -             | -                |
| Fida et al           | 2007 | -           | -            | 0.37/1000          | 0.74/1000     | -                |
| Snell R.S            | 2010 | 6/1000      | 6/1000       | -                  | 6/1000        | -                |
| Golaliipour et al    | 2010 | 11.4/10,000 | 12.7/10,000  | -                  | -             | -                |
| Sunethi et al        | 2011 | 50%         | 41.66%       | 8.33%              | -             | -                |
| Saiyad & Jadav       | 2012 | (41.38%)    | (10.34%)     | (10.34%)           | (13.80%)      | -                |
| Pujari & Pujari      | 2012 | -           | 0.23/1000    | 1.64/1000          | 0.47/1000     | -                |
| Sadler TW            | 2015 | 1/500-1000  | 1/1000       | 1/1000             | 1/1200        | 1/15,000         |
| Moore K.L            | 2016 | 1/1000      | -            | 1/2000             | -             | -                |
| Bhide & Kar          | 2018 | 17.1/10,000 | 8.45/10,000  | -                  | -             | -                |
| Present study        |      | 10 (50%)    | 0.62/1000    | 7 (35%)            | 2 (10%)       | 1 (5%)           |
|                      |      | Births      | Births       | 0.438/1000 Births  | 0.125/10      | 0.063/1000 Births |

Chart 1: Frequency distribution of malformations in central nervous system
Chart 2: Association of CNS malformation with other organ system

| Anencephaly | Meningomyelocele | Hydrocephalus | Holoprosencephaly |
|-------------|-----------------|---------------|-------------------|
| 20%         | 10%             | 5%            | 10%               |
| 10%         | 10%             | 5%            | 10%               |
| 10%         | 5%              | 5%            | 5%                |
| 5%          | 5%              | 5%            | 5%                |

Fig. 1: Anencephaly with occipital meningoencephalocele

Fig. 2: Spina bifida and meningomyelocele with CTEV

Fig. 3: Hydrocephalus with low set ear, CTEV & syndactyly

Fig. 4: Craniorachischisis totalis
Discussion

The present study revealed 26.31% cases of congenital malformation in the central nervous system with an incidence of 1.25 per 1000 birth in comparison to Siddesh et al7 31.6%, Singh A8 20.5%, Singh & Sinha31 12.8%, Fida et al9 1.9/1000, Rajab et al10 1.25/1000 birth, Golalipour et al11 25.4/10000 and Bhide & Kar12 28.93 per 10,000 live births (Table 3). According to Schoenwolf G C,13 open neural tube defects occur in about 0.1% of all live births and the frequency of it as a whole in the United States is approximately 0.1%. Anencephaly was the most common (50%) congenital malformations among central nervous system in the present study. It was comparable with the study of Sunethri et al14 (50%), Moradi et al15 (50%), Kulkarni et al16 (45%) and Saiyad & Jadav17 (41.38%). According to Parthasaraty A18 incidence of anencephaly was observed 1 in 1000 births. In the present study incidence of anencephaly was 0.62/1000 live birth in comparison to Rajab et al10 0.69/1000, Datta & Chaturvedi19 0.69/1000, Tibrewala & Pai20 0.49/1000 and Choudhary et al21 0.52/1000. Anencephaly was recorded by Mathur et al22 3.8/1000, Swain et al23 1.52/1000, Hendrik et al.24 CDC, Golalipour et al11 and Bhide & Kar12 as 4.9, 11.4, 6.1 and 17.1 per 10,000 live birth respectively (table 3). Sadler T W5 stated that anencephaly occurs in 1 per 5,000 births and is more common in females than in males. According to Moore K L,26 anencephaly occurring at least once in every 1000 births and two to four times more common in females than in males. In the present study, the female preponderance was seen with ratio of 1.5:1. Spina-bifida with meningocele occurred was the second most common malformations of the central nervous system (35%) in the present study. The incidence is quite low when compared to Sunethri et al12 (41.66%) and high compared to the observations of Saiyad & Jadav17 (10.34%). On the contrary, the present study was comparable to the observations of Mathur et al22 0.3/1000, Datta & Chaturvedi19 0.34/1000 and Catibusic F H et al2 1/4000 live births. Spina bifida was found by Hendricks et al.24 CDC,25 Golalipour et al11 and Bhide & Kar12 as 6.7, 6.3, 12.7 and 8.45 per 10, 000 live birth respectively which was higher in comparison to the present study of 0.438/1000 live birth. Hydrocephalus was noted in 10% cases which was comparable with Pinar et al27 12.4%. The incidence is quite low 0.125/1000 when compared with Rajab et al9 0.44/1000, Laurence et al28 0.45/1000, Pujari & Pujari29 0.47/1000 and Snell RS4 6/1000. Hydrocephalus develops in at least 80% of patients with meningomyelocele by Catibusic F H et al2 or may be associated with spina bifida and meningocele by Snell R S.4 In the present study hydrocephalus was observed in stillborn male full-term fetus associated with spina bifida and CTEV (Fig. 2). Meningoencephalocele occurs approximately once in every 2000 births by Moore K L6 and 11.6% by Mahadevan and Bhat.30 In the present study occipital meningoencephalocele along with anencephaly was noted in 10% cases with incidence of 0.125 per 1000 birth (Table 2, Chart 2) in comparison to Rajab et al9 0.45/1000 (table 3). Holoprosencephaly observed 1/ 15,614 live birth in comparison to Sadler T W5 1/15,000 live births.

From the present study it had been found that congenital malformation of the central nervous system was one of the leading causes of perinatal mortality in this region of the country. It may present as an isolated defect or may be associated with other organ system malformations.

Conclusion

The present study reveals the pattern and frequency of malformation in the central nervous system and its association with other organ system commonly involved. Anencephaly is the most common malformations followed by spina bifida and meningomyelocele. The other CNS malformations are hydrocephalus, meningoencephalocele and holoprosencephaly. The incidence of congenital malformations in present study is comparatively lower than in other parts of India and abroad. The incidence of congenital anomalies is declining significantly following folic acid administration. The malformations resulting from neural tube defects, can be prevented by taking folic acid daily three months prior to conception and continuing throughout pregnancy.

Conflict of Interest: None

Reference

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