

Original Research Article

## A STUDY OF INCIDENCE OF NEURAL TUBE DEFECTS AND THEIR PATTERN IN A TERTIARY CARE HOSPITAL OF GURUGRAM

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### ABSTRACT

**Objective:** The study was undertaken to determine the proportion and pattern of Neural Tube Defects (NTD) reported at tertiary care teaching hospital in Gurugram. The incidence of NTDs were determined and compared with other studies done in India and other countries.

**Material and methods:** The study was carried out in SGT Medical College Hospital and Research Institute, Gurugram. The total number of deliveries was recorded from 2017- 2019. The aborted fetuses with NTDs were observed in detail externally for the sex, type of NTD and other associated anomalies after obtaining ethical clearance and written informed consent of the parents.

**Results:** The number of deliveries conducted between 2017-2019 at SGT Medical College Hospital and Research Institute, Gurugram was 2500. There were 8 babies born with NTDs (5 female and 4 male). Overall incidence of NTDs in the present study was 3.2/1000 births with female preponderance. The incidence of fetuses with anencephaly, myelocoele, meningomyelocoele, craniorachischisis and encephalocoele were 0.8, 1.2, 0.4, 0.4, and 0.4 per 1000 births respectively.

**Conclusion:** Birth defects like Neural Tube Defects are easily detected by routine screening tests like USG in first and second trimester of pregnancy. Public health measures like preconception folic acid supplements and increasing awareness about maternal care during pregnancy needs to be highlighted to decrease the incidence of congenital anomalies and their comorbidities.

**KEYWORDS:** Neural tube defects (NTDs), Incidence, Anencephaly, Meningomyelocoele, Myelocoele, Craniorachischisis.

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### INTRODUCTION

Neural tube defects (NTDs) are the most common structural malformations of the central nervous system in human beings affecting 1-2

infants per 1000 births. Their incidence varies among different populations. They occur very early during pregnancy between gestational weeks 2 and 6 and are caused by a partial or

complete failure of neural tube closure during embryogenesis at any level of the craniocaudal axis [1].NTD categorized clinically into “open” in which the affected nervous tissues are exposed to the environment or “closed,” in which the defect is covered by skin. Open NTD represent the most common forms of NTD and include anencephaly and meningocele that result from the failure of fusion in the cranial and spinal region of the neural tube, respectively. Anencephaly is characterized by a partial or total absence of the cranial vault and cerebral hemispheres and is invariably lethal [2]. Spina bifida is a general term of NTD affecting the spinal region. It consists of splitting of vertebral arches and may or may not involve the underlying connective tissues.Two different types of spina bifida occurs: Spina bifida occulta and Spina bifida cystica. In spina bifida occulta there is a defect in vertebral arches only and it usually does not involve underlying nervous tissues.Its most common site is L<sub>4</sub>-S<sub>1</sub> and is marked by tuft of hair at the defect site. spina bifida cystica is a severe NTD where neural tissue/meninges protrude through a defect in vertebral arches and skin to form a sac mainly in lumbosacral region and results in neurological deficit.In some cases only meninges protrude called meningocele and in some nervous tissue also herniate through the defect called meningocele. Open NTDs are often associated with Arnold Chiari malformation and hydrocephalous [3]. The causes of NTDs is multifactorial involving both environmental and genetic factors. Environmental factors involved in increasing the risk for NTDs include geography, epidemic trends, socio-economic class, maternal age, maternal diet, maternal diabetes and obesity, antiepileptic drugs like valproic acid and hypervitaminosisA[4,5].

Several studies support a genetic component to NTD and are associated with chromosomal abnormalities, mostly trisomy 13and trisomy 18.NTDs are also associated with genetic syndromes, including Meckel’s syndrome, Anterior sacral meningocele, Currarino syndrome, and anal stenosis[6].The inheritance patterns and recurrence risks for such congenital anomalies do not follow a mendelian pattern[7,8] .Clinical studies having randomized control trials and

population based fortification programme has confirmed the efficacy ofpreconceptional administration of 400µg folic acid in reducing NTDs occurrence as much as 60%70%[9].The Present Study was carried out to elucidate the neural tube defects.

## MATERIALS AND METHODS

The study was carried out in SGT Medical College Hospital and Research Institute, Gurugram. It was a cross-sectional descriptive study where all the cases including still born delivered with neural tube defects (NTD) and those medically terminated due to detection of NTDs were analyzed. Ethical clearance and written informed consent of the parents were taken for the study. The incidence of neural tube defects anomalies were calculated during 2017 to 2019. There were a total of 2500 births including live births, still births and aborted fetuses. The total number of fetuses with neural tube defects were eight. The aborted fetuses with NTDs were observed in detail externally for the sex, type of NTD and other associated anomalies. Dissection of fetuses was not carried out to find out any other internal anomalies.Incidence of NTDs prevalent in present study was compared with the previous studies done in India and other countries.

## OBSERVATION AND RESULTS

The total number of births including live births, still births, aborted fetuses between June 2017 to June 2019 at SGT Medical College Hospital and Research Institute, Gurugram were 2500.Of these deliveries, the number of babies born with NTD was eight (5 female and 3 Male) and details are given in Table 1. The type of NTDs observed in the present study with their incidences are given in Table2. In the present study the incidence of NTD was 3.2 /1000 births. The fetus of Spina bifida cystica labelled as meningocele had the defect in lumbosacral region. The spinal cord along with the meninges were coming out of the defect exposing to the environment. No other associated external deformities were observed (Fig.1). In cases of myelocele one fetus was

showing the defect in cervical region (Fig.5) and rest was showing the defect in lumbosacral region (Fig.2). Out of eight cases of neural tube defects two fetuses were showing the features of Anencephaly. There was absence of a major portion of scalp and cranial vault. Brain tissue and spinal cord were exposed to exterior. In both cases the nose was broad and ears were folded and the eyes were bulging outward. No abnormality of lips or palate was observed. One of the fetus of anencephaly was having rachischiasis (Fig 3) and other was associated with club foot deformity (Fig.4). In the present study, myelocele was more common type of NTD (37.5%) followed by anencephaly (25%). The defects like meningomyelocele (12.5%), craniorachischiasis (12.5%) and encephalocele (12.5%) were less common.

**Fig. 1:** 17- week -old male fetus of meningomyelocele with defect in lumbosacral region.



**Fig. 2:** 18 week –old male fetus of myelocele having defect in lumbosacral region.



**Fig. 3:** 19 week old female fetus of anencephaly with rachischiasis.



**Fig. 4:** 16 week old female fetus of anencephaly with club foot.



**Fig. 5:** 17 week old male fetus of myelocele having defect in cervical region.



**Table 1:** Sex, Gestational age, type of NTD and Associated malformations observed in fetuses.

S.No.	Sex	Gestational age (weeks)	Cranial defects	Spinal defects	Associated malformations
1	Male	17		Myelocele	
2	Female	16	Anencephaly		Club foot
3	Female	19	Craniorachischiasis		
4	Male	17		Meningomyelocele	
5	Female	18	Anencephaly	Rachischiasis	
6	Female	15		Myelocele	Hydrocephalous
7	Female	16	Encephalocele		
8	Male	18		Myelocele	

**Table 2:** Types, Number and Incidence of NTD observed in the present study.

Neural Tube Defects	Number of Fetuses (%)	Incidence/1000 births
Anencephaly	2(25%)	0.8
Myelocele	3(37.5%)	1.2
Meningomyelocele	1(12.5%)	0.4
Craniorachischiasis	1(12.5%)	0.4
Encephalocele	1(12.5%)	0.4

## DISCUSSION

Neural tube defects are a group of severe congenital malformations of central nervous system resulting from failure of neural tube closure during early embryonic life. They may involve meninges, vertebrae, muscle and skin [10]. In the present study the incidence of NTD is 3.2 /1000 births. In United States the incidence of NTD is 1/1000 births having female preponderance [11]. The incidence of NTD in India ranges from 0.5 to 11 per 1000 live births [12]. It was more common in northern states like Punjab, Haryana as compared to southern states[13]. The incidence of NTDs reported by Kulkarni et al , Mini et al , Sharada et al were higher ranging from 7 to 11.42 per 1000 births as compared to present study[14,15,16]. In the present study the incidence of NTD is 3.2/1000 births which is in accordance with the studies done by Suresh et al with incidence of 3.15/1000 births [17]. Creasy and Alberman reported incidence of NTD as 2.8/1000 births which was lower compared to present study [18]. All these studies were done at urban setting in tertiary care teaching hospitals and incidence of NTD has significantly reduced from 11.42 to 2.79 per 1000 births. In most of the previous studies NTDs had female preponderance which

is in accordance with the present study. In present study, myelocele a type of spina bifida cystica was more common (37.5%) followed by anencephaly (25%) which is in contrast to studies done by Kulakrni et al and Mini et al where incidence of anencephaly was more as compared to other NTDs[14,15].

In embryonic life the neural plate is formed approximately 18<sup>th</sup> day after fertilization through a process called neurulation [3]. In human beings neural tube formation occurs through primary and secondary neurulation that occurs at distinct sites along the craniocaudal axis of the embryo .Primary neurulation occurs at 3-4 weeks of gestation and leads to the formation of brain and most of the spinal cord till sacral level. Secondary neurulation occurs at 5-6 weeks of gestation and creates the lowest portion of spinal cord in lower sacral and coccygeal region. Failure of neural tube closure during primary neurulation at any level of body axis from brain to sacral spines leads to the open NTDs [19].

Various theories of Neural Tube Closure were given to describe the neural tube defects in animal models and in humans. Van Allen et al (1993) compared the multisite model vs. the traditional single-site model of neural tube closure for the best explanation for NTDs in humans. With the multi-site neural tube closure model, majority of NTDs can be explained by failure of fusion of one of the closures or their contiguous neuropores. In NTDs the first defect is in the notochord development resulting in failure of the neural folds to fuse in the midline and to make a normal neural tube. The next defect is failure of the mesoderm to develop. Failure of mutual induction of all three germ layers in temporally

related sequence can lead to various types of NTDs [20].

Secondary neurulation begins after closure of posterior neuropore. Secondary neural tube arises from a mass of pluripotent cells derived from the remnant of primitive streak, located at the caudal end of the embryo forming the lowest most region of spinal cord in sacral & coccygeal region. These cells undergo proliferation and condensation followed by cavitation and fusion with the central canal of the neural tube formed by primary neurulation [21]. Defect in secondary neurulation leads to failure of separation of neural tube from other tissues of tail bud leading to tethered cord syndrome including malformed spinal cord, limb buds and bladder & bowel anomalies [22].

Various genetic factors were studied in animal models regulating the neurulation process. Noggin, Chordin and Folistatin secreted by notochord and primitive node leads to the inhibition of BMP4 (Bone Morphogenetic Protein) which is required for the conversion of ectoderm to neuroectoderm and to dorsalize the mesoderm to paraxial mesoderm. Various other genes like WNT, FGF (Fibroblast Growth Factor), and SHH (Sonic Hedge Hog) were also described controlling the different phases of neurulation [23, 24, 25].

Periconceptional administration of folic acid reduces the incidence of N.T.Ds by 60-70%. Folic acid is a water soluble vitamin B absorbed in small intestine through folate transporters- FR  $\alpha$ ,  $\beta$ ,  $\gamma$  [26]. Maternal auto antibodies formed against folate receptors present on placental membrane block the binding of folic acid leading to its deficiency [27]. Folate has important role in synthesis of thymidine and purines. Decrease in FR  $\alpha$  leads to exencephaly [28]. Hence folate deficiency and increased levels of homocysteine leads to increased risk for NTDs. Besides folate machinery other events like cellular apoptosis, premature neurogenesis in neural folds and failure of emigration of neural crest cells had also been implicated in the neural tube defects [29]. Maternal serum AFP (alpha-fetoprotein) and USG are the efficient screening tools in diagnosing the neural tube defects early. High resolution technologies coupled with animal models can help in better

defining of the genetic factors involved in pathophysiology of N.T.Ds [30].

## CONCLUSION

We are still in the early stages of identifying the factors predisposing to neural tube defects due to its multifactorial causation and complexity of traits. Neural tube defects can be prevented by taking folic acid supplementations during reproductive age. Screening tests like AFP (alpha-fetoprotein) and early USG at 16-20 weeks can diagnose the condition early and termination can be decided earliest possible. High resolution techniques in the field of genetics can benefit thousands of families for counselling and better management strategies.

**Conflicts of Interests: None**

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