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Original Research Article

RADIOLOGICAL AND GENETIC EXPRESSION OF NEURAL TUBE DEFECTS

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ABSTRACT

Background: Neural tube defects (NTDs) are the most common birth defects which mainly affect developing foetuses, with a high incidence rate in India and main causes of it been nutritional deficiencies and genetic predisposition. Folic acid supplementation brought decline in the incidence of NTDs.

Materials: This study was conducted on 1000 dead foetuses in Anatomy department, over a period of two years from 2017- 2019 .The dead foetuses were brought from the gynaecology and obstetrics department. A proper family history and obstetrics history was collected. The foetuses were embalmed and later studied for NTDs in detail.

Conclusion: Comparing the results with the previous studies it is clearly evident that the incidence of NTDs have significantly reduced from 11.42/1000 births to 0.2 to 10/1000 births. In most of the previous studies NTDs had a female preponderance whereas in present study there is equal preponderance. In older studies, Spina bifida was the most common NTDs followed by anencephaly. But in the present study it is the same. Incidence of NTDs has reduced due to various reasons like prenatal screening tests forfoetal anomalies and folic acid supplementation.

KEY WORDS: neural tube defects, spina bifida, neuralation,ultrasonography, karyotype.

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INTRODUCTION

Conversion of neural plate into a neural tube by process of folding is known as neuralation. The neuralation is normally completed within 30days after conception, before many women are aware that they are pregnant. Neural tube defects (NTD'S) are severe congenital malformations resulting from complete or partial failure of neural tube to close in the developing embryo during neutralization.

NTDs TYPES ACCORDING TO THE LOCATION [1, 2].

· Cranial region –encephalocele

· Spinal region- spina bifida

· Severe NTDs- craniorachisis (entire neural tube remains open from midbrain to spinal region).

NTDs can be further classified as

· Open type-neural tissue is exposed or covered only by membrane

· Closed type- defect is covered by normal skin

SPINAL CORD NTDs

1. Closed type- Spina bifida occulta

2. Open type

· Spina bifida cystica –meningocele or meningomylocele

· Spina bifida aperta – nervous tissue exposed completely to exterior forms necrotic tissue without meningeal sac

CRANIAL NTDs

Open type

1. Encephalomeningocele- (parietal or occipital region)

2. Anencephaly –brain tissue exposed without meninges.

Severe type –craniorachisistotalis (involving brain and spinal cord).

Neonates with neural tube defects lack functioning of cerebrum, have rudimentary brainstem and they are blind, deaf and unable to feel pain.

Genetic and Non Genetic Environmental factors involving the NTDs-Teratogens involved mainly are[3, 4].

· Low vitamin B12& folic acid levels in mother

· Hyperthermia & intake of anti-epileptic drugs by mother

· High serum alpha feto protein & elevated homocysteine levels in mother

· Chromosomal abnormalities (trisomy 13 & 18) in foetuses

Are predisposing factors

MATERIALS AND METHODS

This study was conducted on 1000 dead foetuses in anatomy department, over a period of two years from 2017-2019.the dead foetuses were brought from the gynaecology and obstetrics department. A proper family and obstetrics history was collected .The foetuses were embalmed and detailed study of these foetuses was done.

OBSERVATIONS AND RESULTS

Four foetuses were observed with different weeks of gestational age.2 were female & 2 were male foetuses. All the foetuses showed different types of NTDs and some had associated anomalies. Mother blood sample, foetal scan reports and genetic analysis were done. These findings were appropriately documented and photographed.

Fig. 1A: Male foetus 20 weeks: Spina bifida cystica with meningocele.

Fig 1B: Spina bifida cystica with meningocele: coronal plane 20 Weeks' foetus.

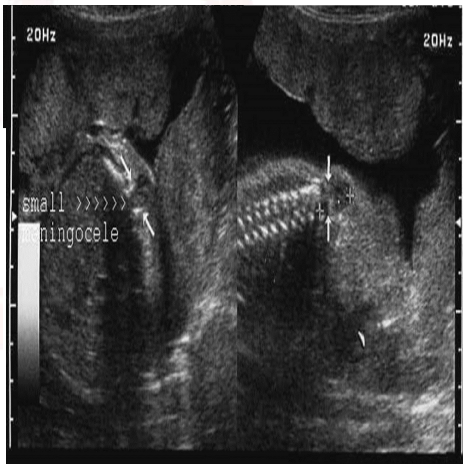
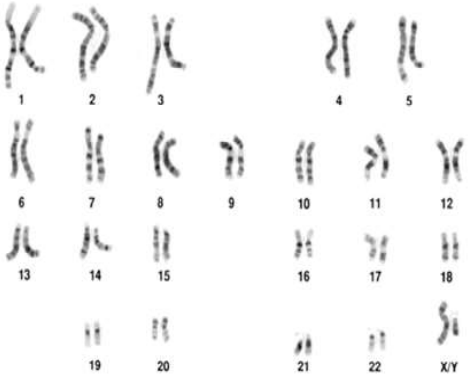


Fig 1C: Spina bifida cystica with meningocele male foetus 20 weeks Genetic analysis (amniotic fluid): normal male karyotyping H/O of mother having hyperthermia during the first 3wks of gestation. Hyperthermia is one of the environmental teratogen which focus on NTDs.



Normal Karyotype

Fig. 2A: Female foetus 19 weeks: Spina bifida cystica Lumbosacral Meningomylocele, associated with bilateral inversion deformity in both the feet.

Fig. 2B: Sagittal view 19 weeks fetus with lumbosacral meningomylocele with bilateral inversion deformity in both the feet

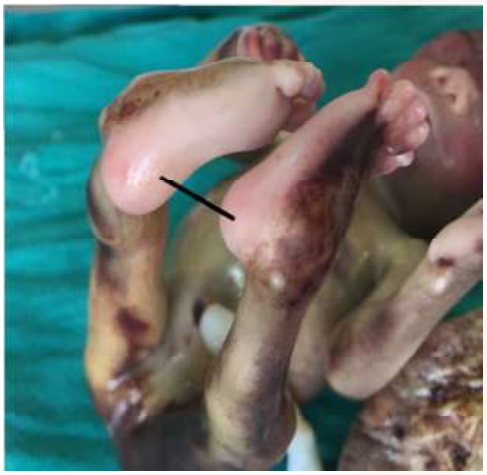
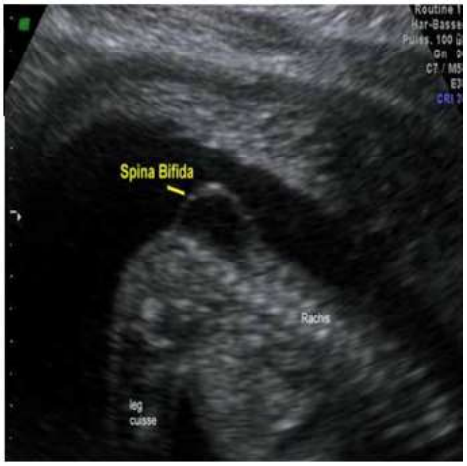


Fig. 2C: Female foetus 19 weeks with lumbosacral meningomylocele with bilateral inversion deformity in both the feet Genetic report (amniotic fluid): Normal female karyotype.

Mothers Blood report: vitamin B12 concentration was significantly low (102pg/ml). (Normal range 180-914pg/ml) Vitamin B12 is metabolically related to foliate pathway. Low B12 status associated with high risk of NTDs.



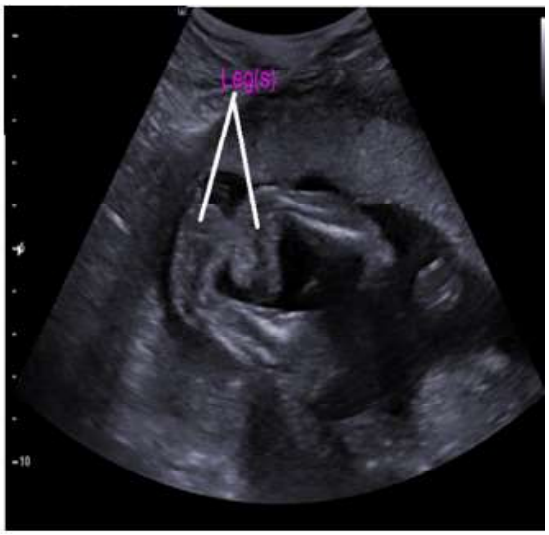


Fig. 3A: Male foetus 16 weeks Spina bifida cystic Lumbar meningomylocele & lemon shaped head (defective calvaria) also associated with severe kypho-scoliotic deformity of the upper spine.

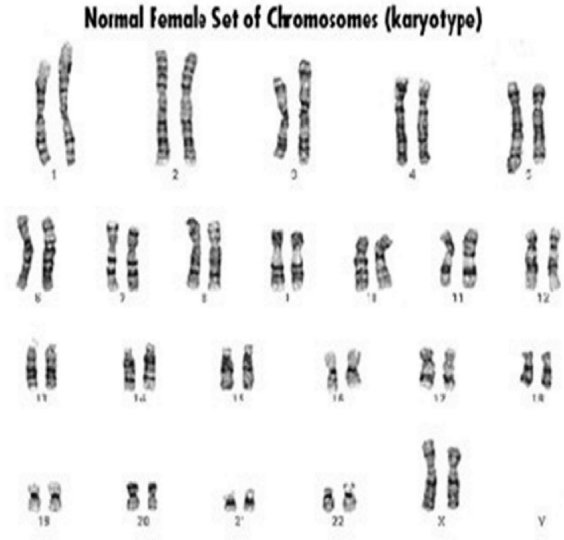


Fig. 3B: Spina bifida cystica with lumbar meningomylocele and lemon shaped head sagittal and coronal view 16 weeks foetus with severe kypho-scoliotic deformity of the upper spine.

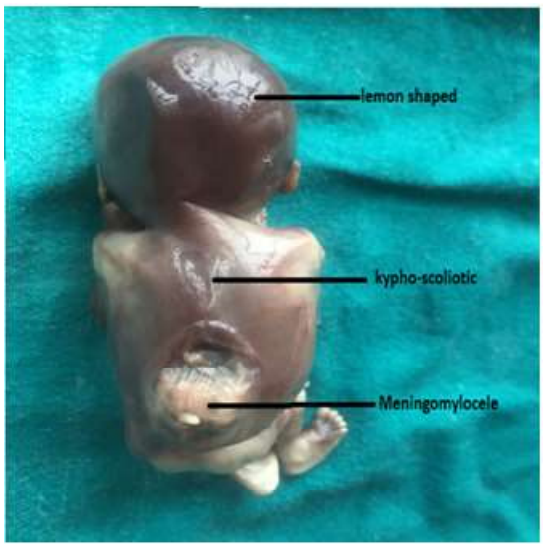
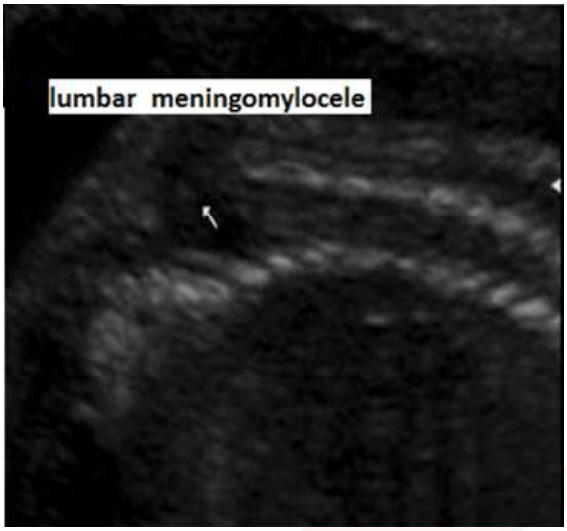
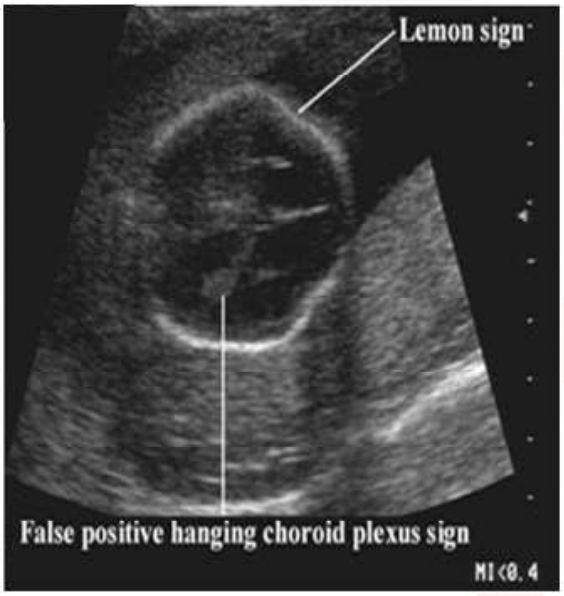


Fig. 3C: Male foetus 16wks: Spina bifida cystica lumbar meningomylocele, lemon shaped head with kypho-scoliotic deformity of the upper spine. Genetic report (amniotic fluid): normal male karyotype Mother with severe folic acid deficiency- 1.2ng/ml (normal 3.56-20ng/ml).





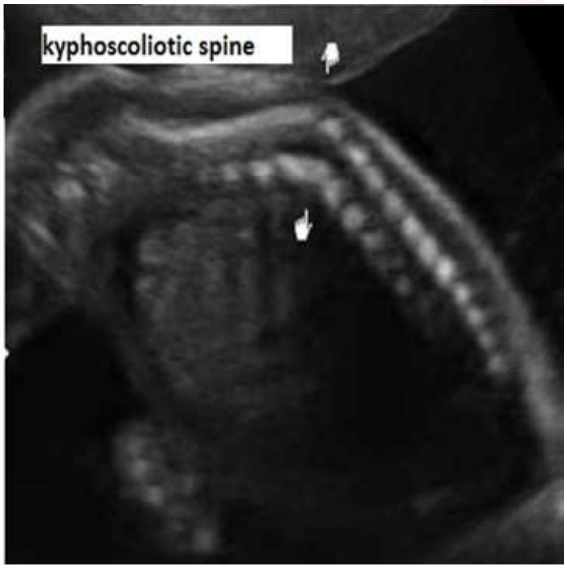


Fig. 4A: Female-20wks Arnold Chiarii syndrome type - II with Spina bifida and clubfeet Hind brain herniation is secondary to Meningomylocele.

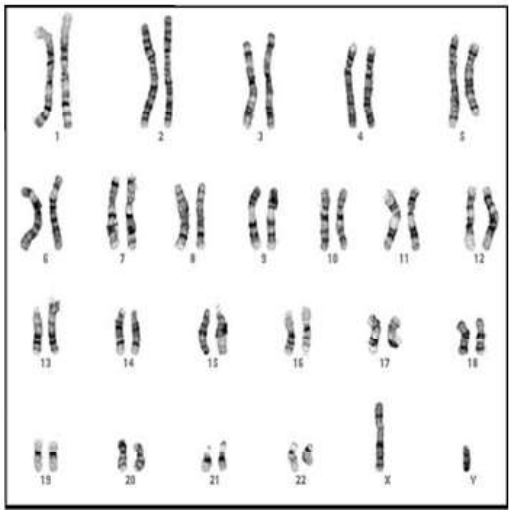


Fig. 4B: Arnold Chiari syndrome type - II with Spina bifida and clubfeet Ultrasonography of fetal cranium (Sagittal and coronal view) Crowded posterior fossa, banana shaped cerebellum is displaced inferiorly through the foramen magnum.

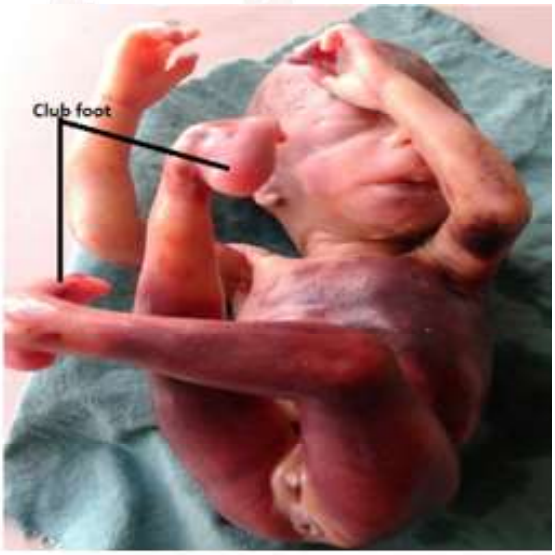
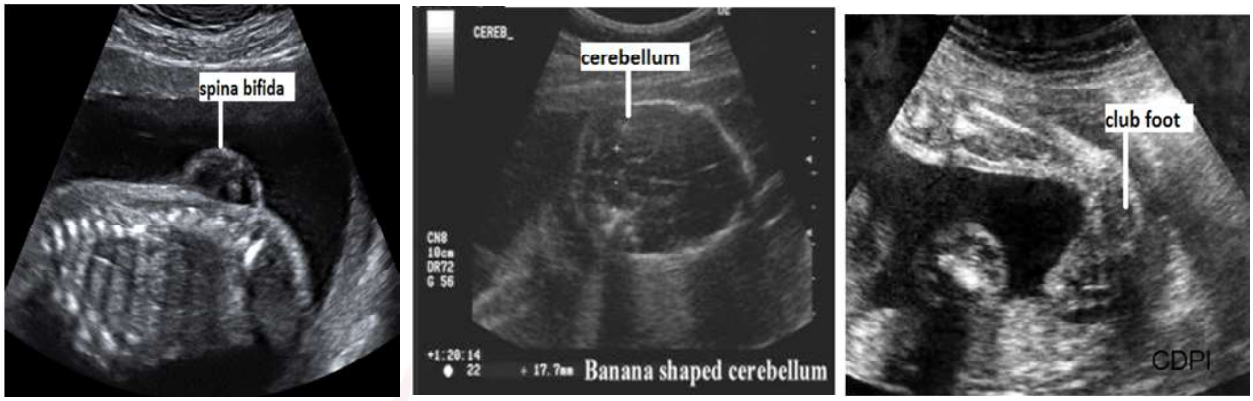


Fig. 4C: Female fetus 20wks Arnold Chari syndrome type - II with Spina bifida and clubfeet Genetic report (amniotic fluid): Karyotype showing trisomy 18 there was no periconceptional folic acid &vitamin B12 supplementation.



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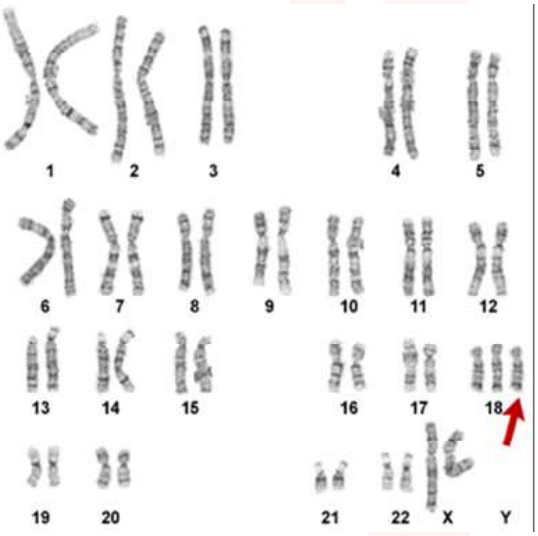

DISCUSSION

NTDs is classified as an embryological induction disorder it results in failure of both neuroectoderm and mesoderm [5, 6]. This inciting event can be traced to days 17-30 days of post fertilization (3-8 weeks).NTDs are CNS anomalies affecting 0.5 to 2 per 1000 pregnancies worldwide, in India 0.6-13/1000 births and more common in females. Females are more often affected than male in having craniorachischisis [7] and spina bifida involving the cervico-thoracic region, males have spina bifida affecting the lumbosacralregion. Positive family history is an important risk factor and recurrence risk is 5% with previous affected child.The main primary defect is a failure of the neural folds to fuse in the midline and form the neural tube during neutralization, the subsequent defect is the maldevelopment of the mesoderm which forms the skeletal and muscular structures that cover the underlying neural structure [8]. The present study has4 neural tube defects per 1000 pregnancies (F2:M2).

Genetic Correlation: The genes which encode and disrupt NTDs include Hectd1, Mib2 and Smurf1/2 [9, 10] these genes help in signaling pathways for neural tube closure. Gene mutations lead to recurrence of NTDs. Consanguinity was suggested to contribute to the high incidence of NTDs. Among folate related genes 5, 10 methylene tetrahydrofolate reductase (MTHFR) has been a principle focus of attention. MTHFR gene alter the functional activity of the MTHFR enzyme which in turn affect the homocysteine levels in the serum. Elevated homocysteine prompts analyses of variants in genes leading to abnormalities of foliate metabolism thus causing neural tube defects.

CONCLUSION

The current study includes 4 NTDs still born fetuses ranging from 16 weeks to full term. Teratogens involved are low vit B12 & folic acid levels, hyperthermia of mother [11], high serum alpha feto protein levels and chromosomal abnormalities (trisomy 18 &13) are predisposing factors contributing for NTDs in this study. Most NTDs are sporadic, both genetic and non-genetic environmental factors provide multifaceted challenge togeneticists, anatomists and gynecologists.

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Conflicts of Interests: None

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