

Anencephaly and its Associated Malformations

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ABSTRACT

Introduction: Anencephaly is a serious neural tube defect in which parts of the brain and skull are not developed. But apart from this it is also associated with other malformations which are not related to neural tube in development.

Aim: The present study was undertaken to find the associated congenital malformations in western region of India and establish a aetiological correlation.

Materials and Methods: The study was conducted using 20 anencephalic fetuses.

Results: Nearly 80% of fetuses had associated malformations. Spina bifida was seen in 9 fetuses and cleft palate in 8. Female fetus with cleft palate had other severe associated gastrointestinal and skeletal malformation.

Conclusion: In cases of anencephaly other associated malformations like spina bifida and cleft palate are commonly seen.

INTRODUCTION

Failure of closure of the cranial neuropore during the fourth week of development results in the abnormal vascularisation of the embryonic exencephalic brain [1]. The nervous tissue subsequently undergoes degeneration and brain remains as a spongy vascular mass with some hind brain structures [2]. Previously called as anencephaly (without brain), it is now called as Meroanencephaly as some functioning neural tissue is always present [3]. As Meroanencephaly is a lethal malformation the research on presence of other associated malformations has largely remained restricted. Ballantyne (1904) [4] as well as David and Illingworth [5] associated diaphragmatic hernia with anencephaly. British Perinatal Mortality Survey [6] of 1958 first stressed on registering the associated malformation in anencephalics. T.J.David [7] tabulated the associated malformations and found spina bifida to be the most common. Many researchers found that the most common associated malformations differed according to the geographical location [8,9]. According to David TJ cardiovascular defects were common in Lancashire while urinary tract defects were common in the Bristol [10]. Apart from CNS malformations gastrointestinal and skeletal abnormalities were the most common according to C Pandurang [11] in a study conducted in India.

MATERIALS AND METHODS

The study was conducted between January 2013 to March 2014 in Lokmanya Tilak Municipal Medical College and general hospital which is a major tertiary care hospital for obstetrics in western India. Ethical clearance was obtained by the institutional ethical committee. Twenty anencephalic fetuses were dissected in the Anatomy department of the institute after obtaining informed consent. The cases originated from still birth, spontaneous abortion and therapeutic abortion. The gestational age was in the range of 16 to 34 weeks. There was no history of diabetes, obesity and infections in the mothers. There was no exposure to any teratogenic drugs. All mothers had received the recommended 0.5mg of folic acid supplementation. The findings were done by external examination, photography and internal examination. Internal examination was done for abdominal and genitourinary viscera only.

Keywords: Anencephaly, Cleft palate, Clubbed foot, Spina bifida

The results were recorded according to the following parameters.

Facial features: - Cleft lip, cleft palate.

CNS: - Spina bifida.

GIT: - Absence or underdeveloped organ.

Genito urinary system: - Hypospadias, penile hypoplasia, renal agenesis.

Skeletal system: - Clubbed foot, clubbed hands.

RESULTS

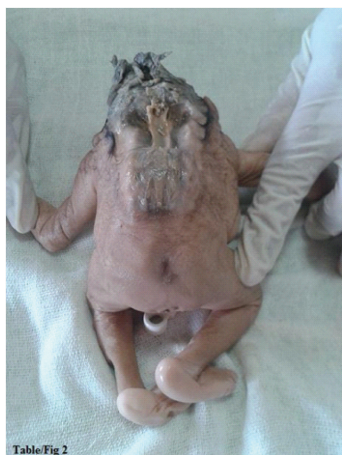
Associated malformations were seen in 16 out of 20 fetuses. There were 12 female and 8 male fetuses. Spina bifida was the most common anomaly followed by facial anomalies which included cleft lip and cleft palate. The details are given in [Table/Fig-1].

DISCUSSION

Anencephaly is associated with anomalies of not only central nervous system but other systems as well. Previous studies have mentioned a wide range for the percentage of fetus with associated malformation. Tan et al., [12] recorded 9.4 % while David TJ [10] recorded 84%. The present study recorded 80% fetus with associated malformations. There were more number of female fetuses (12 cases) as compared to males (8 cases). The percentage

Anomaly	No of cases	Percentage	Remarks
Spina bifida	9	45	Cervical region 7 cases Lumbar region 1 case.
Cleft Palate	8	40	7 male 1 female
Cleft lip	5	25	All has associated cleft palate
Clubbed foot and clubbed hands	7	35	5 males 2 females
Genital abnormalities	2 cases	10	2 males has Hypospadias No abnormality in females
Gastrointestinal system	2 cases	10	1 case gastroschisis. 1 case omphalocele.

[Table/Fig-1]: Showing the distribution of number of cases for different anomaly



Table/Fig 2



Table/Fig 3



Table/Fig 4



Table/Fig 5

[Table/Fig-2]: Fetus with craniospinal rachischisis and kyphosis of thoracic spine **[Table/Fig-3]:** Fetus with thoracolumbar spina bifida **[Table/Fig-4]:** Fetus with gastroschisis, cleft palate, cleft lip and clubbed feet **[Table/Fig-5]:** Fetus with omphalocele

of female fetuses was 60%. All the previous studies have proved that the females outnumber males in cases of anencephaly. The female preponderance noticed by previous authors were David TJ [10] at 66%, Panduranga [11] at 56% Aruna [13] recorded 55%.

In the present study the commonest anomaly associated with anencephaly was spina bifida (9 cases). Associated malformations were more common in cases with spina bifida. Even though spina bifida is more common in lumbar region in general population, craniospinal rachischisis [Table/Fig-2] of the cervical region was found to be commoner in anencephalic fetuses [14]. Craniospinal rachischisis is the most severe form of spina bifida cystica. In this defect the spine lies widely open and the neural plate has spread out on to the surface [15]. The thoracolumbar type spina bifida [Table/Fig-3] was seen in only one case.

Facial abnormalities like cleft palate were seen in 8 cases of which 7 were males and one female. Suggesting a correlation between cleft palate and male sex. Earlier studies have also reported cleft lip and palate to be more common in male anencephalic fetus [10,11,13]. Cleft lip was found in 5 cases in association with cleft palate.

The genital abnormalities were seen in two male cases in the form of Hypospadias. The remaining genital development was normal. There was no genital abnormality detected in females. Studies done by Tan et al., [12], Nielsen et al., [16] and Gopalipour et al., [9] did not find any abnormality in the genital system. David et al found 0.6% cases with abnormalities in the genital system and that too in male fetuses only. One female fetus which had marked deformities such as cleft lip, cleft palate, gastroschisis, clubbed feet and hands also showed normal genital development [Table/Fig-4]. One case of omphalocele was seen [Table/Fig-5]. No abnormality was detected in the urinary system.

Skeletal deformities like clubbed hands and clubbed feet were present in 5 males and 2 female fetuses. All the 5 male cases had associated cleft palate. Skeletal abnormalities found in previous studies were in the range of 1.7% by David TJ [10], 14.5% Vare et al., [17] to 20 % by Tan et al., [12]. The present study recorded a higher number of skeletal abnormalities at 35%.

The cause of anencephaly is still a disputed entity but the defect is failure of closure of rostral neuropore. Anencephaly, even though a defect of the neural tube can affect many other systems selectively [18]. The intake of 0.5mg of folic acid [19] during the course of pregnancy reduces the risk of anencephaly but does it have a similar effects on other anomalies is poorly understood. The presence of spina bifida can be correlated embryologically to the defect in closure of the neuropore. Cleft palate and lip might occur due to the defective neural crest cells. MTHFR gene has been associated with anencephaly and orofacial defects [20] but its increased frequency

in males is poorly understood. Many studies have tried to find the genetic association of anencephaly. LD Botto [21] reported MTHFR gene located on chromosome 1 to be associated with neural tube defects. But EC Melvin [22] failed to reach a consensus on the involvement of p53, PAX3 and MTHFR gene in neural tube defects.

CONCLUSION

Anencephaly is common in females. Associated abnormalities were seen in 80% of cases in the present study. Commonest abnormality was spina bifida. Describing the associated malformations in anencephaly as described in present study is not only of academic and research interest but also helpful to radiologists for correct interpretation and diagnosis. The strong association between cleft palate and male fetus should be considered during the diagnosis. The presence of associated abnormality like spina bifida, cleft palate, clubbed foot, clubbed hands and gastroschisis points to the fact that anencephaly consists of more than one aetiological entity. Studies are required at molecular level to find its association with other anomalies.

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