Incidence of Anencephaly in a tertiary care hospital in North West India

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***Abstract*- Background:** Anencephaly is a neural tube defect (NTD) which is due to defective closure of cranial neuropore. This NTD is associated with other congenital anomalies in most of the cases. This study was undertaken to determine the incidence of anencephaly among congenital malformations seen at autopsy. The study aims to identify the risk factors associated with anencephaly in our population. Attempt was made to correlate the incidence with associated systemic anomalies, maternal age, birth order and sex of the fetus.

Material & method: Data was tabulated on 520 foetal autopsies obtained out of 18744 births in a tertiary care hospital for a period of 3years from August 2011 to July 2014.

Results: Out of the total 520 autopsies, congenital malformations (CMF) were observed in 187 (36%) fetuses obtained from spontaneous /therapeutic abortions. 115 (61.4%) cases showed neural tube defects. NTD's accounted to 22.11% of all fetal autopsies. Anencephaly was the most prevalent anomaly observed in 69 cases (60% of NTD's), 13.3% of total autopsies. In 40 cases (58%) anencephaly was associated with other systemic anomalies such as cardiac defects , GIT defects and polycystic kidneys. No significant statistical correlation could be established regarding the sex of the anencephalic fetus. However mothers in the age group of 20-25 years reported highest number (54.4%) of anencephalic fetuses. Maximum anencephalic fetuses were born to primigravida mothers (38.2%). Regarding their socio-economic status 48% cases were from upper lower class and in 35% cases mothers were high school drop outs.

Conclusion: Prenatal screening of the fetus is of utmost importance to rule out the presence of any CMF. To prevent NTD's, peri-conceptional folic acid supplementation should be provided to low socio-economic females. Pathological examination of the abortus is essential to document associated anomalies.

***Index Terms*-** Anencephaly, Fetal autopsy, Neural tube defects, Systemic anomalies.

I. Introduction

Anencephaly is a neural tube defect that is incompatible with life.[1] Anencephaly (*Gr*. *An*, without+ *enkephalos*, brain) is an anomaly caused by the failure of the rostral end of the neural tube to develop. Failure of closure of the cranial neuropore between the third and fourth week of gestation (23rd and 26th embryonic day; 18-20 somite stage) [2] results in major portion of the brain, skull, and scalp being absent, though brain stem is intact.[3] Although the eyes are present, the optic nerves are absent.[2] Other names like acrania (absence of skull), acephly (absence of head) merocrania, exencephaly and meroanencephaly are also used instead of anencephaly.[4] In anencephaly, the influence of the expanding brain is removed, and secondary adaptive alterations in the cranial base occur. The squamo-occipital bones are under developed compared with the normal standards. In anencephaly the bones derived from chondrocranium are not as severely affected morphologically as those derived from the neurocranium.[5] In some cases closure defect of neural tube extends caudally into spinal cord, and the abnormality is called craniorachischisis. Anencephalic fetuses lack a swallowing reflex, the last 2 months of pregnancy are characterised with polyhydramnios.[6]

The birth prevalence of NTD's including anencephaly, is highly variable and is dependent upon geographical location, race and sex. According to standard textbooks, anencephaly occurs in 1/5000 births.[6] It is twice or four times more common in female fetuses.[7] A wide range of frequency has been quoted from different parts of India. Its about 1.8 to 7 per 1000 live births.[8,10,11]

The cause of anencephaly is disputed. Anencephaly can be induced experimentally in rats by using teratogenic agents and abortuses suggest that the process is similar in humans. Genetic factors are certainly involved because of well- established familial incidence of these defects. [7] The rates of chromosomal abnormalities range from 7-16%. It is more likely to find chromosomal abnormality if anencephaly is associated with other malformations. Trisomy 18 is a common abnormality found at mid-trimester in an anencephalic fetus whereas triploidies are more common in first trimester. [12,13,14] Several candidate genes (more than 100) are now associated with the risk of NTD's. These genes are related to folate, glucose, retinoid, inositol metabolism. Also others are related to apoptosis or developmental pathways such as Sonic Hedgehog, Planar Cell Polarity pathway. There is also evidence that genes related to structure and function of actin cytoskeleton when mutated impedes the elevation of neural folds causing these malformations.[15] Thus the most accepted inheritance of anencephaly is multifactorial inheritance.[7]

A study now confirms a suspected epidemiological link between parents' occupation and anencephaly. A nearly five fold increase in risk of anencephaly for mothers exposed to pesticides resulted while working in agriculture during the acute risk period. Fathers who were exposed to pesticides at any time while working in agriculture had twice the risk of having an anencephalic child. Chlorpyrifos and methyl parathion, have

also been previously linked with possible reproductive ill effects.[16]

Recurrence rate after one affected pregnancy is two to three percent for any open neural tube defect. Rare families have reported with X-linked inheritance. Women taking certain medications for epilepsy like valproic acid ,folic acid antagonists (such as methotrexate), women with insulin-dependent- diabetes-mellitus, hyperthermia and folic acid deficiency are associated with increase risk of NTDs. Radiation ,infectious agents like CMV, rubella, toxoplasma gondii, certain drugs like aminopterin and maternal alcohol abuse especially are known teratogens causing anencephaly.[7] Hibbard and Smithells (1965), were first to suggest a possible link between folate deficiency and NTD's.[17] The birth prevalence of NTDs in the United States has decreased by approximately 25%, to 1/1500 births after fortification of flour with folic acid was instituted in 1998.[2] Advanced maternal age is a stronger risk factor for spina -bifida than for anencephaly.[18]

Anencephaly can be diagnosed by ultrasound examination (USG), MRI, fetoscopy and radiography as extensive parts of brain and calvaria are absent.[7] This anomaly can be diagnosed by 11-12 weeks of pregnancy(by application of alpha protein screening). A study conducted in India, during the antenatal period detected 27 (1.55%) cases of anomalies whereas only 8.48% anomalies were diagnosed by USG.[19] Pathological examination of the abortus is essential, as in most of the cases anencephaly is associated with systemic anomalies.[5]

II. MATERIAL AND METHODS

This study was conducted on 18744 births in a tertiary care centre for a period of 3years from August 2011 to July 2014. 520 fetal autopsies were performed in this institute in the department of anatomy during this period. These cases originated from spontaneous or therapeutic abortions received from the obstetrics and gynaecological department of the institute. Prior to autopsy, prenatal investigations such as ultra sound and radiographs were procured and a brief maternal and family history regarding socioeconomic status, maternal education level & addiction of father to alcohol and tobacco was noted. The updated Kuppuswamy's socioeconomic scale for 2012[20] was used to asses the family and education status. Consent for autopsy was taken from parents /relatives on a Performa prepared in accordance with guidelines provided by the ethics committee which conforms to the provisions of the Declaration of Helsinki in 1995. Autopsies were performed as per guidelines provided by fetal autopsy protocol (Siebert and Kapur, 2001 ; WHO, 2007).[21] The autopsies included reading of the clinical findings, external examination, photography and internal examination. All the observations were recorded paying more attention to associated systemic anomalies. Others parameters registered were Gestational age (supplied by the clinical records), sex of fetus, incidence, frequency in relation to parity, maternal age and isolated or as a part of syndrome. The statistical analysis was performed by using frequency and percentage.

III. RESULTS

Fig. 1 shows the profile of all autopsy cases. 60% fetuses were the result of spontaneous abortions while rest of the fetuses were clinically aborted after manifestation of CMF. 187(36%) fetuses were found to be congenitally malformed; out of these neural tube defects were present in 115(61.4%) fetuses. The overall percentage of NTD was 22.1% in 520 autopsies. The most prevalent NTD was anencephaly observed in 69 (60%) fetuses. The overall percentage of anencephaly was 13.3% in 520 autopsied fetuses.

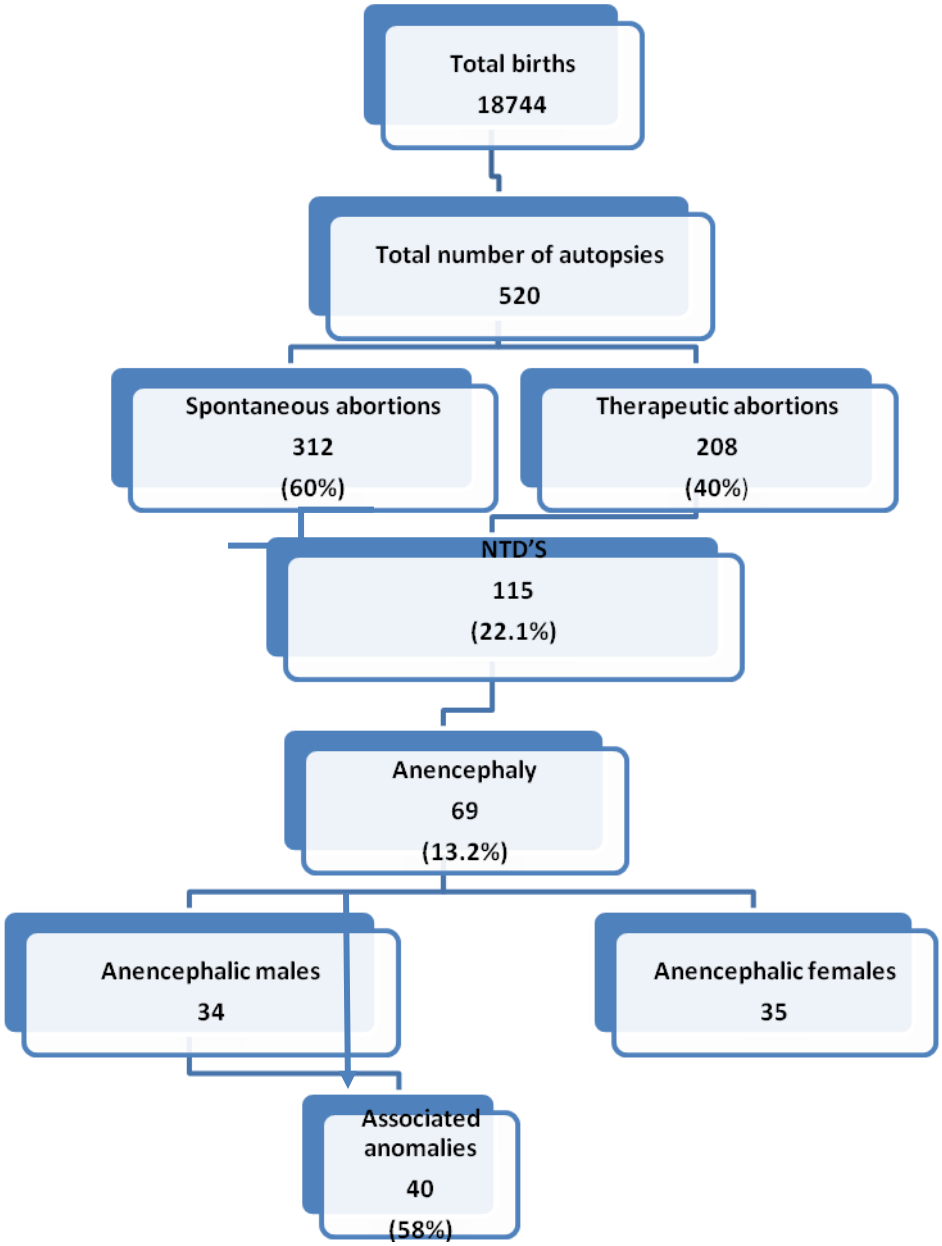

Figure1: .Profile of all autopsy cases.

On a larger scale; when total numbers of hospital births were calculated (table 1) the incidence of anencephaly turned out to be 0.4%.

The incidence of anencephaly was correlated with various maternal and other factors.

Table 1: Annual Incidence of anencephalic births in hospital

Year	Total no. of births	No. of fetal autopsies	Total CMF	Total NTD'S	**Anencephalic births**
2011 (Aug-Dec)	2386	54	25	12	5
2012	5728	179	77	45	23
2013	6200	198	50	32	25
2014	4430	88	35	26	16
Total	18744	520(2.77%)	187(1%)	115(0.6%)	69(0.4%)

a) Maternal Age: minimum age of mother observed was 19 years and maximum was 35years. The maternal age for 54.4% fetuses was between 20-25 years followed by 35% in 26-30 years (Table 2)

Table 2: Frequency of anencephaly in relation to maternal age

Maternal age	NO. Of cases
<20 yrs	1(1.4%)
20-25yrs	37(54.4%)
26-30yrs	24(35.2%)
31-35yrs	6(8.8%)
>35yrs	zero

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b) Parity: Out of 68 mothers 26 were primigravida (38.2%), Twenty were gravida 2 (29.4%), sixteen were gravida 3(23.5%) and four cases were gravida 4(5.8 %), one was gravida 5(1.4%) and one was gravida 6(1.4%). As seen in Fig.2, anencephaly was more prevalent in primigravida (37.6%), the incidence decreased with the increase in parity.

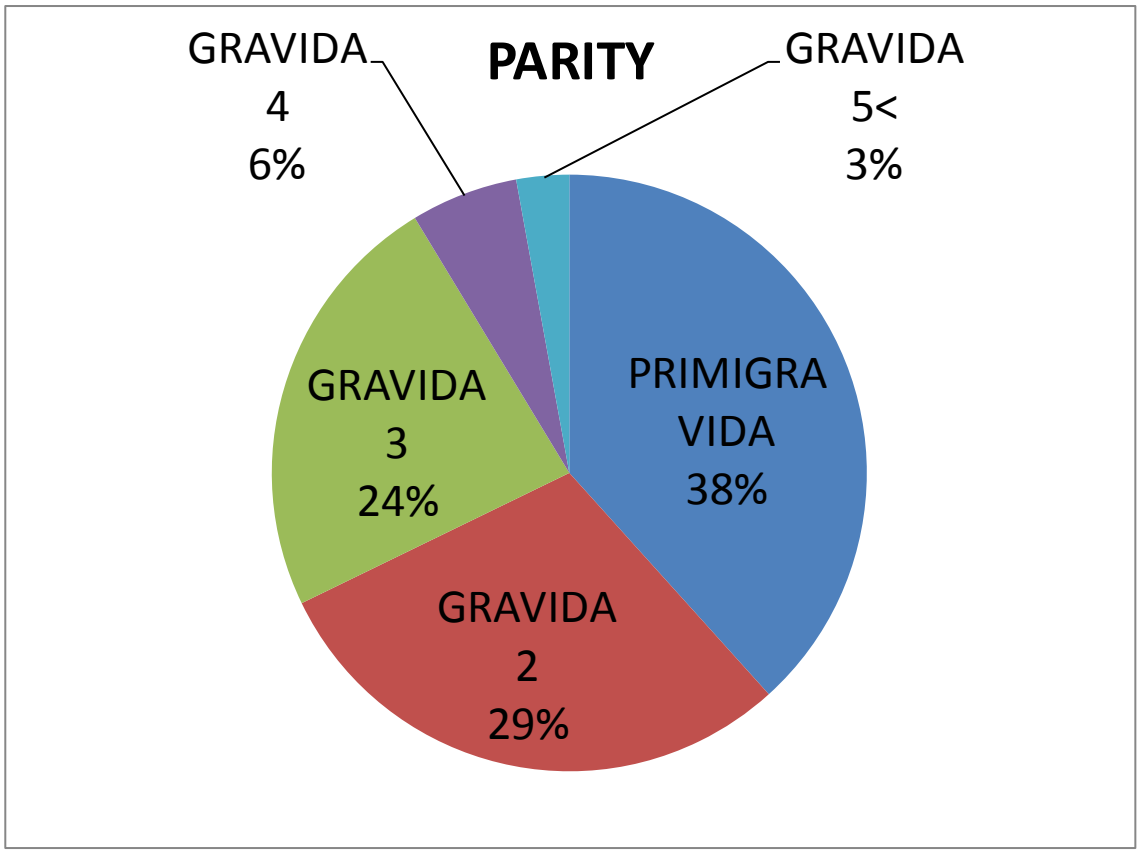

Figure 2: Frequency of anencephaly in relation to parity

c) Sex: No sexual preponderance was noticed. Out of 69 fetuses, 34 were males(49.2%), 35 were females(50.7%)and none of the fetuses had ambiguous genitalia

d) Gestational age: Gestational age ranged from 12 to 29 weeks with mean of 19 weeks.

Spontaneous abortions were seen in 10 cases of anencephaly with minimum gestational age of 19 weeks and maximum of 26^{+6} weeks

Table 3: Frequency of anencephaly in relation to Gestational age

Gestational age	Total No. (%)
11-15 wks	11(15.9%)
16-20 wks	46(66.6%)
21-25wks	9(13%)
26-30 wks	3(4.3%)

The manifestation of anencephaly was maximum (66.6%) in the 16-20 weeks of gestation. In very few cases (4.3%), the anencephaly becomes symptomatic after 6 months of intrauterine life.

The recent National Family Health Survey (NFHS-3) revealed that about 44% of pregnant women sought antenatal care after 16 weeks of gestation as observed in our study also. Most of the mothers were from rural area and they were agricultural labours. The cases were diagnosed at the time of ultrasound examination during their visit to our hospital and they were advised medical termination of pregnancy

Associated anomalies: Anencephaly is not the only malformation present in a fetus, which was proved by the fact that 58% anencephalic fetuses also had some other systemic anomaly (Table 4) 36.23% anencephalic fetuses exhibited other neural tube disorders including rachischisis, meningomyelocoele and encephalocoele. In all anencephalic cases the fetus presented a toad face with protruding eyes, flattened nasal bridge, a very short neck and absence of cerebral hemispheres and skull. (Fig 6) Other Central nervous system **(CNS)** anomalies observed in association were cranio-spinalrachischisis in twenty cases (Fig 4) out of which in five cases it extended to the lumbar region &in three cases to whole of the vertebral column thereby exposing the spinal cord (Fig 5). Spina bifida was observed in four anencephalic fetuses. One case of anencephaly had a meningomyelocoele in thoracic region and another with encephalocoele of occipital region.

In nine fetuses (11.5%), anencephaly was associated with dysmorphic facial features, including cleft lip in two cases. One fetus presented with micrognathia, webbed neck, bilobed right lung, absent scortum with inverted foot and a dysmorphic pinna. Low set ears were observed in five cases & in one anencephalic fetus a single nostril was seen. (Fig 6).

In 17.3% anencephalic fetuses respiratory anomalies were also present as hypoplasia of lung (bilateral-2, unilateral -2). In one case no fissure was present in both right and left lungs. Bilobed right lung was present in eight cases.

Anencephalic fetuses also exhibited cardiovascular anomalies (CVS) in 13.4% cases, GIT anomalies in 18.8%, uro-genital defects in 18.8%, and skeletal anomalies in 10% fetuses.

The CVS anomalies were presence of single umbilical artery in six cases. Dextrocardia as a part of situs inverses was observed in one case (Fig 7) and non development of diaphragm in another case (Fig 8). Position of heart chambers were reversed in one case.

The GIT anomalies observed were diaphragmatic hernias in five cases. In one fetus it was combined with ascites and ectopic position of appendix. In another case the ascending colon along with transverse colon pushed into midline and a diaphragmatic hernia was present. Sub hepatic appendix was observed in three anencephalic fetuses reflecting delay in development of other systems.

Malrotation of gut was spotted in four anencephalic fetuses. Anencephaly along with omphalocoele was observed in two cases, out of which in one case the ascending colon was present in the left hypogastric region. Another case showing imperforate anus with common opening of ureter and anus was spotted.

The skeletal anomalies were observed in 10% of anencephalic fetuses. Polydactyly was present in (bilateral -2 ,unilateral-1) three fetuses, in one case associated skeletal anomalies were cleft palate with cleft lip. Other skeletal anomalies were in the form of scoliosis and fusion of lower limbs (Fig 9).

Genito- urinary abnormalities were present in 18.8% of anencephalic fetuses. Bladder with dilated left ureter was detected as a part of Prune Belly syndrome. Unilateral absence of kidney was noted in one case and horse shoe kidney in another. Two anencephalic fetuses had both their ureters dilated .Bilateral polycystic kidneys were present in three cases.

Table 4: Systemic anomalies associated with anencephaly

SYSTEM	Associated anomalies (No. of cases)
C.N.S	cranio-spinalrachischisis (20) , Spina bifida (4), meningomylocoele (1)
Head and Neck	cleft lip (2), Micrognathia with webbed neck, dysmorphic pinna (1), low set ears(5), single nostril (1)
Respiratory	B/L Hypoplastic lungs (2), right lung hypoplasia (8), Bilobed right lung (2)

Cardiovascular	single umbilical artery (6), dextrocardia (2), reversal of heart chambers (1)
GIT	Diaphragmatic hernia (4),malrotation of gut (4), Omphalocele (2), Imperforate anus (1), sigmoid colon opening in ureter (1), common opening of ureter & anus(1)
Skeletal	club foot(3), bilateral polydactyly (2), fused lower limbs (1), scoliosis (1), Simian crease (2)
Genitor-urinary	Absent scortum (1), unilateral kidney(1), horse shoe kidney (1), dilated ureters (bilateral-2, unilateral-1), B/L polycystic kidneys (3)

In two instances Anencephaly was part of a well defined syndrome such as Meckel Gruber syndrome and OEIS complex. Two cases of Meckel Gruber syndrome (Polycystic kidneys, polydactyly, liver fibrosis hypoplastic lungs) were discovered. OEIS complex (Omphalocele, cloacal exstrophy, imperforate anus, spinal defects was spotted in one fetus.

Social factors

The families were divided into five socioeconomic stratas according to Kuppuswamy's socioeconomic status scale (2012).[20] .Almost half of the families (48%) were grouped in the upper lower status followed by lower middle in 17.3% instances.

Table 5: Frequency of Anencephaly in relation to the socioeconomic status and the mother's education status (Kuppuswamy 's socio-economic status scale)[20]

Status	No of cases (%)	Mothers Education	No. of cases (%)
Lower <5	9 (13%)	Illiterate	12(17.4%)
Upper lower (5-10)	34 (49.2%)	Primary	16(23.2%)
Lower middle (11-15)	12 (17.3%)	Middle	5(7.2%)
Upper middle (16-25)	11 (15.9%)	High	24(34.8%)
Upper (26-29)	3 (4.3%)	Graduate & above	12(17.4%)

Mother's education status:-

Mother's education and thereby awareness did not prove to be deciding factor as in 35% anencephalic fetuses, mothers were educated upto high school.

Family History revealed that out of 69, 10 cases reported previous unhealthy pregnancy. In three cases, parents reported aborting previous anencephalic fetus. Recurrence rate after one affected pregnancy is 2-3% for any open neural tube defect.

Substance abuses

In the matter of substance abuse, none of the mothers confirmed the intake of alcohol or any tobacco product. Whereas 22(31.8%) fathers admitted intake of alcohol while 17(24.6%) fathers were addicted to tobacco products in form of ghutkas, bidis and cigarettes.

Discussion

NTDs are considered to be polygenic, multifactorial condition wherein many genes, nutrients, environmental factors including infections, drugs and maternal disease like diabetes individually or in combination play a role.[7] The maternal risk factors that are associated with anencephaly are illiteracy, increasing gravidity, history of previous miscarriages, positive history of birth defects, high or low age of mothers during pregnancy. [1,5,22] Other factors include increased stress, women employed in industry or agriculture,[16] low socioeconomic status and maternal antipyretic consumption,[4] and consanguineous marriages.[1,8]

This study provides detailed information on the incidence of NTD's, anencephaly with its associated anomalies in the northwest population of India. In the present study frequency of neural tube defect was 6.1/1000 live births in the period 2011-2014 comparable to previous study of Mahadeven et al (5.7/1000 births)[8] in South India . A wide range of frequency has been quoted from different parts of India and it was 3.9/1000 in Lucknow,7/1000 in East Delhi[10] and 11.4/1000 births in Davangere; Karnataka.[8]

Study by Golalipour et al , 2010[1] reported that NTD's accounted for 21.7% of all notified congenital birth defects,with an incidence of 28/10000 live births in northern Iran.[,1]

Some studies (Chinara & Singh,1982; Kara basi et al,2009; Dutta et al,2010) have reported the incidence of GIT and genitourinary defects to be the highest of all the CMF .[25] The present study confirms the existing view that neural tube defects are most prevalent congenital malformations as compared to defects in other systems i.e (61%) of all the CMF. This observation is in agreement with the other two fetal studies of the same region (Mohan et al;2004 and Sankar,et al, 2006, Kapoor et al;2013)[25].

Anencephaly is the most prevalent neural tube defect observed in western and some Indian studies.[1,8,11,17] Study in South India reported a frequency of 1.8/1000 in Pondicherry as compared to 3/1000 in Delhi.[8,10,] Outside India, the incidence of anencephaly was observed as 1.2/ 1000 in Iran, 1.04/ 1000 in China, 0.54/1000 in Singapore, and 5.9/1000 in Dublin.[1] The present study reports the incidence as 3.68/1000 births which is comparable to the eastern countries. The prevalence of anencephaly is higher in India. The cause of this discrepancy can be attributed to maternal malnutrition, low education and lack of social awareness.

The association between anencephaly and maternal age is disputable. While some authors are of the opinion that risk of anencephaly increases with advancing age, other studies advocate that it is more prevalent in younger women. The present observations corroborate with the later; i.e 54.4% anencephalic

babies were born to mothers between 20-25 years. Commonest child bearing age of women in India is 20- 28 year.[4] Mean age of the mother observed in our study was 26.9 years (range from 19-35 years). Our findings are consistent with published literature.[4,5] In contrast, (Caffey & Jessop ,1957; Golalipour etal,2010) observed the prevalence of anencephaly to be more in women over30 and above 35 years respectively.

The association between anencephaly and birth order has been described as U-shaped by Elwood et.al ,1978 , in contrast no association of parity with the aetiology and outcome in neural tube defects have been shown by Paduranga et al;2012[4] According to other studies anencephaly was common in primigravida.[8,17] Similarily in our study anencephaly was more prevalent in primigravida (37.6%), and the incidence decreased with parity in contrast to the study by Paduranga et al;2012.

The present analysis showed equal preponderance of anencephaly in both the sexes with 34 males and 35 females. On the contrary some authors have noted female preponderance in the occurrence of anencephaly.[4,5,22]

The occurrence of anencephaly could be genetic as is suggested by the presence of associated anomalies. Nielson et al; 2006[23] have mentioned the chromosomal abnormalities in 16% of anencephalic cases.[23] The associated anomaly could be some other neural tube defect, or systemic anomaly. Table 7 shows the system wise occurrence of associated anomaly in comparison to available literature.

The most prevalent associated anomaly was neural tube disorders (13%) including rachischisis, spina bifida and meningomyelocoele. This observation is in concurrence with other authors.[5.23] The other associated anomalies include hypoplasia of lungs(5.8%), single umbilical artery(8.7%), diaphragmatic hernia(5.8), malrotation of gut(5.8%),and musculoskeletal defects(11.5%). The present findings are consistent with literature(Table 6).

Table 6: Comparison of associated anomalies with anencephaly

System	Tan et al (1984)[17]	Vare et al (1971)[11]	Nielson et al(2006)[23]	Golali pour et al (2010)[1]	Panduranga et al (2012)[4]	Eslavath et al (2013)[5]	Present study(2015)
Total incidence of CMF	9.4	-	43	42.9	73	77.7	58
Head & neck	No	7.5	14	3.5	2.5	11.1	13
Respiratory System	3	NAD	NAD	NAD	2.5	NAD	17.3
CVS	3	7.5	4.75	1.7	14.5	33.3	13
GIT	29	32	NAD	5.3	14.5	22.2	13
Renal	3	27	12	3.5	NAD	NAD	11.5
Musculo-skeletal	20	14.5	16.5	8.9	14.5	11.1	10.1
Genital	NAD	5	NAD	NAD	12	NAD	1.4
Diaphragmatic hernia	NAD	5 2cases	2.3	NAD	1	NAD	5.7 4cases

NAD= No anomaly detected

In USA, the prevalence of anencephaly was highest among Hispanic births, followed by non-Hispanic white births, with the lowest prevalence among non- Hispanic black births. Considering the parental ethnicity, the prevalence of anencephaly was 12, 16, and 7 per 10000 in Fars, Turkman, and Sistani ethnicity in Northern Iran.[1] The race specific incidence of anencephaly was 7.6/10000 live births in Malaya population , higher than 5.5/10000 in the Chinese . The difference in races and ethnicities could possibly suggest role of dietary factors and a genetic disposition.

In support of dietary deficiency, it was noticed that , there was a decline in anencephaly after starting the fortification program in South Africa, USA, Canada and Iran .[1] In Singapore, the decline was from 0.54/1000 in 1993 to 0.32/1000 in 2002.[17] Significant decline in anencephaly was observed among Hispanic births and non-Hispanic white births after fortification.[1]

Therefore the major thrust of primary prevention of NTDs has been on nutritional supplementation with folic acid apart from controlling the maternal diseases like diabetes and avoiding medications. Role of 0.4 mg of periconceptional folic acid leading to reduction in NTDs was demonstrated by Medical Research Council Vitamin study,[24] and also by Kulkarni *et al*. in India.[9] Currently there is no national program for primary prevention of NTD in India. National anemia prevention program provides 0.5 mg of folic acid along with 100mg of elemental iron from third month of pregnancy. The recent National Family Health Survey (NFHS-3) [26] revealed that about 44% of pregnant women sought antenatal care after 16 weeks of gestation as observed in our study as well. Thus only a small percentage of women receive Periconceptional folic acid supplementation.[4] Fortification of flour in India is not uniform; it varies from state to state with highest percentage in Gujarat. The benefit of fortification of flour still needs to be established in India.

In the present study also anencephaly was more commonly seen in mothers belonging to low socioeconomic class (62.2 %.) as compared to 4.3% in upper class estimated according to Kuppuswamy's socioeconomic scale 2012. However illiteracy could not be diagnosed as a relevant parameter as anencephaly was present with equal incidence of 17.4% in illiterates and graduates respectively. No association with consanguinity could be noted as consanguineous marriages are not common in India.

Anencephaly can be diagnosed as early as 11-14 weeks of gestation by USG and by measuring the values of serum alpha feto protein level in maternal blood. A high prenatal detection rate (100%) for anencephaly was reported from the Czech republic for anencephaly.[1] However in a developing country like India, sensitization is required for pregnant females to get antenatal check-up as soon as possible.

Conclusions

Better knowledge of unexpected fetal loss is the promise for better parental counselling and for prevention of recurrences. Understanding and identifying the risk factors associated with anencephaly in our population, allows approaches to avoid them and thereby lower the incidence of anencephaly in our population. Prenatal screening in a tertiary care hospital is of utmost importance to rule out CMF. 1st trimester antenatal check up of mothers should be made mandatory. To prevent NTD, dietary supplements should be provided to low socioeconomic pregnant females. Peri-conceptional and 1st trimester folic acid supplementation is of prime importance.. There should be obligatory reporting of all CMF all over the country to assess the incidence accurately. Autopsy is the gold standard to document the incidence, possible causes and associated systemic anomalies.

Table 7: Comparison of anencephaly & its various parameters with available literature

Authors	Live Births	Fetal Autopsy	Incidence Of CMF	Incidence of NTD	Incidence of anencephaly	Mothers age	Parity	Sexual difference (M/F)
Eslavath et al (2013)		103	34cases 33%	17cases 50% of CMF	9cases 13.8%	20-29yrs	P(55.5%) G2(33.3%) G3(11%)	5:4
Paduranga et al (2012)		41	-	-		19-28yrs	P(48.5%) G2(10%) G3(31.5%) G4(10%)	27:9:A
Golailipour Et al (2010)	49534		-	2.8/1000	1.2/1000 Prevalence 12/10000	1.31/1000 >35yrs Not significant		27:29
Nielsen et al (2006)		1984	-	4.9%	2.1%	-	-	51:46
Mahadevan et al (2005)	54738			5.7/1000	1.8/1000	80% in 21-30 yrs	P-40.6%	0.6:1

Tan et al (1984)	171773				0.54/1000	25-29yrs	P(41%) G2(24.7%) G3(21.5%) G4<(13%)	1.38:1
Coffey et al (1957	23000				5.9/1000	30-34yrs	>Primigravida	1:4.2
Present Study	18744	520	36% of autopsy	22.1% Of autopsy	6.1/1000	20-25yrs	P(37.6%) G2(28.9%) G3(23%) G4<(8.6%)	34:35

P=Primigravida;,G=Gravida, M=male, F=female, A:=ambigious

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Table 1:Annual Incidence of anencephalic births in hospital

Year	Total no. Of births	No. of fetal autopsies	Total CMF	Total NTD'S	Anencephalic births
2011 Aug-Dec	2386	54	25	12	5
2012	5728	179	77	45	23
2013	6200	198	50	32	25
2014	4430	88	35	26	16
Total	18744	520(2.77%)	187(1%)	115(0.6%)	69(0.4%)

Table 2: Frequency of anencephaly in relation to maternal age

Maternal age	No. of cases (%)
<20 yrs	1(1.4%)
20-25yrs	37(54.4%)
26-30yrs	24(35.2%)
31-35yrs	6(8.8%)
>35yrs	zero

Table 3: Frequency of anencephaly in relation to Gestational age

Gestational age	Total No(%)
11-15 wks	11(15.9%)
16-20 wks	46(66.6%)
21-25wks	9(13%)
26-30 wks	3(4.3%)

Table 4: Systemic anomalies associated with anencephaly

SYSTEM	Associated anomalies (No. of cases)
C.N.S	craniorachischisis (20) , Spina bifida (4), meningomylocoele (1)
Head and Neck	cleft lip (2), Micrognathia with webbed neck, dysmorphic pinna (1), low set ears(5), single nostril (1)
Respiratory	B/L Hypoplastic lungs (2), right lung hypoplasia (8), Bilobed right lung (2)
Cardiovascular	single umbilical artery (6), dextrocardia (2), reversal of heart chambers (1)
GIT	Diaphragmatic hernia (4),malrotation of gut (4), Omphalocele (2), Imperforate anus (1), sigmoid colon opening in ureter (1), common opening of ureter & anus(1)
Skeletal	club foot(3), bilateral polydactyly (2), fused lower limbs (1), scoliosis (1), Simian crease (2)
Genitor-urinary	Absent scortum (1), unilateral kidney(1),horse shoe kidney (1), dilated ureters (bilateral-2, unilateral-1), B/L polycystic kidneys (3)

Table 5 : Frequency of Anencephaly in relation to the socioeconomic status and the mother's education status (Kuppuswamy 's socio-economic status scale)

Status	No of cases (%)	Mothers Education	No. of cases (%)
Lower <5	9 (13%)	Illiterate	12(17.4%)
Upper lower (5-10)	34 (49.2%)	Primary	16(23.2%)
Lower middle (11-15)	12 (17.3%)	Middle	5(7.2%)
Upper middle (16-25)	11 (15.9%)	High	24(34.8%)
Upper (26-29)	3 (4.3%)	Graduate & above	12(17.4%)

Table 6 : Comparison of associated anomalies with anencephaly

System	Tan et al (1984)[17]	Vare et al(1971)[11]	Nielson et al(2006)[23]	Golali pur et al (2010)[1]	Panduranga et al (2012)[4]	Eslavath et al (2013)[5]	Present study (2015)
Total incidence of CMF	9.4	-	43	42.9	73	77.7	58
Head & neck	No	7.5	14	3.5	2.5	11.1	13
Respiratory System	3	NAD	NAD	NAD	2.5	NAD	17.3
CVS	3	7.5	4.75	1.7	14.5	33.3	13
GIT	29	32	NAD	5.3	14.5	22.2	13
Renal	3	27	12	3.5	NAD	NAD	11.5
Musculo-skeletal	20	14.5	16.5	8.9	14.5	11.1	10.1
Genital	NAD	5	NAD	NAD	12	NAD	1.4
Diaphragmatic hernia	NAD	5 2cases	2.3	NAD	1	NAD	5.7 4cases

NAD = No anomaly detected

Table 7: Comparison of anencephaly & its various parameters with available literature

Authors	Live Births	Fetal Autopsy	Incidence Of CMF	Incidence of NTD	Incidence of anencephaly	Mothers age	Parity	Sexual difference (M:F)
Eslavath et al (2013)		103	34cases 33%	17cases 50% of CMF	9cases 13.8%	20-29yrs	P(55.5%) G2(33.3%) G3(11%)	5:4
Paduranga et al (2012)		41	-	-		19-28yrs	P(48.5%) G2(10%) G3(31.5%) G4(10%)	27:9:A
Golailipour Et al (2010)	49534		-	2.8/1000	1.2/1000 Prevalence 12/10000	1.31/1000 >35yrs Not significant		27:29
Nielsen et al (2006)		1984	-	4.9%	2.1%	-	-	51:46
Mahadevan et al (2005)	54738			5.7/1000	1.8/1000	80% in 21-30 yrs	P-40.6%	0.6:1
Tan et al (1984)	171773				0.54/1000	25-29yrs	P(41%) G2(24.7%) G3(21.5%) G4<(13%)	1.38:1
Coffey et al (1957	23000				5.9/1000	30-34yrs	>Primigravida	1:4.2
Present study	18744	520	36% of autopsy	22.1% Of autopsy	6.1/1000	20-25yrs	P(37.6%) G2(28.9%) G3(23%) G4<(8.6%)	34:35

P= Primigravida, G=gravid, M=male, F=female, A= ambigious

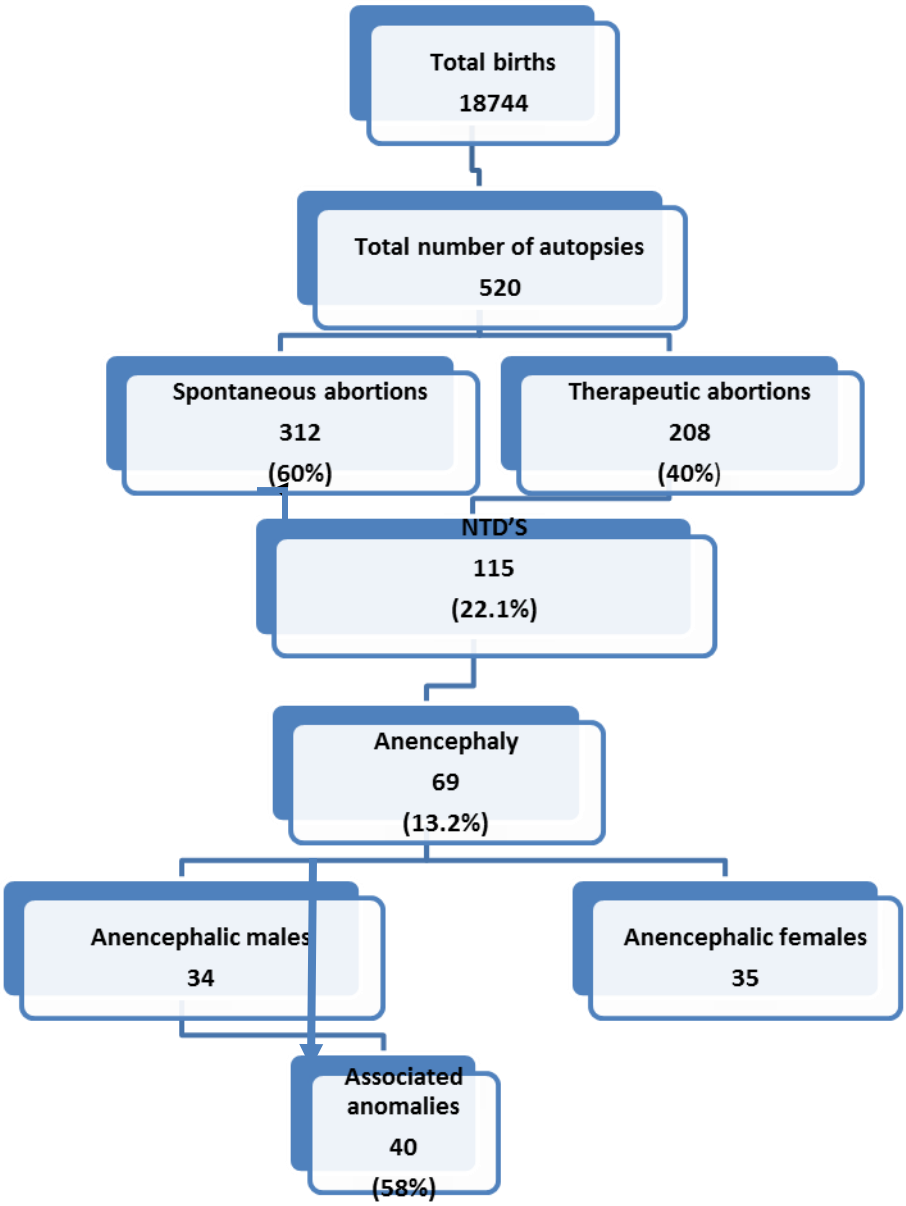

Fig 1:Profile of all autopsy cases

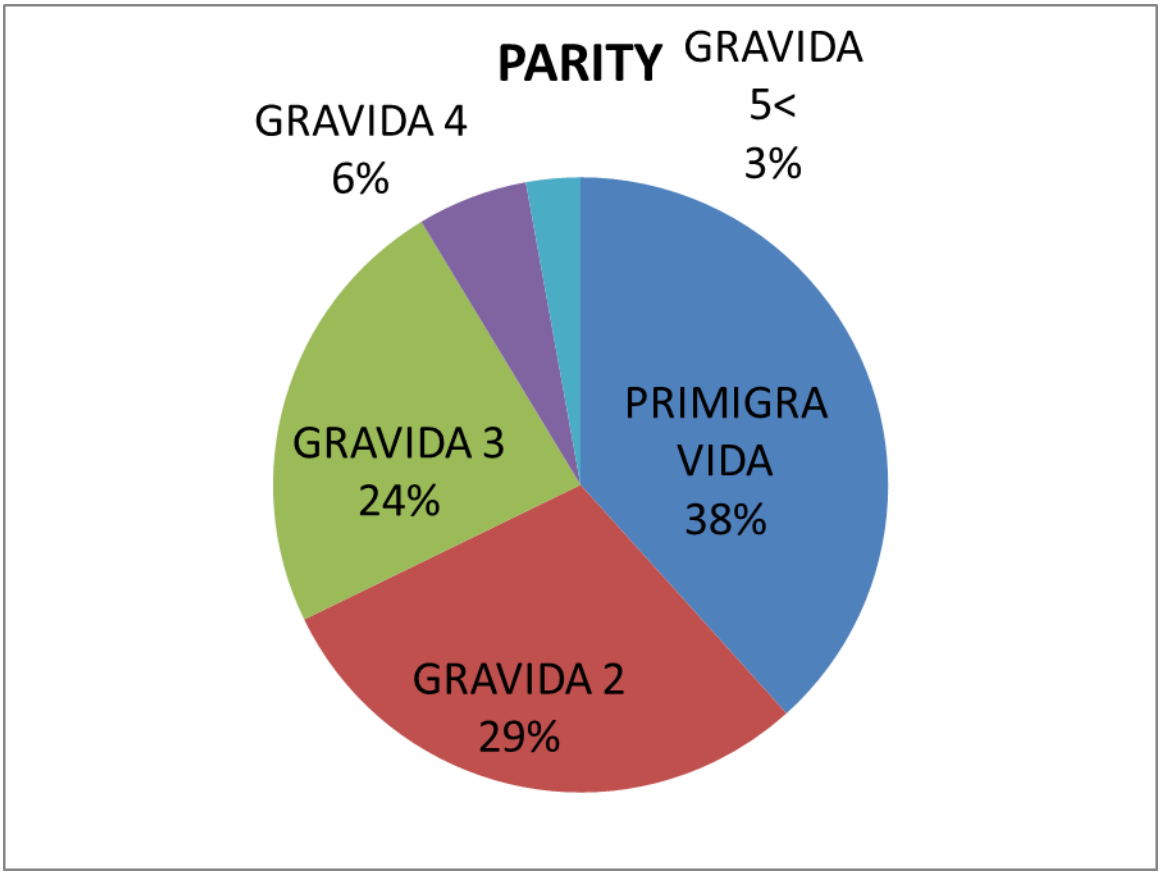

Fig. 2: Frequency of anencephaly in relation to parity

Figures with legends

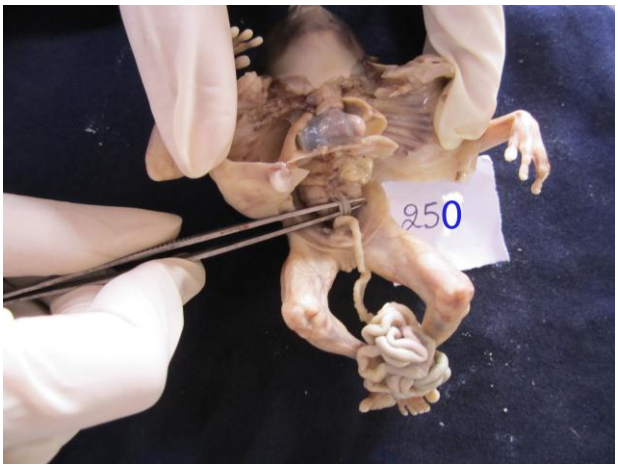

Figure 3: Anencephaly with uro-genital disorders (Horse shoe kidney, bilateral dilated ureters and sigmoid colon opening in urinary bladder)

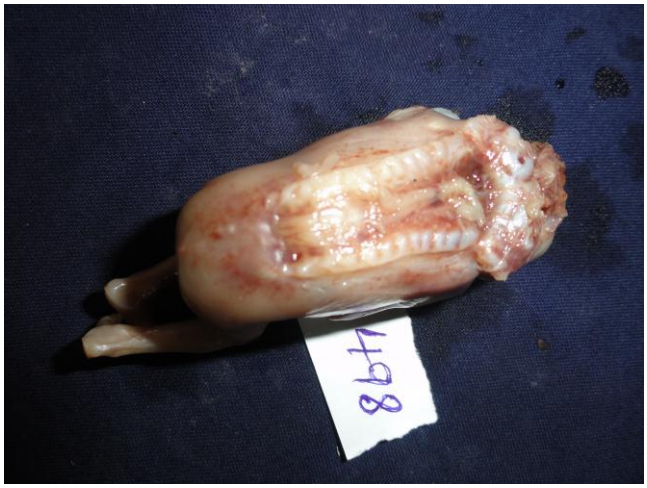

Figure 4: Anencephaly and craniorachischisis

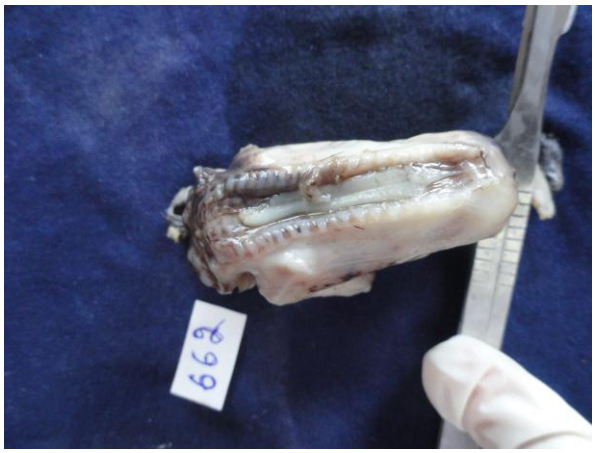

Figure 5: Anencephaly with open spinal cord

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Figure 6: Anencephalic fetus with toad face and single nostril (Proboscis)

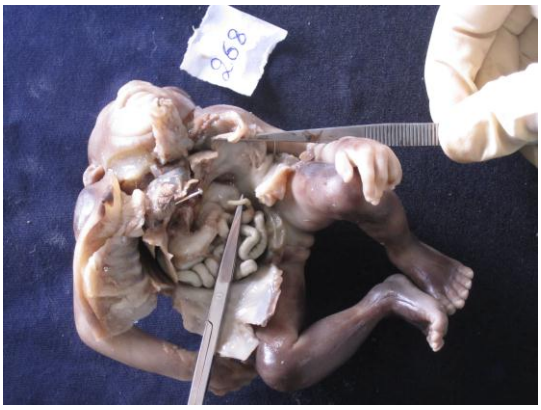

Figure 7: Anencephaly with situs inversus

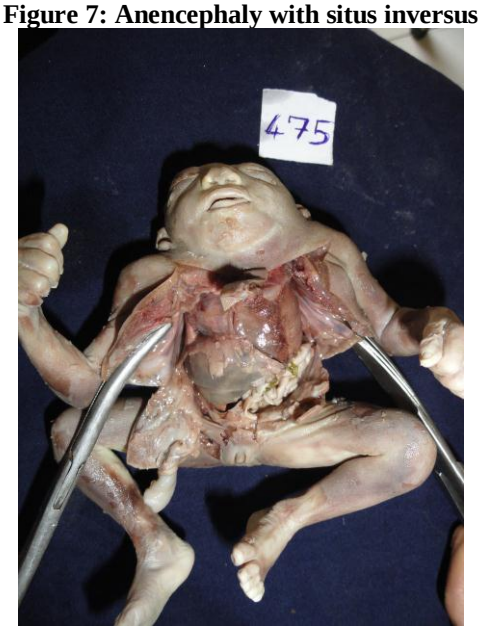

Fig 8: Anencephaly with dextrocardia and diaphragmatic hernia

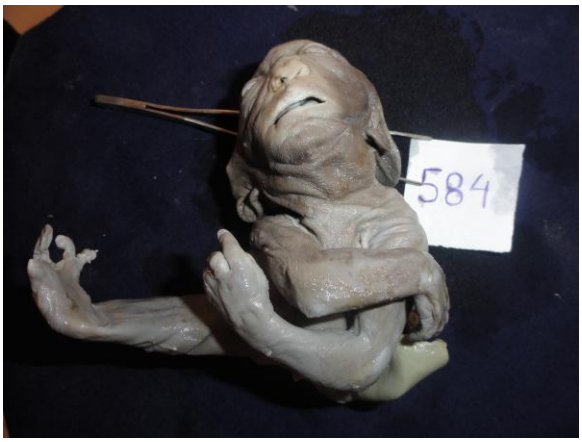

Figure 9: Anencephaly with fused lower limbs