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Original Research Article

# Incidence of associated systemic anomalies in foetuses with neural tube defect in Uttarakhand population

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## Abstract

**Background:** Uttarakhand is a hilly area and females from the interior region are illiterate agricultural laborers. Pregnant females of these distant areas cannot visit for regular antenatal checkups and have folic acids, iron, and vitamins. These deficiencies may lead to neural tube defects, among which Anencephaly is common. This lethal neural tube defect results in defective closure of the rostral pore of the neural tube. Neural tube defect is associated with other 50% of other systemic anomalies. Most of the studies are ultrasonographic but we identified anencephaly grossly and tabulated all associated systemic anomalies, affected by maternal age, birth order, and sex of the fetus in the Uttarakhand population.

**Materials and Methods:** 21 anencephalic fetuses were collected from the labor room of Government Medical College, Haldwani after permission from the college ethical committee and consent from the guardians of all fetuses, the study was done for the periods of two years, gross features, and systemic anomalies after autopsy, and histological reading was done, fetuses were tabulated according to gestational age and gender. A vigorous maternal history was noted.

**Results:** Out of 21 cases, 11 anencephalic cases have systemic anomalies, maximum female fetuses were associated with skeletal anomalies meningomyelocele, gastrointestinal anomalies followed by polycystic kidney disease mainly observed in primigravida, prevalence more in females less than 20 years or more than 36 years of age, not having previous anencephalic aborted fetus, intake of folic acid and suffering from any diseases.

**Conclusion**: Parenteral counseling and antenatal visits, routine tests, and USG must be advised and folic acid supplements must be provided to pregnant females.

**Keywords:** Anencephaly, Fetal autopsy, Neural tube defects, Polycystic kidney disease.

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## 1. Introduction

Neural tube defects (NTDs) are a group of congenital malformations with an incidence of 1/1000 live births worldwide,[1] causing significant infant morbidity and mortality. They are known to have a multifactorial-polygenic origin with etiology of both genetic factors (70% prevalence) and environmental factors including maternal nutritional deficiency of folic acid in the first term that has a crucial role, a dose of 4 mg folic acid daily for 20 weeks increases red blood-cell folate levels (1000-1400 nmol/L) and reduces the neural tube defect risk,[3] these all factors are important and contributory.[2] NTD can be classified into open or closed types.

(a)-Open NTDs are the most common type of defect which include anencephaly, which occurs due to the defective closure of the rostral pore in the neural tube, absence of cranial vault, and subsequent disruption of the cerebral cortex development with a severely damaged brain another one is (b-Closed NTDs are due to failure of secondary neurulation and are generally confined to the Spinal cord where neural tissue is not exposed. The closed neural tube defects occur post-neurulation and include lipoma with a dorsal defect (lip myelomeningocele, lipomyelocele), especially when a subcutaneous mass is present. Anencephaly is the most severe fetal NTD, it could be noticed during the third or fourth week (day 26 to 28) after conception, leaving the skull bones undeveloped that usually surround the head unformed.[3]

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The different malformations that occurred along with anencephaly include cleft lip, cleft palate, polycystic kidney, spina bifida, simian crease, malrotation of gut, intestinal obstruction, encephalocele, craniorachischisis, esophageal atresia, diaphragmatic hernia, bladder exstrophy, or renal agenesis. The diagnosis of anencephaly can be made either by ultrasound examination or by alpha-fetoprotein test, still, amniocentesis and MRI, and a pathological and physical examination of the abortus are required, among all cases, anencephaly is associated with systemic anomalies[1] many syndromes are also associated with it as Downs syndrome, Meckel–Gruber syndrome (MKS) that is a lethal ciliopathy characterized by the triad of cystic renal dysplasia, occipital encephalocele, and postaxial polydactyly. There are many studies done related to anencephaly and its causes related to maternal factors in many states of India but still no research is notified in the Uttarakhand region, which is more prone to these cases, the reason behind this is pregnant females are not getting the proper investigation and folic acid in during antennal periods. Hence, the proposed study undertaken to assess the incidence of anencephaly cases in Uttarakhand, their deformities, and associated systematic anomalies, both morphometric and histological findings with associated maternal factors are tabulated.

## 2. Materials and Methods

### *2.1. Sample collection process*

This study comprised 74 human fetuses collected from the labor room of the Obstetrics and Gynecology department at Sushila Tiwari Memorial Hospital, Haldwani. Sample size derived (19) as follows-

$$Sample\ size\ = \frac{Z_{1-\alpha/2}{}^2 p(1-p)}{d^2}$$

$Z_{1-\alpha/2}$ = Is standard normal variate (at 5% type 1 error (P< 0.05) S it is 1.96 and at 1% type 1 error (P<0.001) it is 2.58). As in the majority of studies, P values are considered significant below 0.05 hence 1.96 is used in a formula.

p Expected proportion in population based on previous studies and pilot studies.

d = absolute error or precision – has to be decided by the researcher.

So now the sample size

$$= \frac{1.96 \times 1.96 \times 0.05\ (1-0.05)}{0.05 \times 0.05}$$

= 73

This is a retrospective study where all the patients diagnosed with features of NTD by ultrasound or delivered babies with NTD were taken in the study group. Detailed history with all records was taken from pregnant females and recorded as per the Department of Anatomy of Government Medical College, Haldwani format. This is a part of a thesis study done in two years, foetuses were collected for the thesis studies among which this specific study was done for NTD. The fetuses of 10 to 40 weeks were collected with inclusion criteria of spontaneous abortion, intrauterine death, and stillborn fetuses. All received fetuses were preserved in 10% formalin (Ajmani's Method), and embalming was done in the Department of Anatomy with due regard on ethical grounds after seeking permission from the college ethical committee (136-IEC/01/13 and proper written consent from the guardians. Estimation of fetal gestational age was done with the help of hospital records, LMP details given by the pregnant female, and ultrasound reports.

### *2.2. Morphometrical analysis*

During the autopsy, clinical findings, external gross features, internal systemic organs examination, and photography along with histopathology of the tissue were done to confirm the presence of anomalies at the microscopic level also by using hematoxylin and eosin staining.

## 3. Results

During the study, 74 dead fetuses were obtained by therapeutic or spontaneous abortions with neural tube defects among which 21 (28.37%) had only anencephaly and 11 (52.3%) were anencephaly with associated different systemic anomalies. The maternal mean age of presenting 11 females was 28 years (19-38 years), 7 primigravids (63.6%), and 4 (36.36%) multigravida details are tabulated in **Table 1**.

Among 11 cases, 5 (45.5%) were females & 4 (36.3%) males; and 2 were undetermined sex of gestational age between 12 to 34 weeks. Head circumference measured from 8 cm to 24 cm. Extensive antenatal history and all morphometric & histological features of 11 anencephalic fetuses with different associated systemic anomalies (100%) with head circumference ranging from 8 cm to 26 cm, many morphological changes prior and systemic changes after dissection of all 11 fetuses are shown with different associated systemic anomalies (100%) along with anencephaly described in **Table 2**.

**Table 1:** Maternal history

| Case | Age | Gravida | Presenting complaint | Previous T/T history | ANC & Folic acid T/T | Family H/O |
|---|---|---|---|---|---|---|
| 1 | 28 | $G_4P_1A_2$ | ANC for USG | | Negative | h/o anencephalic baby |
| 2 | 19 | Primi | Weakness and decreased fetal movement | Epilepsy, pernicious anemia | Negative | |
| 3 | 32 | Primi | ANC for USG | Hypertension, diabetes, infertility, smoking | Positive | |
| 4 | 35 | $G_5P_1A_3$ | Pain Abdomen | Poor hygiene, poor diet, poor build, | Negative | 2 anencephalic, preterm live birth |
| 5 | 24 | Primi | Routine ANC for USG | Busy schedule, regular alcohol intake, frequent smoking, pernicious anemia | Positive | |
| 6 | 30 | Primi | Vaginal Spotting | Iron deficiency anemia, epilepsy, asthma, infertility | Positive | |
| 7 | 22 | Primi | Weakness, pain abdomen, vaginal spotting | Low BMI, poor diet, | Negative | Husband has Down syndrome, |
| 8 | 28 | $G_3PA_1$ | In labor pains at term | Hypertensive, hyperthyroidism | Positive | Anencephalic fetus, stillborn fetus |
| 9 | 21 | Primi | Decreased fetal movement | High BMI, PCOD, hyperthyroidism, diabetes, infertility | Positive | First-degree relatives have H/o anencephalic fetus |
| 10 | 29 | $G_4P_1A_2$ | Weakness, shortness of breath | Malnourished, anemic, seizures | Negative | 2 Anencephaly, second child died due to pneumonia, congenital limb defect of husband, |
| 11 | 26 | Primi | Regular ANC visit | Alcohol, smoke | Negative | |

### *3.1. Case 1*

A 28-year-old multigravida ($G_4P_1A_2$) presented with 23 weeks 5 days pregnancy for routine antenatal examination with no history of consanguineous marriage and teratogenic drugs, she did not take folic acid in previous pregnancies and current pregnancy, with poor health hygiene, having earlier history of anencephalic fetal abortion. Routine antenatal screening displayed an anencephalic fetus with bradycardia, termination was done. The terminated fetus had excess hairs on the whole body, i.e., lanugo, cleft palate, cleft lip with lobulated tongue in the oral cavity, low set of ears with a short neck, simian crease in left palm, metatarsus adducts with 6 fingers in both lower limbs. Fetal autopsy describes poorly developed cerebrum, cerebellum & brain stem, right lung had 3 fissures with 4 lobes, dilatation of bowel loop leading to intestinal obstruction, right shifting of sigmoid colon, malrotation of the gut, poorly developed genitalia, bilateral dilated cystic kidney.

### *3.2. Case 2*

A termed dead female 34 weeks fetus was delivered by 19 years primigravida, she was on antiepileptic drugs had a complaint of pernicious anemia and never took folic acid, on her first visit to the hospital she complained of weakness and sensed decreased fetal movement antenatal ultrasonography revealed the absence of cardiac activity with oligohydramnios. Termination of pregnancy was suggested, a dead fetus was presenting abnormal spinal curvature, sacrococcygeal soft tissue mass, protrusion of meninges with brain tissue resulting in occipital encephalocele, low set ears with a short neck, cleft lip & palate, witch tooth, crowding of teeth, disproportionately large and protuberant distended abdomen with diffuse subcutaneous edema, bilateral postaxial polydactyly (6 digits) in upper and lower limbs, bilateral talipes equinovarus. Autopsy shows a small-sized heart, bilateral polycystic nephromegaly, agenesis of the urinary bladder, intestinal obstruction, megacolon with intestinal obstruction, enlarged deformed thin liver & spleen, and hypoplastic lungs were present, and underdeveloped genitals. It is Meckel's gruber syndrome with a classical triad of occipital encephalocele, infantile polycystic kidneys, and postaxial polydactyly.

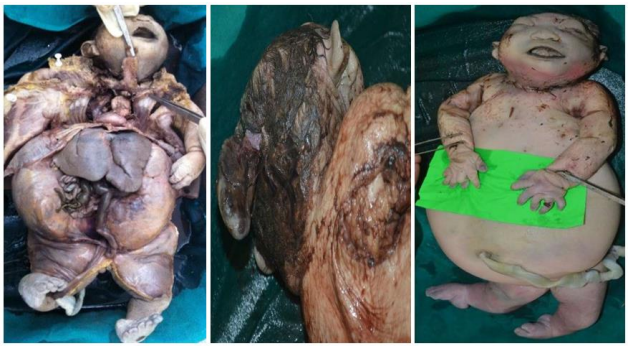

**Figure 1:** Case 2- Polydactyly, Encephalocele, Polycystic kidney- Meckel-Gruber syndrome

**Table 2:** Different associated systemic anomaly with anencephaly

| | A&S | CNS& HC | UL | LL | Heart | Lungs | KUB | Abdomen | Genitalia | Low-set ears & neck | Oral |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F 24 | Anencephaly, 18 cm | Simian crease | Metatarsus adductus With six fingers | Normal | Right lung had 3 fissures with 4 lobes | PKD, nephromegaly (b/l) | Intestinal obstruction megacolon presents malrotation of the gut | Underdeveloped | +nt | Cleft palate, cleft lip with lobulated tongue |
| 2 | F 34 | Anencephaly, 26 cm, occipital encephalocele | Postaxial polydactyly six fingers in both hands | Club foot, six fingers in both leg | Normal | Normal | Cystic dysplasia, nephromegaly (b/l), bladder absent | Intestinal obstruction megacolon presents malrotation of the gut | underdeveloped | +nt | Cleft lip with cleft palate, witch tooth present |
| 3 | M 14 | Anencephaly, 18 cm, Encephalocele defect in the cervical region | Normal | Normal | A single ventricle on the left side, | Normal | short ureter, megacystic bladder | Malrotation of gut | normal | +nt | Cleft palate |
| 4 | Undefined 21 | Anencephaly, 19 cm, occipital encephalocele | Syndactyly 4 metacarpals in the right hand | six Fingers on both legs | Situs inversus | Pulmonary hypoplasia | Absent | Diaphragmatic hernia, malrotation, intestinal obstruction | absent | +nt | Cleft lip with cleft palate |
| 5 | F 18 | Anencephaly,18cm , Craniorachischsis, kyphoscoliosis | normal, simian crease present | Club feet | Normal | left lung had 2 fissures & 3 lobes | Both kidneys were absent | normal | underdeveloped | +nt webbed neck | Cleft palate, presence of witch tooth |
| 6 | M 28 | Anencephaly 22cm, spina bifida present with meningomyelocele | Club hand, simian crease present | Club feet | Absence of tricuspid valve | Normal | Multiple renal arteries +nt with double ureter | Pancreas absent | normal | +nt | Cleft palate with lobulated tongue |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 7 | F 12 | Anencephaly 8 cm, encephalocele | Syndactyly 4 metacarpals in left hand | Metatarsus adductus | Mitral stenosis | Underdeveloped | b/l Polycystic kidney, bladder agenesis | Intestinal obstruction | underdeveloped | +nt | Cleft lip with cleft palate |
| 8 | M 36 | Anencephaly, 25 cm, microcephaly | Postaxial polydactyly six fingers in one and seven in the other hand | Metatarsus varus | Normal | Normal | absent | Intestine absent, hepatomegaly | underdeveloped | +nt webbed neck | Cleft palate with lobulated tongue |
| 9 | M 32 | Anencephaly 19 cm, Cranio-spinalrachischisis | Normal | Normal | Inversion of vessel with Ductus arteriosus | Shifting of trachea, hypoplastic left lung | Normal | Diaphragmatic hernia | Normal | +nt | Cleft palate |
| 10 | Undefined 26 | Anencephaly, 22 cm, meningomyelocele | Clubbed hand | Club feet | Underdeveloped heart | Compressed | Absent | Diaphragmatic hernia, Intestine obstruction, hepatomegaly | Absent | +nt stretched backward, webbed | Cleft palate |
| 11 | F 14 | Anencephaly, 12 cm Spina Bifida | Normal | Clubbed feet | Ventricular septal defect | Hypoplastic lung | Multiple renal arteries | Normal | Normal | Webbed neck | Normal |

*3.3. Case 3*

Absent cardiac activity in 14 weeks was noticed during a routine ultrasound of the second trimester in 32-year primigravida presented with a history of hypertension, and diabetes. She was earlier on infertility treatment from two years ago and has, a positive history of frequent smoking. She visits hospitals regularly and takes folic acid & vitamins. An aborted male fetus presenting with an encephalocele extended up to the cervical region, extended neck, and cleft palate after dissecting the thoracic area heart appeared with a single left ventricle and two outlets (aorta & pulmonary trunk), short ureter with mega cystic bladder and malrotation of the gut.

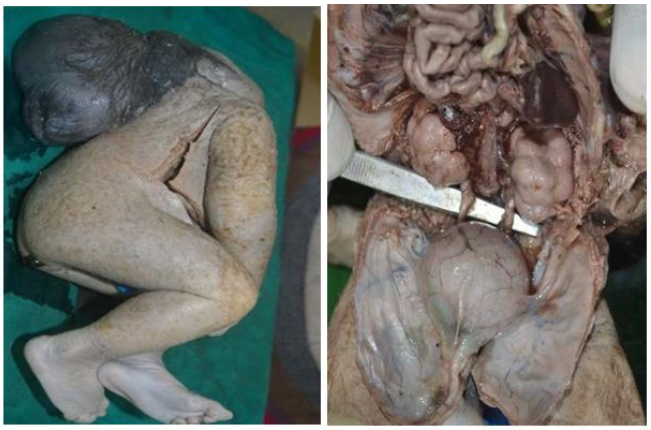

**Figure 2:** Case 3-Occipital encephalocele having defect in cervical region

*3.4. Case 4*

35-year multigravida ($G_5P_1A_3$) with a previous history of two anencephalic fetal abortions and a preterm (26 weeks) live birth, poor hygiene, never took folic acid in any of her pregnancy ever. Being a farmer, she had to work all the time on the farms with less rest, she was not on a proper diet such as good iron, protein, vitamins & minerals, and her physique was lean and thin. She complained of abdominal pain and was admitted to the hospital, where she delivered 21 weeks anencephalic fetus of undefined gender presenting with encephalocele, syndactyly 4metacarpals on the right side, bilateral 6 toes, low set ears with cleft lips, and cleft palate. Autopsy reveals congenital diaphragmatic hernia with thin and compressed hypoplastic lungs, situs inversus, KUB region & genitalia not developed, malrotation, and obstruction of the gut. Histology of the lungs determines that the lung area is not mature enough as per fetal age, the absence of cartilage and alveolar bronchus represents a canalicular stage of the lungs which is suggestive of 16 to 26 weeks gestational age.

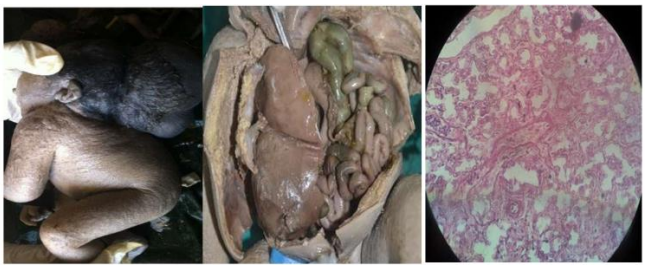

**Figure 3:** Case 4-occipital encephalocele, Diaphragmatic hernia, LUNG H&E X600

*3.5. Case 5*

A 24-year well-educated primigravida was living alone and shifted to Haldwani for some project work. She has a very hectic work schedule with a history of regular smoking and alcohol intake. She was already on treatment for pernicious anemia. She is aware of the importance of antenatal visits, ultrasonography, and folic acid & vitamin B12 intake, she is doing it all properly. During her routine antenatal visit her USG report depicted an 18-week anencephalic fetus. The consultant suggested abortion after the autopsied fetus exhibited cranio-spinal-rachischisis, extended up to the lumbar region, kyphoscoliosis, simian crease with club feet, webbed neck, cleft palate with witch tooth, left lung had 2 fissures & 3 lobes absence of both kidneys, underdeveloped genitals.

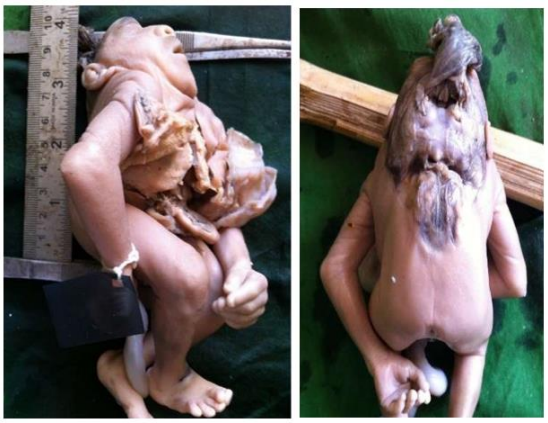

**Figure 4:** Case 5- Cranio-spinalrachischisis

*3.6. Case 6*

30-year-old obese, anemic (iron deficiency) primigravida was on folic acid and vitamin supplements, admitted with a complaint of vaginal spotting, she was already getting treatments for epileptic, asthma, and infertility. A dead anencephalic male fetus of 28 weeks was delivered presenting with spina bifida with meningomyelocele, Club hand & feet, simian crease on the right hand, low set of ears with webbed neck, cleft palate with lobulated tongue, on autopsy tricuspid valve was absent, multiple renal arteries were present with double ureter and absence of pancreas.

**Figure 5:** Case 6-Meningiomyelocele with multiple renal arteries

*3.7. Case 7*

7-22 weeks primigravida, being a wife with a Down syndromic husband belonging to low socio-economic status with low BMI appearing pale and feeling weakness, after taking a detailed history on her diet, she said that she has never been for an antenatal checkup and not had folic acid and vitamins, she was not taking protein, vitamin, and iron-rich diet regularly. During working on the field, she slipped and presented with pain abdomen with vaginal spotting, an anencephalic dead fetus was delivered in the labor room with encephalocele, syndactyly of 4 metacarpals in left-hand metatarsus adducts, webbed neck with cleft lip with cleft palate during autopsy mitral stenosis, both lungs were underdeveloped Polycystic kidney was noticed. Renal histology shows marked multiple dilatations of the vesicle, loss of the parenchymal tissue replaced by cystic dilatation, and few fibrous tissues in between multiple cysts of various sizes, less developed, degenerating glomeruli with ill differentiated medulla, bladder agenesis, intestinal obstruction, and underdeveloped genitalia.

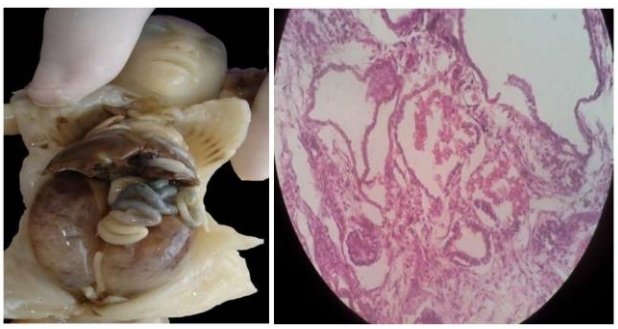

**Figure 6**: Case 7-(b/l) Polycystic kidney, bladder agenesis

*3.8. Case 8*

A 28-year third gravida ($G_3P_1A_1$) with a previous history of aborted 22 weeks anencephalic fetus, was on folic acid but had a history of raised blood pressure and hyperthyroidism treatment, presented at 36 weeks of gestation in labor in the emergency. Her previous pregnancy was uneventful with a 3-year-old male baby after that she delivered a stillborn male fetus. Aborted anencephalic fetus revealed many gross features such as protruding eyes, oral cavity with cleft palate, two incisor teeth and lobulated tongue, postaxial polydactyly with six fingers in left & seven in right, metatarsus Varus, low-set ears with webbed neck. On dissecting it thoroughly microcephaly was visible, the forebrain has a thalamus, but the cerebrum and cerebellum were absent, genu was developed in the corpus callosum & partially developed brainstem, the whole abdomen is covered by an enlarged liver with a lacking intestine, even both the kidneys along with ureter and bladder were absent.

*3.9. Case 9*

A 21-year primigravida at 21 weeks gestational age of high BMI (>40, obese) presented with a complaint of decreased fetal movements and also gave a positive history of diabetes, hyperthyroidism, polycystic ovarian disease, history of the fetus with neural tube defect in first degree relative earlier and undergone the infertility treatment previously and she was consuming folic acid and vitamins regularly. She was suggested for USG, and the radiologist reported an anencephalic fetus. On external examination of the fetus, lanugo hairs were present, cleft palate in the oral cavity, broad nose, folded ears, swollen eyelids, and cranio-spinalrachischis extended up to the thoracic region. In autopsy brain tissue was in a closed sac, cerebrum, and brainstem were absent while the cerebellum was underdeveloped. Diaphragmatic hernia resulted in inversion of a vessel with ductus arteriosus, shifting of the trachea, hypoplastic left lung, and intestinal obstruction with malrotation of the gut.

**Figure 7:** Case 9 diaphragmatic hernia

*3.10. Case 10*

A 29-year multigravida ($G_4P_1A_2$) at 26 weeks of gestation presented in OPD for the first time, she was malnourished, her hygiene was deplorable, anemic, never took folic acid & vitamins, with a positive history of seizures but never took any treatment for that, the previously 2 aborted fetuses were anencephalic, the third child died due to pneumonia at the age of 8 months the husband has congenital limb defect (polydactyly). During physical examination she complained of weakness and shortness of breath for 2 days, the consultant did not detect fetal movement, and she underwent

sonography that is suggestive of an anencephalic fetus with polyhydramnios and absent cardiac activity. The aborted fetus manifested external gross external features were a toad face with protruding eyes, a flattened nasal bridge, a cleft palate, a very short webbed and backward stretched neck, a meningomyelocele extended to thoracic region clubbed hand with feet. After dissecting it revealed an underdeveloped genitourinary system, a diaphragmatic hernia resulting in compression of the lungs, and an underdeveloped heart, the enormously enlarged liver was covering half of the lower abdomen and obstructing the intestine. Histology of the liver depicts the distortion of cytoarchitecture, unclear demarcation of the hepatic and portal lobule, hepatocytes not arranged in a radiating manner, reduction in the number of central veins and portal triad, sinusoid was more dilated, fibrous tissue appeared around the central vein and hematopoietic cells had been reduced considerably.

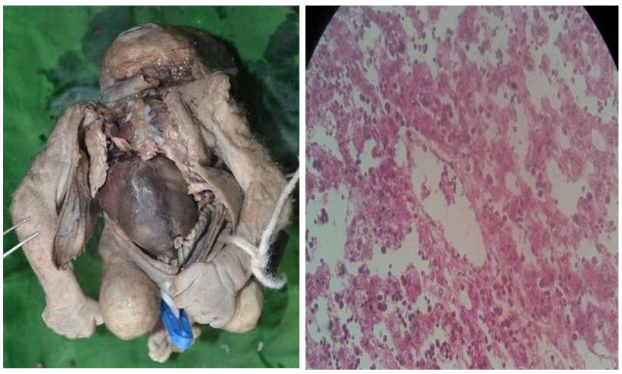

**Figure 8:** Case 10- undefined gender, PKD-polycystic kidney disease, LIVER H &E X600 dilated Sinusoids with deranged hepatocytes and presence of fibrous tissue

*3.11. Case 11*

26-year-old primigravida with a history of regular smoking and alcohol consumption presented on regular antenatal checkup with a sonographic report of congenital anomaly, abortion done on consent and fetus manifested anencephaly with spina bifida, frog eyes, webbed neck, clubbed feet, death mainly due to severely compressed hypoplastic lungs, ventricular septal defect. Doctors had prescribed folic acid and vitamins, but she never took any of these supplements.

**Table 3:** Incidence of anencephaly according to maternal age, parity, and gender difference by following studies

| Authors | Fetal Autopsy | Incidence Of CMF | Incidence of NTD | Incidence of anencephaly | Mothers age | Parity | Sexual difference (M/F) |
|---|---|---|---|---|---|---|---|
| **Present study** | 250 | 74 | 21 | 11 | 19-38 Years | P(63.6%) G(36.3%) | 4:5:2 |
| Rashmi[15] (2023) | | | | 6.5/1000 | 21-35 Years | P(66.66%) G2(16.66%) G3 (16.66%). | 8:2 |
| Chandan[16] (2022) | 500 | 30% | 14% | 25/500 | 20-39 years | P-57.1% G(2,3)-42.9% | 49:51 |
| Singh[8] (2015) | 520 | 36% of autopsy | 21% of autopsy | 6.1/1000 | 20-25 years | P(37.6%) G2(28.9%) G3(23%) G4<(8.6%) | 34:35 |
| Eslavath[14] (2013) | 103 | 34cases 33% | 17 cases 50% of CMF | 9cases 13.8% | 20-29yrs | P(55.5%) G2(33.3%) G3(11%) | 5:4 |
| Paduranga[13] (2012) | 41 | | | | 19-28 yrs | P(48.5%) G2(10%) G3(31.5%) G4(10%) | 27:9:A |
| Golailipour[7] (2010) | | | 2.8/1000 | 1.2/1000 Prevalence 12/10000 | 1.31/1000 >35yrs Not significant | | 27:29 |
| Nielsen[12] (2006) | 1984 | | 4.9% | 2.1% | | | 51:46 |

**Table 4:** Comparison of involvement of systemic pathological parameters done in a previous study with the present study system

| System involved | Neilsen[12] (2006) | Golalipour[4] (2010) | Panduranga[13] (2012) | Eslavath[14] (2013) | Singh[8] (2015) | Rashmi[15] (2023) | Present study |
|---|---|---|---|---|---|---|---|
| Total anomaly | 43 | 42.9 | 73 | 77.7 | 58 | 100 | 74 |
| Anencephaly | 14 | 3.5 | 2.5 | NAD | 13 | 83.3 | 21 |
| Respiratory | NAD | NAD | 2.5 | 11.1 | 17.3 | NAD | 7 |
| Cardiovascular | 4.75 | 1.7 | 14.5 | 11.1 | 13 | NAD | 6 |
| GIT | NAD | 5.3 | 14.5 | 33.3 | 13 | 66.6 | 10 |
| Skeletal | 16.5 | 8.9 | 14.5 | 22.2 | 10.1 | 50 | 11 |
| Renal | 12 | 3.5 | NAD | 14.5 | 11.5 | 33.3 | 10 |
| Genital | NAD | NAD | 11.1 | 11.1 | 1.4 | NAD | 7 |
| Diaphragmatic Hernia | 2.3 | NAD | 1 | NAD | 5.74 | NAD | 3 |

## 4. Discussion

The incidence of anencephaly varies in different countries, In India, a study by Cherian[5] showed that the incidence rate is 6·57–8·21 per 1000 live births. A vast hospital-based study has shown results that 60 % of spontaneous abortions & were clinically aborted, 36% were congenitally malformed with 61.4% NTD,[6] and 0.12% incidence in India was noted.

The prevalence of anencephaly (**Table 2**) is more in mothers of age below 20 and above 35,[6] whereas our study depicts that the mean maternal age was 28 years [21–35], among spontaneous abortion and stillborn fetuses, female cases were leading with a male by gestational age of 14–36 weeks with a ratio of 1.38–1.[6,8] NTD is commonly seen in females (**Table 3**) were not on folic acid and vitamins with poor hygiene, are undernourished have any treatment for any condition like epilepsy, diabetes, or hypertension, or are on infertility treatment while the multigravidas show positive abortion history of neural tube defect, few researched it also favors race or ethnicity; gravidity, and history of previous cesarean delivery, Missing values for gravidity (34,694) livebirths (24,276) late prenatal care (227,769), cigarette use (46,572), body mass index (222,916), hypertension (6280), diabetes mellitus (6280), history of preterm birth (6280), infertility treatment (6280).[9]

Typical features of anencephaly such as acrania (absence of skull), acephaly (absence of head), and microencephaly, and associated with anomalies of different systems (**Table 4**). Spina bifida is the most common anomaly associated with anencephaly[12] and the second most common is GIT (intestinal obstruction of megacolon and malrotation of the gut) included with cleft palate, lobulated tongue, witched teeth.[14]

Although congenital heart diseases are the most common birth defects and the leading cause of infant death worldwide after Kidney, mostly polycystic kidney disease, ureter, and bladders had gross histological alterations in comparison to normal foetuses,[10] while skeletal and GIT cases are maximum in our case then-after kidney and genitals. Group of multiple anomalies due to altered Gene frequency in Meckel's syndrome is approximately 0.028 among Hindu parents of Gujarat State in India, we also determined one case of Meckel's Gruber with almost all systems involved. Studies on 67 cases depict the constant typical triad of large polycystic kidneys (100%), occipital encephalocele (90%i), and postaxial polydactyly (83.3%),[10] both males and females are affected equally with a recurrence rate of 1 in 4 (25%) and the mortality rate is 100% while it may be overcome by oral folic acid supplementation, or dietary folate intake in-addition with a multivitamin/micronutrient supplement, choline-rich foods (meat, egg yolk), lower rates of neural tube defects and other congenital heart and urinary tract defects, oral facial clefts, and limb-reduction anomalies (*high*) and obstetrical complications. If women (12–45 years) considering a pregnancy about the benefits of taking an oral daily multivitamin, 2.6-µg dose of vitamin $B_{12}$ containing folic acid (0.4–1.0 mg) to optimize serum and red blood cell folate levels (*strong, high*), in obesity & high risk (positive previous or first degree relatives) dose may be increased up to five times as required*)*, she should take a folic acid supplement containing the recommended dosage for women at *increased risk* (4–5 mg).[17]

## 5. Conclusion

Anencephaly is a neural tube defect (NTD) that is due to defective closure of cranial neuropore in multigravida mostly poor and undernourished females with previous abortive fetuses of neural tube defect, having genetic anomalies, unable to visit for health checkups and not taking folic acids & vitamins, overaged primigravida are undergoing some treatments in Uttarakhand region. Most cases were diagnosed through ultrasound and were advised for medical termination of pregnancy. In our comprehensive study of 74 cases, 21 were determined with anencephaly, 11 cases were associated with systemic anomalies, bulk cases were of skeletal anomalies followed by GIT & renal anomalies, and a rare anomaly "Meckel's Gruber Syndrome" lethal condition was noticed. Nevertheless, caution is advised and better

knowledge of unexpected fetal loss, parental counseling, and prenatal screening done for prevention of recurrences, females must be advised for routine antenatal checkups and proper intake of folic acids and vitamins. Further research, particularly considering maternal history as a potential confounder, is warranted to enhance our understanding of the complex interplay between maternal history and neonatal outcome.

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## 7. Conflict of Interest

None.

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