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*Original Research Article.*

# Demographic Factors, Autopsy Findings and Syndrome Diagnosis in Congenital Anomalies with Imperforate Anus

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## ABSTRACT

**Introduction:** Imperforate anus is a relatively rare birth defect in which rectum is malformed. Cases of isolate imperforate anus exist, but most commonly, this condition is found as a part of syndromes and congenital anomalies. Therefore, we conducted a prospective fetal autopsy study to know the association of imperforate anus in congenital anomalies, analyse the demographic factors and correctly diagnose the syndromes.

**Materials and Methods:** Perinatal deaths with congenital anomalies over a period of 1 year at our institute were included in the study. Standard protocol for autopsy was followed in each case. External examination and anthropometric measurements were carried out. Autopsy was conducted according to Virchow's technique by giving a modified "Y" shaped incision starting from below the ears to symphysis pubis encircling umbilicus on the left side. Both thorax and abdomen were opened. Internal examination including viscera was done and samples were collected for histopathological examination. Results were noted and analysed.

**Results:** Out of the 57cases with congenital anomalies, 9 cases were found to be associated with imperforate anus which included VACTERL anomaly with Prune Belly syndrome, Edward's syndrome, Fraser syndrome, OEIS complex (2 cases), Ellis-Van-Creveld syndrome, TRAP baby and Gastroschisis (2 cases).

**Conclusion:** Autopsy has an important role in the diagnosis of syndromes and associations with imperforate anus. Our study also pointed at the contribution of demographic and maternal risk factors towards these syndromes.

**Keywords:** Imperforate Anus, Edward's Syndrome, Fraser Syndrome, Ellis-Van-Creveld Syndrome, Gastroschisis, OEIS Complex, TRAP Baby, VACTERL Association.

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## INTRODUCTION

Imperforate anus is a congenital anomaly with an incidence of 1:1500 to 1:5000 in newborns.[1] It can be found as an isolated anomaly or as a part of several syndromes. Usually imperforate anus is not diagnosed until birth. It's prenatal diagnosis is difficult but maybe assisted by ultrasound detection of a dilated bowel or rectum. Defects range from the very minor or easily treatable abnormality with excellent functional prognosis to those that are complex and difficult to manage having very poor outcome. With early diagnosis, management of associated anomalies and efficient meticulous surgical repair, patients have the best chance for a good functional outcome.

## MATERIALS AND METHODS

This study comprised of a perinatal autopsy series of cases with congenital anomalies over a period of 1 year at the Pathology Department of S.C.B. Medical College, Cuttack. A prospective study was conducted after ethical clearance by the institute committee. The clinical and radiological data were documented.

External examination like hair, ear lobes, cleft lip, cleft palate, nail bed, nipples, chest, abdomen, spine, fingers & toes, talipes equinovarus, talipes equinovalgus, genitalia and anus were looked for. Anthropometric measurements like weight of baby, crown rump length (CRL), crown heal length (CHL), head circumference (HC), chest circumference (CC), foot length (FL) were recorded.

Virchow's technique of autopsy was followed starting with modified "Y" shaped incision from both mastoid process down to symphysis pubis and encircling umbilicus on left side. After reflecting skin, fascia and muscle coats, internal organs were exposed and grossly examined for any abnormality. Samples were collected for histopathological examination.

**Table 1: Gestational age and sex of anomalous cases**

| Anomalies/syndromes | Gestational age (in weeks) | Sex of foetus |
|---|---|---|
| **1.VACTERL ANOMALY with Prune Belly syndrome** | 28 | Ambiguous genitalia |
| **2.Trisomy18(EDWARD'S syndrome)** | 32 | Ambiguous genitalia |
| **3.Fraser syndrome** | 26 | Male |
| **4.OEIS complex** | 28 | Ambiguous genitalia |
| **5.OEIS Complex** | 26 | Ambiguous genitalia |
| **6.Ellis-van-Creveld syndrome** | 32 | Ambiguous genitalia |
| **7.TRAP baby** | 28 | Female |
| **8.Gastroschisis** | 22 | Ambiguous genitalia |
| **9.Gastroschisis** | 28 | Ambiguous genitalia |

**Table 2: Distribution of reproductive factors for mothers**

| Anomalies | Maternal age (in years) | Number of previous births | Previous miscarriage | Outcome of index pregnancy | Multiple births in index pregnancy |
|---|---|---|---|---|---|
| **1.VACTERL anomaly** | 37, Second gravida | 1 | 0 | Stillbirth | 0 |
| **2.Trisomy 18** | 36, second gravida | 1 | 0 | Stillbirth | 0 |
| **3.Fraser syndrome** | 28, Primi | 0 | 0 | Stillbirth | 0 |
| **4.OEIS complex (1)** | 42, Fifth gravida | 2 | 1 | Stillbirth | 0 |
| **5.OEIS complex (2)** | 38, Primi | 0 | 0 | Stillbirth | 0 |
| **6.TRAP baby** | 22, Primi | 1 | 0 | Termination of pregnancy | Twins-one normal one stillborn |
| **7.Ellis-Van Creveld syndrome** | 36,primi | 1 | 0 | Stillbirth | 0 |
| **8.Gastroschisis (1)** | 23, Primi | 0 | 0 | Stillbirth | 0 |
| **9.Gastroschisis (2)** | 35, Primi | 0 | 0 | Stillbirth | 0 |

**Table 3: Maternal risk factors**

| Cases | Obesity | Iron and folate intake | Compliance to ANC | Socio-economic status | Diabetes |
|---|---|---|---|---|---|
| **1.VACTERL anomaly with Prune Belly** | Yes | Yes | Regular | Low | No |
| **2.Trisomy 18** | Yes | No | No | Low | No |
| **3.Fraser syndrome** | Yes | yes | Regular | Low | No |
| **4.OEIS complex** | Yes | No | No | Upper-middle | No |
| **5.OEIS complex** | Yes | No | No | Low | No |
| **6.TRAP baby** | No | Yes | Irregular | Low | No |
| **7.Ellis-van Creveld syndrome(EVC)** | No | Yes | Regular | Low | No |
| **8.Gastroschisis** | No | Yes | Irregular | Low | No |
| **9.Gastroschisis** | Yes | No | Irregular | Low | No |

**Table 4: Anthropometric measurements**

| Anomalies | Body weight (in kg) | CRL (in cms) | CHL (in cms) | HC (in cms) | CC (in cms) | FL (in cms) |
|---|---|---|---|---|---|---|
| **1. VACTERL with Prune Belly** | 2.4 | 24 | 41 | 29 | 30 | 6 |
| **2. Trisomy 18** | 2.5 | 26 | 43 | 22 | 23 | 5.5 |
| **3. Fraser syndrome** | 1.45 | 30 | 44 | 29 | 31 | 5.8 |
| **4. OEIS complex** | 2.6 | 23 | 37 | 31 | 22 | 6 |
| **5. OEIS complex** | 2.45 | 23.5 | 36 | 30 | 23 | 5.2 |
| **6. TRAP baby** | 1.75(AGA) | | | - | 33 | 4.5 |
| **7. EVC** | 900gms(SGA) | 28 | 37 | 30 | 27 | 5 |
| **8. Gastroschisis** | 2.2 | 13.5 | 28.5 | 21.5 | 14 | 4.5-R 3.5-L |
| **9. Gastroschisis** | 2.4 | 24 | 30 | 20.5 | 15 | 4.0-R 3.6-L |

EVC-Ellis Van Crveld Syndrome, CRL- Crown-rump length, CHL- Crown-heel length,
HC-Head circumference, CC-Chest circumference, FL-Foot length

## RESULTS

Out of the 57 cases with congenital anomalies, 9 cases were found to be associated with imperforate anus. As imperforate anus was found in conjunction with other anomalies also, they were compiled into certain conditions and syndromes. These associations included VACTERL anomaly with Prune Belly syndrome, Edward's syndrome, Fraser syndrome, OEIS complex (2 cases), TRAP baby, Ellis-Van-Creveld syndrome, and Gastroschisis (2 cases). The common gestational age was 26-28weeks (Table 1). Ambiguous genitalia were found in most (7.7% cases) except TRAP baby which was a female and Fraser syndrome which was a male. All were stillborn. In TRAP baby, there was termination of pregnancy, one baby was normal and other was stillborn. Low socio-economic status was found in majority (88.8% cases). Imperforate anus was most common in elderly primi (>35 years)-Table 2. Other maternal risk factor was obesity; but diabetes was not found in our series (Table 3). Major associated anomaly was genitourinary (50%) followed by musculoskeletal (22%) and gastrointestinal (12%) abnormalities. Histopathological examination of viscera like lungs, heart, liver, kidney and rectum revealed normal architecture without any obvious abnormality.

### CASE 1: VACTERL ANOMALY WITH PRUNE-BELLY SYNDROME

A 28-week fetus was delivered vaginally by a 37 year old second gravida. USG revealed gross abdominal distension, an enlarged bladder. Heart was pushed to one side, while the lungs couldn't be visualised. External examination following delivery showed normal placenta, distended abdomen and lax abdominal wall. Umbilical cord was high placed measuring 37cm with knots. There was a single umbilical artery. Internal examination revealed deformed thorax with enlarged bilobed heart. Imperforate anus was present with patent urachus and gonads were absent.[2] Right foot revealed talipes equinovalgus deformity.

### CASE 2: TRISOMY 18 (EDWARD'S SYNDROME)

Intrauterine death (IUD) of the fetus occurred at gestational age of 32 weeks. After deliver, autopsy was conducted. On external examination, there was microphthalmos, cleft lip, cleft palate and bilateral low-set ears. Right hand showed syndactyly and imperforate anus was found. Internal examination showed collapsed lungs, absent intestine, bilateral enlarged lobulated kidneys and undescended testis in the lumbar region.

### CASE 3: FRASER SYNDROME

Fetus of 26 weeks of gestational age was born to a mother aged 28 years. External examination showed complete cryptophthalmos of right eye, syndactyly of hand and low set malformed ears. Internal examination revealed imperforate anus, bilateral renal agenesis and testis at pelvic brim.

### CASES 4 & 5: OEIS COMPLEX- (OMPHALOCELE, EXTROPHY OF CLOACA, IMPERFORATE ANUS AND SPINAL DEFECTS)

Antenatal check-up of a 42 years old fifth gravida female with normal previous obstetric history on USG showed a single live intrauterine fetus of 16 weeks with no congenital anomalies. But at 28 weeks, she delivered a congenitally abnormal fetus. Placenta was normal. External examination showed omphalocele, absent external genitalia and imperforate anus.[3] Right foot presented with talipes equinovalgus. There was exostrophy of meconium stained bladder and lumbosacral meningocoele measuring 6.5cm in diameter containing 16ml straw coloured fluid. There was absence of appendix, gonads, single kidney and scoliosis in fetal spine. There was a 2nd case of OEIS complex also delivered at 26 weeks of gestational age by a 38 year old primi and showed all features of OEIS complex.

### CASE 6: ELLIS VAN CREVELD SYNDROME

36 year old primi during USG showed single dead fetus of gestational age 32 weeks with absence of right kidney which was delivered vaginally. External examination revealed flat pinna, very short forearms, syndactyly and polydactyly in left foot with finger nail abnormality.[4] Imperforate anus was also seen. X-ray revealed abnormal bones in upper limbs. Internal examination revealed atrial septal defect in heart and absent kidneys (bilateral).

### CASE 7: TRAP ANOMALY

22 year old primi in 3rd trimester came for routine antenatal check-up. USG revealed monoamniotic monochorionic twin of gestational age 33weeks and 2days .Twin A was a live female fetus with no congenital anomaly. Twin B was anomalous baby and received blood perfusion from Twin A. Placenta was fundo-posterior, grade 2. So, pregnancy was terminated. External examination showed grossly deformed lower limbs with soft globular upper portion. No head, neck and upper limbs were seen. Skin was edematous with swollen legs and abdomen. Internal examination revealed absence of heart, lungs and brain, bilateral kidneys with ureters opening into normal bladder and presence of coils of intestine.

### CASE 8 & 9: GASTROSCHISIS

23 year old primi during ultrasonography at 23rd week of gestation revealed herniation of all abdominal contents. A stillborn fetus was delivered vaginally. On external examination, there was absence of plantar crease, ear cartilage, nipple, external genitalia and anus.[5] All abdominal contents herniated to outside. Bilateral pelvic deformity was present with bilateral feet showing congenital talipes equinovarus deformity. Spine showed kyphosis. 2no case was of 35 year old primi with a still birth of 28 weeks fetus and on external examination revealed large defect in abdominal wall with imperforate anus. Abdominal contents were present outside.

## DISCUSSION

Imperforate anus is a condition often found in association with other serious anomalies leading to significant morbidity and mortality. Prenatal diagnosis of imperforate anus has been described earlier mostly as case reports.[6] Out of 57 cases of congenital anomalies, 9 had imperforate anus. Majority of them (7 out of 9=77.7%) had ambiguous genitalia, one was a male and the other a female. In a study conducted by Lisi A.et al a male preponderance has been described previously with a ratio of male to female being 1.3:1.[7] Anorectal malformations affect several socio-economic and ethnic groups. In present study, 88.8% (8 out of 9cases) belonged to low socio-economic group which was comparable to Moore SW and Murphy F et al's study where the figure was 74.2%.[8,9]

Maternal age more than 35 years was a significant finding in our study comprising of 55.5% (5out of 9cases). Nadine's study made a similar study in 2010 where he found percentage to be 65.4%.[10] Obesity in mothers was found in 66.6% cases (6 out of 9). This was agreeable to results by Bloomberg MI et al.[11] By categorizing maternal obesity into 3 classes –adiposities I (BMI 30-34.9), adiposities' II (BMI 35-39.9) and morbid obesity (BMI ≥ 40), they showed a particularly strong risk of anorectal malformation for morbid obesity.

Imperforate anus frequently manifests with other malformations. In this study, genitourinary anomalies comprise about 50%, musculoskeletal 22%, gastrointestinal 12%, craniofacial 10%, cardiovascular 04% and central nervous system (2%). The figures were 30%, 21%, 18%, 8%, 12% and 11% respectively in a study by Cushiera Aet al.[12]

Maternal diabetes has been shown to be a significant risk factor in a study done by Frias JL et al.[13] Our study didn't show any association with diabetes. In our study, prenatal diagnosis by ultrasound was missed in all cases. The prenatal detection rate was 15.9% according to a study done by Brantberg H et al.[14] A decreased risk of congenital anomalies was seen in mothers complying to regular antenatal check-ups and taking folate adequately by a study conducted by Sarah D et al in 2003.[15] 33.3% cases (3 out of 9) in our study underwent regular antenatal check-ups and 55.5%(5 out of 9 cases) regularly had folate intake. Cornel MC et al established maternal smoking before or during pregnancy as a risk factor for imperforate anus.[16] Alcohol consumption by mothers showed a direct relation in previous study done by Yuan P et al.[17] None of the mothers included in our study had these habits.

Other risk factors include illicit drug and caffeine intake. Some studies have reported on the potential role of maternal occupational hazards with a significantly increased risk with maternal cleaners and janitors.

Cytogenetics was done only in Trisomy 18 from skin sample. No role of cytogenetics has been reported in OEIS complex, TRAP anomaly and Gastroschisis so far. We failed to do this in cases of Fraser syndrome, Ellis Van Creveld syndrome and VACTERL anomaly due to unwillingness of parents of the concerned.

## CONCLUSION

There has been a decline in autopsy rate and studies being conducted today. Perinatal autopsy has an important role in syndrome diagnosis of imperforate anus and associated anomalies. It can act as an adjunct to ultrasound examination where prenatal diagnosis of syndrome or isolated imperforate anus has been missed. Thus by a proper correlation and compilation of autopsy studies, prenatal USG, data documentation we can counsel parents properly and predict the recurrence of anomalies in future pregnancies.

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