ORIGINAL ARTICLE

INCIDENCE AND SEXUAL PREPONDERANCE OF CONGENITAL MALFORMATIONS IN NICU, AT RIMS, RAICHUR

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ABSTRACT: This is a prospective study of congenital anomalies in babies admitted to NICU at RIMS teaching hospital from September 2014 to March 2015 and half yearly incidence was noted. The anomalies were classified into gastrointestinal, cardiovascular, nervous system, orofacial abnormalities, musculoskeletal and multisystem disorders. Each of them was further observed for sexual preponderance.

KEYWORDS: Congenital anomalies, Incidence, Sexual preponderance, Antenatal diagnosis, Risk factors.

INTRODUCTION: According to WHO, the term congenital anomaly includes any morphological, functional, biochemical or molecular defects that can develop in the embryo and fetus from conception until birth, that is present at birth whether detected at the time or not.(1) Birth defects are one of the leading causes for neonatal and infant mortality as well as morbidity as along with cancer in developed countries. However, in developing nation like India, malnutrition and infections are the leading cases of infant mortality and morbidity. But with improving conditions and access to better health care, the detection, work up and treatment of congenital anomalies is gaining significance

This study was done to determine the overall incidence of congenital malformations, as well as incidence affecting various organ systems. The cases of congenital anomalies admitted at RIMS, NICU have been reported in incidence, comparison to other available studies and sex ratio of each organ system.

METHODS AND METHODOLOGY: Patients were selected regardless of the indication for admission. A total of 1190 babies admitted in the NICU, RIMS during the 6 months from 1st September 2014 to 28th February 2015 were considered. Out of them, 762 cases were inborn in the RIMS hospital and 428 cases were out born and referred from outside. A total of 46 congenital anomaly cases were recorded of these 1190 admissions. All the cases of congenital anomalies were considered to determine the incidence of congenital anomalies in RIMS. The 2 cases of sexual ambiguity were excluded from studies related to sexual preponderances. The remaining 44 cases were used to statistically derive the sexual preponderance in various congenital anomalies that were reported in the NICU of RIMS. The cases were classified into cardiac, gastrointestinal, nervous system, musculoskeletal, orofacial and multisystem defects; and incidence of anomalies in each of them were noted.

OBSERVATIONS: The overall half yearly incidence, anomalies in various organ systems and sexual distribution from our study is depicted in the following tables.

Congenital anomaly	No. of Patients	Total No. of Patients
Gastrointestinal System		
Imperforate Anus	5	18
Ruptured omphalocoele with prolapsed bowel	1	
Hirschsprung Disease	1	
Umbilical hernia	1	
Diaphragmatic hernia	2	
Hypertrophic pyloric stenosis	1	
duodenal obstruction	2	
Trachea-oesophageal fistula	1	
Pure oesophageal atresia	3	
Cystic abdominal mass	1	
Cardiovascular System		
Patent Ductus Arteriosis	2	9
Ventricular Septal Defect	3	
Tetrology of Fallots	1	
Ectopia Cardis	1	
Tricuspid Atresia	1	
Complex congenital cardiac anomaly	1	
Central Nervous System		
Occipital meningoencephalocoele	1	8
Meningomyelocoele	3	
Spina bifida	2	
Congenital hydrocephalus	2	
Musculoskeletal		
Congenital Talipus Equino Varus	2	4
Arhrogrypsosis multiplex congenital	1	
KYPHOSCOLIOSIS, Short Neck, Polydactily	1	
Oro-facial		
Cleft lip	2	4
Cleft Palate	0	
Cleft lip and palate	1	
Pierre-robin Syndrome	1	
AMBIGIOUS GENITALIA	2	2

Multisystem Involvement		
Situs inversus totalis	1	1
Total	**46**	**46**

Table 1

Distribution and incidence in males and females is shown below. The following data has been diagrammatically represented in figures 1 and 2.

	Occurrence	**Male**	**Female**	**Male incidence**	**Female incidence**
GIT	18	10	8	55.6%	44.4%
CVS	9	3	6	33.3%	66.7%
CNS	8	2	6	25%	75%
Musculoskeletal	4	4	0	100%	0%
Oro-Facial	4	0	4	0%	100%
Multisystem	1	1	0	100%	0%
Sexual Ambiguity	2	-	-	-	-
Total	**46**	**20**	**24**		
Half Yearly Incidence				1.67%	2.01%

Table 2

DISCUSSION: Cardiovascular System: The congenital heart defects noted by us include Patent ductus arteriousus, ectopia cardis, tricuspid atresia, ventricular septal defects and complex congenital cardiac anomalies. The half yearly incidence was 0.75% with male: female ratio of 1:2. Geographical distribution of the congenital cardiac anomalies records a worldwide incidence of 8-10 per 1000 live births, as well as that of India which is 2.52-5.2 per 1000 live births. Asia has reported the highest congenital heart diseases prevalence at 9.3 per 1000 live births compared to Europe and North America at 8.2 and 6.9 respectively.

This is likely to be an underestimate, however, because an unknown number of cases go unreported, particularly those delivered by unqualified personnel in rural areas where monitoring is inadequate.[2]

Central Nervous System: There are two types of NTDs: open, which are more common, and closed. Open NTDs occur when the brain and/or spinal cord are exposed at birth are anencephaly, encephaloceles, hydranencephaly, iniencephaly, schizencephaly, and spina bifida. Rarer types of NTDs are called closed NTDs. Closed NTDs occur when the spinal defect is covered by skin. Common examples of closed NTDs are lipomyelomeningocele, lipomeningocele, and tethered cord.[3]

INCIDENCE: The half yearly incidence was 0.67% with male: female ratio of 1:3. The neural tube defects are among the most common birth defects.[4]

- Currently, the highest reported incidence is in Northern China (3.7 cases per 1000 live births). Indian and Eastern Mediterranean populations (with the exception of Israeli Jews) also have relatively high incidences of NTDs.[5]
- Vitamin B_{12} is an important receptor in the folate biopathway such that studies have shown deficiency in vitamin B_{12} contributes to risk of NTDs as well,[6] importantly, a deficiency of folate itself does not cause neural tube defects. The association seen between reduced neural tube defects and folic acid supplementation is due to a gene-environment interaction such as venerability caused by the C677T Methylenetetrahydrofolate reductase (MTHFR) variant. Supplementing folic acid during pregnancy reduces the prevalence of NTDs by not exposing this otherwise sub-clinical mutation to aggravating conditions.[7]
- It is more prevalent in first birth and in young and elderly mothers. Recurrence risk after one affected child is 4%. Open neural tube defects are associated with maternal polyhydramnios.[8]
- Other causes include antimetabolite medications such as methotrexate, maternal diabetes, exposure to radiation, alcohol consumption. Studies have shown that both maternal cigarette smoking and maternal exposure to second hand smoke increased the risk for neural tube defects in offspring. Studies have suggested that cigarette smoke, including second hand exposure, is not only hazardous to the mother, but may also interfere with neural tube closure in the developing embryo.[9]

Prenatal Diagnosis: Maternal serum Alpha feto protein is elevated in open neural tube defects. Amniotic fluid acetyl choline esterase is elevated and has a better diagnostic value than AFP.[8] Women who may become pregnant are advised to get 400 micrograms of folic acid daily. Women who are pregnant should receive 1.0 mg (1000 mcg), and women who have previously given birth to a child with a neural tube defect should get 4.0 mg/5.0 mg daily.[10]

OROFACIAL ABNORMALITIES: Non-syndromic cleft lip and palate, which forms the largest subgroup of craniofacial anomalies. The sex ratio in patients with clefts varies. Cleft lip and cleft lip and palate occurs significantly more often in males, and cleft palate occurs significantly more often in females.

In our study there was remarkable female preponderance with the occurrence of all four orofacial anomalies in females with half yearly incidence was 0.34%.

Risk Factors: Maternal factors include the following:

- Drugs such as phenytoin, isotretinoin, valproic acid, benzodiazepenes and corticosteroids.
- Maternal smoking especially in first trimester, alcohol consumption particularly binge drinking.
- Maternal diabetes, obesity and nutritional deficiency of folate and zinc.

Recurrence Risk[11]:

- If the parents are normal and have one child affected, the probability of the next child being affected is 2%.

- If however, there is a similarly affected child and a parent with a cleft, the probability increases to 7-15 %.

Table 3: The following table depicts the occurrence at our centre.

Anomaly	Incidence
Cleft lip only	2
Cleft palate only	0
Combined cleft lip and palate	1
Pierri robin syndrome	1

Table 3

Gastrointestinal system: Hirschsprung's disease: The disease, which affects about 1 in every 5,000 newborns, is 5 times more frequent in males than in females.

Factors that may increase the risk of Hirschsprung's disease include:

- Having a sibling who has Hirschsprung's disease: Hirschsprung's disease can be inherited. If you have one child who has the condition, future biological children also might be at risk.
- Being male: Hirschsprung's disease is more common in males.
- Having other inherited conditions: Hirschsprung's disease is associated with certain inherited conditions, such as inherited heart problems and Down syndrome. It may also be associated with multiple endocrine neoplasia, type IIB.

Anorectal Malformations: Risk factors: It's a relitavely common anomaly with an estimated incidence of 1 in 5000 live births and males are more predisposed. It has increased incidence along with other abnormalities known as VACTREL (V- vertebral anomalies, A- Anal atresia, C- CVS anomalies, T- Trecheoesophageal fistula, E- esophageal atrresia, R- Renal anomalies, and Limb defects) It is also associated with trisomies of 18 and 21 and other syndromes. Paternal smoking, alcohol in first trimester, obesity, excess caffine intake, diabetes mellitus

Tracheoesophageal Fistula and Esophageal Atresia: With respect to race/ethnicity, several studies have reported esophageal atresia and tracheoesophageal fistula to be more common in whites than in nonwhites or Hispanics.(12)

The influence of maternal age on esophageal atresia and tracheoesophageal fistula risk has been reported to be higher among both older and younger mothers or increasing with greater maternal age.(13)

Infant sex has been reported to influence esophageal atresia and tracheoesophageal fistula risk, with the conditions being more common among males than among females.(14)

Lower birth weight and lower gestational age increases the risk. Esophageal atresia has been associated with intrauterine growth retardation. There is decreased risk of these esophageal and tracheal conditions with increasing parity.(15)

Both esophageal atresia and tracheoesophageal fistula are more common among multiple gestation pregnancies.[16]

CONGENITAL DIAPHRAGMATIC HERNIA:

Risk Factors: more common in underweight mothers,[17] maternal thyroid dysfunction,[18] anticonvulsant use and multiple births. No association was found between maternal age and parity. It is more common in males than females.

Musculoskeletal System: Worldwide incidence is about 1 in 3000, with increased incidence in Finland and the Bedouin community in Israel.[19]

Risk-Factors: Decreased intrauterine movement, oligohydramnios (low volume or abnormal distribution of intrauterine fluid), and defects in the fetal blood supply, hyperthermia, limb immobilization and viral infections.[20]

Single gene defects (X-linked recessive, autosomal recessive and autosomal dominant), mitochondrial defects and chromosomal disorders (for example: trisomy 18).[21]

70-80% of the cases of arthrogryposis are caused by neurological abnormalities.[22]

AMBIGUOUS GENITALIA: The worldwide incidence is 1/10,000–20,000.

Risk Factors: excessive or deficient androgen effect, others result from teratogenic effects. The cause of many of these birth defects is unknown. Common causes include 5α-reductase deficiency, 17β-Hydroxysteroid dehydrogenase deficiency, Androgen insensitivity syndrome, Aromatase deficiency, Aromatase excess syndrome, Complete androgen insensitivity syndrome, Congenital adrenal hyperplasia, Leydig cell hypoplasia, Mild androgen insensitivity syndrome, Mixed gonadal dysgenesis, Partial androgen insensitivity syndrome.

CONCLUSION: Congenital anomalies are one of the important causes for infant mortality and morbidity.

These pregnancies should be considered as high risk. Antenatal diagnoses of congenital anomalies therefore, play a very important role for the specific management and better outcome of such pregnancies.

Counselling of parents for subsequent conceptions should be done as genetic risk factors are one of the leading cause for the occurrence of congenital anomalies. With advanced medical technology and tertiary care a baby born with congenital malformations can be managed appropriately with favourable prognosis.

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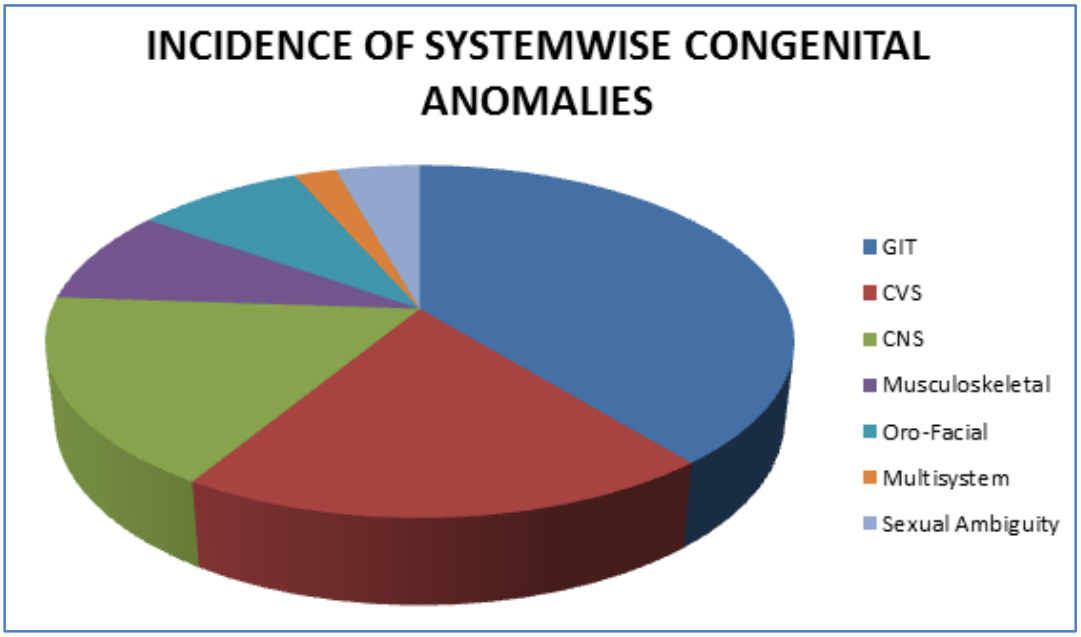

Fig. 1

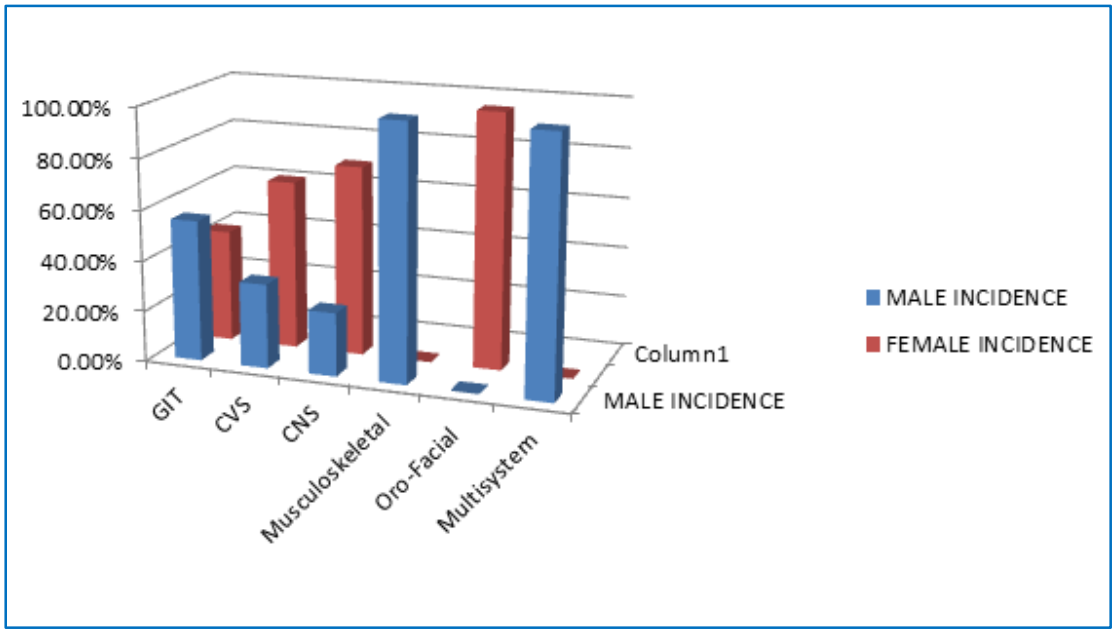

Fig. 2: System wise incidence of congenital anomalies in males and females

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