DOI: 10.5281/zenodo.8229787
16
Original research article

STUDY OF FETUSES WITH GROSS CONGENITAL ANOMALIES

Dr Purvi Malaviya: 2nd Year Resident Doctor, Department of Obstetrics and Gynaecology, Smt SCL Municipal General Hospital, Smt NHL mun. Meical college Ahmedabad pin 380006
Dr Neha Panchal: 1st Year Resident Doctor, Department of Obstetrics and Gynaecology, Smt SCL Municipal General Hospital, Smt NHL mun. Meical college Ahmedabad pin 380006
Dr Kinjal Sailor: 1st Resident Doctor, Department of Obstetrics and Gynaecology, Smt SCL Municipal General Hospital, Smt NHL mun. Meical college Ahmedabad pin 380006
Dr Samipa J Shah: Professor and Head of the Unit, Department of Obstetrics and Gynaecology, Smt SCL Municipal General Hospital, Smt NHL mun. Meical college Ahmedabad pin 380006
corresponding author: Dr Neha Panchal: panchalneha57@gmail.com

ABSTRACT:

INTRODUCTION:
Congenital malformations can be defined as structural or functional anomalies that occur during intrauterine life. Also called birth defects, congenital disorders, congenital abnormalities or congenital anomalies, these conditions develop prenatally and may be identified before or at birth, or later in life. An estimated 2,40,000 new-borns die worldwide within 28 days of birth every year due to congenital anomalies. Birth defects can result in long-term disability with a significant impact on individuals, families and health-care systems.

Method:
This is a prospective observational study which was conducted at our tertiary care centre. Total 2642 births were recorded in a period of one and a half year from January 2023 to June 2023. All booked, antenatal patients with diagnosed anomalous fetuses as well as unbooked, and those referred from outside with established diagnosis of congenital anomalies were included in our study.

Result:
incidence of congenital malformations during this study was 1.135%. increased chances of congenital malformations with increasing maternal age, highest risk being 18-20years 0.40% 21-25years 0.96% 26-30years 1.47% 31-35years 2.47% >35years 6.76% 18-20years 21-25years 26-30years 31-35years >35years 56 involved with age >35 years (6. 75%). Liqour abnormalities are often associated with congenital malformations. Elderly primigravida also have increased incidence of congenital - malformations (5.56%)

Conclusion:
Congenital anomalies can contribute to long-term disability, which may have significant impacts on individual, families, health-care system and society. Preventive public health measures to decrease the frequency of congenital anomaly can be taken by treating risk factors or reinforcement of protective measures. An estimated 6% of babies worldwide are born with a congenital disorder, and in our institute incidence is 1.135% due to preventive measures.

Keywords: FETUSES, GROSS CONGENITAL ANOMALIES, FETUSES WITH GROSS CONGENITAL ANOMALIES

INTRODUCTION

Congenital malformations can be defined as structural or functional anomalies that occur during intrauterine life. Also called birth defects, congenital disorders, congenital abnormalities or congenital anomalies, these conditions develop prenatally and may be identified before or at birth, or later in life. An estimated 2,40,000 new-borns die worldwide within 28 days of birth every year due to congenital anomalies. Birth defects can result in long-term disability with a significant impact on individuals, families and health-care systems.1 The causes of congenital malformations can be divided into following categories- 1) Genetic 2) Socioeconomic and demographic factors 3) Environmental factors including maternal infections 4) Unknown. Preventive public health measures work to decrease the frequency of certain birth defects through the removal of risk factors or the reinforcement of protective factors. Important interventions include adequate dietary intake of folic acid in adolescent girls and mothers, controlling diabetes pri-or to and during pregnancy, reducing or eliminating environmental exposure to hazardous substances, vaccination against rubella and screening for infections and their appropriate treatment. Preconception screening includes obtaining family histories and carrier screening and is particularly valuable in countries where consanguineous marriage is common. Peri-conception screening includes the use of ultrasound to screen for trisomies and major structural abnormalities during the first trimester, and for severe fetal anomalies during the second trimester. Maternal blood can be screened for placental markers to aid in prediction of risk of chromosomal abnormalities or NTDs, or for free fetal DNA to screen for many chromosomal abnormalities. Diagnostic tests such as chorionic villous sampling and amniocentesis can be used to diagnose chromosomal abnormalities in high-risk women. Neonatal screening is also an important step towards detection of congenital anomalies. This helps to reduce mortality and morbidity by facilitating earlier referral and the initiation of medical or surgical treatment. With early detection of congenital anomalies, timely termination of pregnancy can be done. This study is conducted to determine the prevalence, epidemiology and type of malformations at our tertiary care centre as congenital malformations are a major cause of global burden of disease.

CLASSIFICATION OF CONGENITAL ANOMALIES

1) Classification based on timing of insult:

a) MALFORMATION

A malformation is a morphologic defect of an organ, part of an organ, or region of the body due to an intrinsically abnormal developmental process. Example: renal agenesis and neural tube defects.

b) DISRUPTION

Disruptions result from the extrinsic breakdown of or an interference with an originally normal developmental process, and the resulting anomaly can include an organ, part of an organ, or a larger region of the body. example: amniotic band sequence

c) DEFORMATION

Deformational anomalies are produced by aberrant mechanical forces that distort otherwise normal structures. Example-fibroids, bicornuate uterus, multiple gestation and oligohydraminos.

2) Clinical classification of birth defects

a) SINGLE SYSTEM DEFECT- Involvement of either a single organ system or only a local region of the body such as cleft lip/palate and congenital heart defects

b) -MULTIPLE MALFORMATION SYNDROME

If a combination of congenital malformations occurs repeatedly in a consistent pattern and usually implies a common etiology, similar natural history and a known recurrence risk, it can be called a syndrome.

c) ASSOCIATION

Clinical entities in which two or more congenital anomalies occur together more often than expected by chance alone and have no well-defined etiology. A common example of an association is the VACTERL association which includes vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, renal and limb anomalies.

d) SEQUENCES

A single primary anomaly or mechanical factor initiates a series of events that lead to multiple anomalies of the same or separated organ systems and/or body areas. A common example is the Potter sequence in which primary Abnormality of renal agenesis leads to oligohydramnios, limb Deformities, flat facies, and pulmonary hypoplasia.

e) COMPLEXES

A set of morphologic defects that share a common or adjacent Region during embryogenesis, for example hemifacial microsomia.

ETIOLOGICAL CLASSIFICATION OF BIRTH DEFECTS:

1) GENETIC AND CHROMOSOMAL DISORDER-

Genetic disorders are inherited as autosomal dominant disorders, in which Each child has a 50% hence of inheriting the disorder, or as autosomal Recessive disorders, in which each child has a 25% chance of being Affected, a 50% chance of being a carrier, and a 25% chance of being Unaffected. Sex-linked disorders almost always are associated with the X Chromosome and are predominantly recessive

a) Single Gene Mendelian disorder:

- Autosomal dominant- Achondroplasia, Adult Polycystic Kidney Disease, Marfan syndrome, Familial hypercholesterolemia, Osteogenesis imperfecta, Hereditary spherocytosis, Huntington Chorea, Neurofibromatosis, von Willebrand disease etc.
- Autosomal recessive- Sickle cell disease, Thalassemia, Phenylketonuria, Cystic fibrosis, Glycogen storage diseases, TaySachs disease,Oculocutaneous albinism
- X-linked dominant- Alport syndrome, Rett syndrome, X-linked Hypophosphatemia
- X-linked recessiveBruton-type hypogammaglobulinemia, Haemophilia A, G-6PD deficiency

b) Chromosomal abnormalities:

- Numerical (Aneuploidy, Triploidy, Mosaicism): Down's syndrome, (trisomy 21), Edward's yndrome (trisomy 18). Patau syndrome (trisomy13), Turner's syndrome (X0), Klinefelter's syndrome(XXY).
- Structural (Deletion, Inversion, Translocation): Structural changes in Chromosomes usually result from breakage in one or more of the Chromosomes followed by rearrangement or deletion of the Chromosome parts.

c) Multifactorial inheritance disorders: Multifactorial inheritance Disorders are caused by multiple genes and, in many cases, Environmental factors.

d) Mitochondrial gene disorders: The mitochondria contain their own DNA, which is distinct from nuclear DNA. This DNA, which is Inherited maternally, is subject to mutations at a higher rate than Nuclear DNA, and it has no repair mechanisms. Disorders of Mitochondrial genes interfere with oxidative phosphorylation and the Production of cellular energy. The range of mitochondrial gene Disorders is diverse, with neuromuscular

disorders predominating. Examples include Chronic progressive external ophthalmoplegia, Kearns-Sayre syndrome, Leber hereditary optic neuropathy, Leigh Disease, MELAS, MERRF, Myoclonic epilepsy with ragged red fibres Etc.

2) <u>DISORDERS DUE TO ENVIRONMENTAL INFLUENCES:</u>

a) Chemicals and drugs:

i. Alcohol- Fetal alcohol syndrome

ii. Warfarin- Choanal atresia, stippled epiphyses, agenesis of corpus callosum, optic atrophy

iii. Retinoids- Ventriculomegaly, microtia, anotia, cleft palate, thymic aplasia, conotruncal heart defects

iv. Thalidomide- Phocomelia, abnormal development of long bones, cardiac anomalies, gastrointestinal
anomalies

v. Antiepileptics:

Phenytoin- Anomalies of heart, failure of CNS closure, cleft palate

Valproate- Facial dysmorphy, neural tube defects

Phenobarbitone- Cleft lip and palate

vi. Antifungals:

Fluconazole- Oral clefts, cardiac, skull, long bone and joint Abnormalities

vii. Psychiatric medications:

Lithium- Anomalies of heart, Ebstein's anomaly

SSRIs/SNRIs- ASD, VSD, persistent pulmonary hypertension of The new-born

viii. Anti-inflammatory:

NSAIDS- Bronchopulmonary dysplasia, intraventricular haemorrhage, Necrotizing enterocolitis

Leflunomide- Hydrocephalus, skeletal abnormalities

ix. ACE inhibitors and ARB- ACE-inhibitor fetopathy

x. Immunosuppressants:

Corticosteroids- Cleft palate, renal atrophy

Mycophenolate mofetil- Mycophenolate embryopathy, pregnancy Loss

xi. Sex hormones:

Androgens- Masculinization of external genitalia

Danazol- Virilization of female fetus

Diethylstilbestrol- Vaginal clear cell adenocarcinoma, genital tract Abnormalities

b) Maternal infections:

i. Protozoal:

Toxoplasmosis- Hydrocephalus, mental retardation, Chorioretinitis

ii. Viral:

Varicella- Congenital varicella syndrome33 which includes Chorioretinitis, microphthalmia, cortical
atrophy, hydronephrosis, Limb hypoplasia

Cytomegalovirus- Microcephaly, microphthalmia, chorioretinitis, Periventricular calcifications

Influenza- Neural tube defects

Rubella- Congenital rubella syndrome36 which includes cataracts, Cardiac septal defects, microcephaly,
pulmonary stenosis

Coxsackie- Myocarditis

Parvovirus- Hydrops fetalis37, still birth, pregnancy loss

Zika virus- Congenital zika syndrome which includes severe Microcephaly, subcortical calcifications,
macular scarring, Congenital contractures such as club foot or arthrogryposis, etc.
iii.. Bacterial: Treponema pallidum- Depressed nasal bridge, deafness, hydrops Fetalis

c) Maternal diseases:

i. Diabetes- caudal regression syndrome, congenital heart diseases, Neural tube defects
ii. Hypothyroidism- goitre

d) Radiation: Radiation is teratogenic and mutagenic, and has the Capacity to effect inheritable changes in genetic materials. Administration of therapeutic doses of radioactive iodine during the 13thweek of gestation, the time when the fetal thyroid is beginning to Concentrate iodine, has been shown to interfere with thyroid Development.

3) MULTIFACTORIAL/POLYGENIC:

a) Maternal age- Incidence of congenital anomalies increases with Advancing age, >35 years. There is a clear association between increasing Maternal age and Down's syndrome.
b) Consanguinity- The risk is more in couples having consanguineous Marriage.
c) Maternal nutrition –
i. Obesity has been found to have a close correlation with neural tube Defects, cardiac anomalies, omphalocele, etc.
ii. Vitamin C, D and folic acid deficiency leads to many congenital Anomalies

Materials and Methods

This is a prospective observational study which was conducted at our tertiary care centre. Total 2642 births were recorded in a period of one and a half year from January 2023 to June 2023. All booked, antenatal patients with diagnosed anomalous fetuses as well as unbooked, and those referred from outside with established diagnosis of congenital anomalies were included in our study. Babies diagnosed with congenital anomalies at birth were also included. A total of 30 cases of congenital malformations were recorded during the study period. The mother's details were entered in the proforma which contained the following particulars, like maternal age, gravidity, consanguinity, any exposure to teratogens or history of infection in 1st trimester, history of medical disorders like diabetes, hypertension and hypothyroidism, history of ART or previous history of anomalous child or abortions or stillbirths. Antenatal scans were noted. Once the diagnosis of congenital anomaly was made, proforma was filled to document the type of anomaly and maternal and neonatal outcome. The newborns were subjected to detailed examination from head to toe within 48 hours of birth. Neonates that were identified with congenital anomalies were admitted in NICU for further observation and management. Investigations were carried out wherever needed and surgical intervention carried out wherever- required by transferring to a centre equipped with pediatric surgery facilities.

Observation and Discussion

Over an period of 6 months, 2642 birth were recorded from which 30 cases of Congenital Anomalies were diagnosed.

TABLE 1: INCIDENCE OF CONGENITAL ANOMALIES

An estimated 6% of babies worldwide are born with a congenital disorder, resulting in hundreds of thousands of associated deaths.

Total no. of deliveries	No. of malformation	Percentage
2642	30	1.135%

The above table shows that incidence of congenital malformations during this study was 1.135% which was comparable to following studies.

TABLE 2: DISTRIBUTION OF MALFORMATION ACCORDING TO MATERNAL AGE

Maternal age (year)	Total deliveries N=2642	No of malformation N=30	Percentage
18-20	489	2	0.40%
21-25	1248	12	0.96%
26-30	743	11	1.47%
31-35	134	3	2.47%
>35	24	2	6.76%

The above table show that there is increased chances of congenital malformations with increasing maternal age, highest risk being 18-20years 0.40% 21-25years 0.96% 26-30years 1.47% 31-35years 2.47% >35years 6.76% 18-20years 21-25years 26-30years 31-35years >35years 56 involved with age >35 years (6.75%).

TABLE 3: CORRELATION OF LIQOUR ABNORMALITIES WITH INCIDENCE OF MALFORMATIONS

Liquor	Total deliveries N=2642	No. of malformation	Percentage
Polyhydramnios (AFI>25cm)	415	11	2.65%
Oligohydramnios (AFI<5cm)	684	6	0.87%
Normal	1608	13	0.80%

Liqour abnormalities are often associated with congenital malformations. The above table that there is increased association of anomalies with polyhydramnios (2.65%). Polyhydramnios is associated with Liqour Total deliveries (N=2642).

TABLE 4: DISTRIBUTION OF CONGENITAL MALFORMATIONS ACCORDING TO CONSANGUINITY

Consanguinity	No. of malformation N=30	Percentage
Consanguineous	18	60%
Non consanguineous	12	40%

TABLE 8: CORRELATION OF ANTENATAL RISK FACTORS WITH INCIDENCE OF MALFORMATIONS

Risk Factor	No. of malformation (N=30)	Percentage
Diabetic mothers	5	16.67%
Elderly primi	4	13.33%
Hypertensive mothers	3	10.00%
Hypothyroid mothers	2	6.67%
Teenage pregnancies	2	6.67%
Use of ART	2	6.67%
H/O fever in 1 trimester	2	6.67%
Use of teratogens in 1 trimester	2	6.67%
Past H/O congential anomaly	3	10.00%
No intake of folic acid in 1 trimester	5	16.67%

Above table show that there is increased incidence of congenital malformations in diabetic mothers (16.67%). This was comparable to study done by Sheffield and Koster (4.8% for gestational diabetes and 6.1% for pregestational diabetes) 69. Pre- gestational glycemic control and counselling help to decrease the rate of anomalies in diabetic pregnancies.

Pregnancy with previous anomalous child have a higher incidence of anomaly in second pregnancy as shown in our study (4.45%). Malik et al observed that 8.3% of the pregnancies with previous anomalous child had anomaly in subsequent pregnancies61.
Elderly primigravida also have increased incidence of congenital - malformations (5.56%) and findings were consistent with Pradhan et al in his study (2.51%)70. Pregnancy with hypertension also have higher incidence of malformations (4.45%) and similar findings were observed by Malik et al (5%)61

SCREENING

PRECONCEPTION SCREENING

1Preconception screening: to identify those at risk of conceiving a child with a birth defect since inherited disorders tend to cluster within family Using family history to identify individuals at risk of having affected Children. Carrier screening for common recessive disorders (e.g., thalassaemia and sickle cell disorders).

PERI-CONCEPTION SCREENING

Peri-conception screening: offers genetic counselling to women 35 years or Older. Along with routine ultrasound other tests can be used for screening During the first trimester and the second trimester of pregnancy for e.g. Dual marker, triple marker, quadruple marker, NIPT etc

Conclusion

Congenital anomalies can contribute to long-term disability, which may have significant impacts on individual, families, health-care system and society. Preventive public health measures to decrease the frequency of congenital anomaly can be taken by treating risk factors or reinforcement of protective measures.
The risk factors for congenital anomalies are women>35 years of age, multigravida, elderlyprimi, previous history of anomalous child, consanguineous marriage, use of Artificial Reproductive Techniques, medical disorders like diabetes, hypothyroid etc.
Preconception and peri-conception screening are tools which can be used to identify individuals at risk of specific disorders.
Ultrasonography is an important diagnostic as well as screening tool for timely diagnosis and management of fetal congenital anomalies. It has high sensitivity for diagnosis of anomalies. Other than USG, various biochemical markers are also available for screening in 1^{st} as well as 2^{nd} trimester.
The causes of congenital malformations can be divided into following categories-
1) Genetic
2) Socioeconomic and demographic factors
3) Environmental factors including maternal infections
4) Unknown
An estimated 6% of babies worldwide are born with a congenital disorder, and in our institute incidence is 1.135% due to preventive measures
Preventive public health measures work to decrease the frequency of certain birth defects through the removal of risk factors or the reinforcement of protective factors. Important interventions include adequate dietary intake of folic acid in adolescent girls and mothers, controlling diabetes prior to and during pregnancy, reducing or eliminating environmental exposure to hazardous substances, vaccination against rubella and screening for infections and their appropriate treatment.
Preconception screening includes obtaining family histories and carrier screening and is particularly valuable in countries where consanguineous marriage is common. Peri-conception screening includes the use of ultrasound to screen for trisomies and major structural abnormalities during the first trimester, and for severe fetal anomalies during the second

trimester. Maternal blood can be screened for placental markers to aid in prediction of risk of chromosomal abnormalities or NTDs, or for free fetal DNA to screen for many chromosomal abnormalities.
Diagnostic tests such as chorionic villous sampling and amniocentesis can be used to diagnose chromosomal abnormalities in high risk women.
Neonatal screening is also an important step towards detection of congenital anomalies. This helps to reduce mortality and morbidity by facilitating earlier referral and the initiation of medical or surgical treatment.
With early detection of congenital anomalies, timely termination of pregnancy can be done.
This study is conducted to determine the prevalence, epidemiology and type of malformations at our tertiary care centre as congenital malformations are a major cause of global burden of disease.
Timely termination is the required goal in case of lethal anomalies. Screening of newborns also helps to reduce mortality and morbidity by facilitating earlier referral and the initiation of appropriate treatment.
Timely termination is the required goal in case of lethal anomalies. Screening of newborns also helps to reduce mortality and morbidity by facilitating earlier referral and the initiation of appropriate treatment.

Conflict of interest: Nil
Funding: NIL
Acknowledgement: Nil

References

1. World health organization. Birth defects. https://www.who.int/news-room/fact-sheets/detail/birth-defects
2. Schumacher GH, Gill H, Gill H. Zur Geschichte angeborener Fehlbildungen unter besonderer Berücksichtigung der Doppelbildungen. Vom 18. bis 20. Jahrhundert [The history of congenital malformations with special reference to conjoined twins. 2. The 18th to the 20th centuries]. Anat Anz. 1987;164(4):291-303. German. PMID: 3326427.
3. Research on the Artificial Production of Monstrosities, or Essays on Experimental Teratogenesis (Dareste, 1876)
4. DeSesso, JM. The arrogance of teratology: A brief chronology of attitudes throughout history. Birth Defects Research. 2019; 111: 123– 141.
5. Kelley, Kristin, "Amniocentesis Prior to 1980". Embryo Project Encyclopedia(2010-09-02).ISSN:1940-5030 http://embryo.asu.edu/handle/10776/2072.