J. Fetal Med. (March 2021) 8:41–48
https://doi.org/10.1007/s40556-020-00287-y

ORIGINAL ARTICLE

Clinical Profile of Women with Congenital Fetal Malformations: A Retrospective Cohort Study

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Received: 31 August 2020 / Accepted: 21 December 2020 / Published online: 20 January 2021

Abstract

Background Though this is an era of imaging, many women with fetal congenital malformations are presenting beyond 20 weeks of pregnancy posing problems in decision making. This study was undertaken to determine the prevalence of congenital fetal malformations presenting to tertiary health care and to analyse the gestational age at presentation and spectrum of malformations and the clinical and socio-demographic factors.

Material and Methods This was a retrospective analysis of hospitalised women with diagnosis of congenital fetal malformations (CFM) from January 2017 to December 2017. The data was retrieved from Medical Records Section after due permissions and analysed with respect to socio-demographic status, age, consanguinity, type of congenital anomaly and gestational age at presentation.

Results The prevalence of CFM was 1.56%. The majority (64%) of CFM were detected during the second trimester and 27% were detected in the 3rd trimester. The most common anomalies were CNS followed by multiple anomalies and 72% and 65% of them were live born respectively. The majority (90%) belonged to lower middle socioeconomic group and were from rural background (82%). The majority of women were less than 30 years of age (77.6%) and 38% were primigravidae. Consanguinity was present in 34%, medical disorders were associated in 29% and 3% had family history of congenital fetal anomalies.

Conclusion The most common anomalies were CNS and majority were primigravidae. The most common medical disorder associated was diabetes. It is possible that they are deficient in folic acid and vitamin B12. Hence pre-conceptional control of medical disorders, nutritional counselling regarding intake of micronutrients and awareness programmes to take pre-conceptional folic acid and vitamin B12 are the need of the hour for prevention.

Keywords Fetal congenital malformations · CNS · Multiple congenital anomalies · Socio-demographic status · Folic acid

Introduction

Congenital anomalies are structural or functional anomalies that occur during intrauterine life and can be identified prenatally or at birth. These have long term disability and have significant impact on individuals, families, health care systems and Societies. Worldwide it is estimated that 3,03,000 new-borns die per year within 4 weeks of life and thus primary preventive strategies need to be adopted [1]. In India, a meta-analysis estimated congenital fetal anomalies to occur in 4,72,177 per year with a pooled prevalence of 184.48 per 10,000 births [2]. The etiology is not exactly known for all congenital malformations even in developed countries. In a study conducted in Boston, etiology was identified only in 26% of women which included a large database between 1972 to 2012 among 289,365 births. [3]. Prevention of birth of children with congenital malformations is possible by adopting measures at various levels like primary, secondary and tertiary [4]. An analysis of the spectrum of fetal congenital anomalies and the sociodemographic profile may give some clues to adopt

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some strategies for their prevention. This retrospective analysis was undertaken with the objectives of analysing the sociodemographic profile of women with congenital fetal anomalies presenting to a tertiary care centre over one year and to know the type and spectrum of these malformations.

Material and Methods

This was a retrospective cohort study conducted in 2018 at JIPMER, Puducherry, India. The case records of women who were hospitalised during the preceding year (Jan 2017–December 2017) were retrieved from the Medical Records Section after due permissions. Data was recorded with respect to age, socio-demographic details, family history, marital history of consanguinity, past history, associated medical disorders, gestational age at presentation, type of malformation and pregnancy management and fetal outcome. Data was analysed and presented as proportions and frequencies.

Results

The prevalence of congenital malformations during the one year of the study period was 1.56% (260/16,694 deliveries).The socio-demographic and clinical profile is represented in Table 1. The majority (82%) were from rural areas and 90% belonged to lower middle socioeconomic status (modified BG Prasad classification). History of consanguineous marriage was present in 34%, family history of congenital anomalies in 3% and past history of congenital anomalies in 5%. The majority (38%) were primigravidae and 35% were second gravidae. Women > 30 years constituted 22.3%. In women > 30 years of age, 24.1% had central nervous system (CNS) malformations, 15.5% had multiple system anomalies, 17.24% had renal, 15.5% had cardiovascular system (CVS) anomalies, 12.06% had musculo-skeletal system anomalies, 6.9% had gastro-intestinal system malformations and 8.62% were found to be syndromic fetuses (4 had Down syndrome and 1 had Edward syndrome). Medical disorders complicated 29% of women with CFM and of them, 37% were diabetic, 32% were hypertensive and 21% were hypothyroid. Overall, Sixty five percent were diagnosed during the 2nd trimester, 27% during the 3rd trimester and only 8.5% in the first trimester.

The type of congenital malformations involving various systems is represented in Table 2. The most common were CNS (25.76%) followed by multiple system (21.15%) involvement and then renal anomalies (13%). Cardiac anomalies, Musculoskeletal, and Gastrointestinal (GI) anomalies constituted 12.3%, 11.9% and 10.76% respectively. Other anomalies were lymphangioma, diastematomyelia, CPAM (Congenital pulmonary adenomatoid

Table 1 Socio-demographic and clinical profile of women with congenitally anomalous fetuses

S. No.	Characteristic	Number N = 260	Percentage
1	Residence		
	Rural	212	81.5
	Urban	48	18.46
2	Socio-economic status		
	Upper	27	10.38
	Upper middle	–	–
	Middle	–	–
	Lower middle	233	89.61
	Lower	–	–
3	Marital status		
	Non consanguineous marriage	172	66.15
	Consanguineous marriage	88	33.84
4	History of congenital malformations		
	Family history	8	3.07
	Previous history of anomalies	13	5
5	Clinical characteristics		
A	Age group		
	15–20 years	22	8.46
	20–25 years	83	31.9
	25–30 years	97	37.3
	> 30 years	58	22.3
	≤ 30 Years	202	77.69
B	Pregnancy order		
	Primi-gravidae	99	38
	Second gravidae	90	34.6
	Third gravidae	53	20.38
	> 3 Pregnancies	18	6.92
C	History of drug intake	5	1.9
	Anti-epileptics	2	–
	Warfarin	1	–
	Others	2	–
D	Medical disorders	70	28.92
	Hypertensive disorders	22	31.4
	Diabetes mellitus	26	37.1
	Thyroid disease	15	21.4
	Heart disease	3	4.28
	Bronchial asthma	4	5.71
E	Gestational age at diagnosis		
	First trimester	22	8.46
	Second trimester	168	64.61
	Third trimester	70	26.92

Table 2 Types of gross congenital fetal malformations

S. No.	System involved	Number N = 260	Percentage
1	CNS	67	25.76
2	Multiple systems	55	21.15
3	Renal system	34	13.07
4	CVS	32	12.3
5	Musculo-skeletal system	31	11.9
6	Gastro-intestinal system	28	10.76
7	Others	13	5

malformation), Micrognathia, cystic hygroma and neck swelling of unknown cause.

The historical associated factors for CFM are shown in Table 3. In women with history of consanguineous marriage, 25% of foetuses had CNS malformations, 23.8% had multiple system anomalies, 14.7% had cardio-vascular malformations, 13.6% had renal, 12.5% had musculoskeletal and 10.2% had gastro-intestinal system anomalies. Out of 8 cases with family history of congenital malformations, 2 had atrial septal defect, 1 had Ebstein's anomaly, 3 fetuses were found to have CNS anomalies (2 with hydrocephalus and 1 with meningomyelocoele) and two had hydronephrosis. Thirteen women were found to have recurrent anomalies, 5 had cardiovascular malformations (2 with ventricular septal defect, 2 with atrial septal defect and one with left ventricular outflow tract obstruction), 5 had CNS malformations (2 had meningocoele and meningomyelocoele respectively, 1 had spina bifida and 2 had hydrocephalus), 2 had renal malformations (unilateral renal agenesis and hydronephrosis respectively) 1 had Congenital Diaphragmatic Hernia (CDH). History of drug intake was present in 1.9%. Two women were on valproate, one of the fetuses had meningocoele and the other had meningomyelocoele. Two women were on anti-cholinestrase enzyme inhibitors, their fetuses were found to have renal hypoplasia and atrial septal defect respectively. One of the fetuses had microcephaly and the mother was on warfarin. Overall, ten percent were diabetic and 5.8% were hypothyroid. Seventy two percent had overt diabetes and 28% had gestational diabetes. Periconceptional blood sugar values were not checked in all women with overt diabetes, hence we have not analysed this aspect. In diabetic women, 46.1% had CNS malformations, 42.3% had cardiovascular and 11.5% had renal malformations.

CNS malformations and their outcome is represented in Table 4. More than 70% of foetuses with CNS anomaly were live born and the most common CNS anomaly was hydrocephalus (38.8%). Meningomyelocele constituted 15%. Multiple fetal anomalies and their details are represented in Table 5. The most common combined systems malformed were CNS + CVS + GI (32.7%) and CNS + CVS in 20%. Of the foetuses with multiple anomalies 65% were live born. Table 6 shows the anomalies in third trimester and their outcome. There were 70 women in third trimester diagnosed with anomalies. Seventy six percent of them underwent malformation scan in second trimester, while 24% presented directly in the third trimester. Ninety seven percent were live births and the most common system involved was renal (25.7%). The second most common group of malformations detected in the third trimester were of Central Nervous System (18.6%). In CNS anomalies, 2 fetuses with hydrocephalus were still born. All the foetuses with Cardiovascular, Musculoskeletal, Gastrointestinal and multiple anomalies detected in third trimester were live born.

Discussion

One of the strategies of early diagnosis is to identify the risk factors of congenital malformations and target those with risk factors to specific interventions. A study undertaken to know the risk factors (The Latin American Collaborative Study of Congenital Malformations (ECLAMC),

Table 3 Type of gross congenital malformations and historical associated factors

S. No	Type of congenital fetal malformation	Historical associated factors			
		Consanguineous marriage (N = 88)	Family history (N = 8)	Drug intake(N = 5)	Diabetes mellitus (N = 26)
1	CNS	22 (25%)	3 (37.5%)	3 (60%)	12 (46.1%)
2	Renal system	12 (13.6%)	2 (25%)	1 (20%)	3 (11.5%)
3	CVS	13 (14.7%)	3 (37.5%)	1 (20%)	11 (42.3%)
4	Musculo-skeletal system	11 (12.5%)	–	–	–
5	Gastro-intestinal system	9 (10.2%)	–	–	–
6	Multiple system	21 (23.8%)	–	–	–

Table 4 CNS malformations—outcome

S.No	Type of anomaly	Mean gestational age at diagnosis (weeks)	Number (%) N = 67	Outcome			
				MTP N = 16 (24%)	Still born N = 3	Live born N = 48	Total live births
1	Anencephaly	16	6 (8.9%)	6	–	–	48 (71.6%)
2	Hydrocephalus	20	26 (38.8%)	6	2	18	
3	Spina bifida	22	7 (10.4%)	1	1	5	
4	Meningomyelocoele	31	10 (14.9%)	–	–	10	
5	Meningocoele	30	6 (8.9%)	–	–	6	
6	Microcephaly	28	5 (7.46%)	–	–	5	
7	Arnold chiari	32	7 (1.4%)	3	–	4	

Table 5 Multiple fetal anomalies—outcome

S. No.	Systems involved or Sndrom.ic fetuses	Mean gestational age at diagnosis (weeks)	Number (%) N = 55	Outcome			
				MTP N = 17 (30.9%)	Still born N = 2	Live born N = 36 (65.45%)	Total live births
1	CNS + CVS + GI	26	18 (32.7%)	5	2	11	36 (65.4%)
2	CNS + GI	24	9 (16.4%)	4	–	5	
3	CVS + GI	20	10 (18.2%)	4	–	6	
4	CNS + CVS	22	11 (20%)	3	–	8	
5	DOWN'S syndrome	22	5 (9%)	1	–	4	
6	Edwards's syndrome	28	1 (1.8%)	–	–	1	
7	VACTERL' syndrome	30	1 (1.8%)	–	–	1	

in 2001–2010 found increasing maternal age, family history of congenital malformations, intrauterine growth restriction and acute febrile illness during the first trimester to be associated with severity of congenital malformations [5]. A study from north India on demographic profile of women seeking MTP reported 75% from rural areas and most of them were 20–25 years of age[6]. In this cohort of South Indian population, 82% were from rural background and the most common age group was 25 to 30 years. This difference may be due to the fact that the current study included all congenital malformations and not only those seeking MTP. A study from Tamil Nadu in South India also found maternal age to be more than 25 years and history of consanguineous marriage was reported as 15.7% [7] but the current study found a high association (33.8%) of consanguineous marriages. Family history of anomalies was recorded in 3% in the current study and it was 8.4% in the study of Prema and colleagues [7]. Diabetes mellitus was present in 10% of women in the current study and a very high association (32%) was reported by Prema and colleagues [7]. They reported a prevalence of 1.93% of congenital anomalies which is similar to the present study (1.56%). A study from Haryana has reported a 1.7% prevalence of congenital malformations. [8].

The commonest system affected reported is central nervous system in India; South India 48% [8], North India 35.6% [7]. The present study also found CNS to be the commonest (25.8%) system that was affected. But differences still exist in various geographic areas. Gastro-intestinal system anomalies were the commonest (35%) followed by CNS (26.6%) in a study conducted in Jammu [9]. Cardiac anomalies were the commonest among newborn live births in a study reported from central India [10].However, Sarkar et al reported that musculoskeletal anomalies were commonest in their study in Eastern India [11].

The most common type of CNS malformations reported from Bosnia and Herzgovina were neural tube defects

Table 6 Malformations detected in third trimester

S. No.	Type of anomaly	Number (%) N = 70	Outcome		
			Still born N = 2	Live born N = 68	Total live births
1	Renal	18 (25.7%)	–	18	68 (97%)
	Hydronephrosis	11		11	
	Unilateral renal agenesis	3		3	
	Dysplastic kidney	4		4	
2	CNS	13 (18.6%)	2	11	
	Hydrocephalus	3	2	1	
	Spina Bifida	1		1	
	Meningomyelocoele	2		2	
	Meningocoele	1		1	
	Microcephaly	3		3	
	Arnold Chiari	3		3	
3	Gastro-Intestinal system	12 (17.1%)	–	12	
	Congenital diaphragmatic hernia	5		5	
	Intra-abdominal cyst	6		6	
	Splenic cyst	1		1	
4	CVS	9 (12.8%)	–	9	
	Ventricular septal defect	5		5	
	Atrial septal defect	3		3	
	Total anomalous pulmonary venous connection	1		1	
5	Musculo-Skeletal system	7 (10%)	–	7	
	CTEV	5		5	
	Achondroplasia	2		2	
6	Multiple anomalies	8 (11.4%)	–	8	
7	Others	3 (4.28%)	–	3	

(38.6%), hydrocephalus (26.8%), microcephaly (18.9%) and agenesis of the corpus callosum (7.9%) [12]. In the present study, we found hydrocephalus (38.8%) to be the most common CNS malformation followed by other neural tube defects (34.2%) (meningomyelocoele 14.9%, spina bifida 10.4%, meningocoele 8.9%) and microcephaly in 7.46%.

Dursen Arzu et al in their study on distribution of congenital anomalies in a neonatal intensive care unit in Turkey reported 32.9% of babies to have multiple anomalies [13]. In the present study, we found that 21.1% had multiple system anomalies and CNS + CVS + GI malformations were the most common (32.7%). Prema and colleagues in their study in South India reported that only 4.2% of babies were syndromic [7]. Taksande et al from Central India also found that 4.08% of the babies had various syndromes [10].

Most of the malformations are detected before 20 weeks of gestation, however some phenotypic expressions become apparent only after 20 weeks like short limbs in achondroplasia, abnormal shape of the head in craniosynostosis and dilated bowel loops in bowel atresia. There are some anomalies which may develop only during the third trimester like ventriculomegaly following maternal infection, and ovarian cysts secondary to maternal estrogenic stimulation. Ficara et al did a prospective study of 52,400 women in UK to determine the value of routine ultrasound at 35–37 weeks of gestation in women with normal second trimester anomaly scan. They found that 24.8% of anomalies were detected for the first time between 35 and 37 weeks of gestation. The most common anomalies first seen in third trimester ultrasound were hydronephrosis, mild ventriculomegaly, ventricular septal defect, duplex kidney, ovarian cyst and arachnoid cyst [14]. Manegold et al also performed a routine third trimester ultrasound at 28–32 weeks after previous 2 normal ultrasounds at 11–14 weeks and 20–24 weeks. They found that an additional 15% of anomalies were detected in the third trimester. The most common anomalies were of the urogenital system followed by cardiovascular, gastro-intestinal and

central nervous system [15]. In the present study, we found that 26.9% of anomalies were detected in the third trimester. Of these renal malformations constituted 25.7% followed by CNS (18.6%). These organ systems show alterations later as it has to do with fetal growth and increased function like urine output and development of foetal brain [16, 17]. EUROCAT study reported that as high as 53% of anomalies were detected after 24 weeks or were missed [18].

The most common anomaly detected in the third trimester was hydronephrosis (11/18). It affects 1–5% of all pregnancies and infants with mild hydronephrosis are also at risk of febrile urinary tract infections. Monitoring and post natal follow up is important in these cases [19, 20]. Hydrocephalous was the most commonly detected central nervous system malformation in the third trimester. The main causes are structural like Aqueductal stenosis, Dandy walker malformation, Arnold chiari II, corpus callosum agenesis, but it can also be caused by infections or intracranial haemorrhage. Since fetal development continues after the second trimester, some findings can only be identified later [16]. One of the common findings is corpus callosum agenesis, which can be missed even in the hands of experts.

Out of cardiovascular system anomalies, mostly small ventricular septum defects were detected in third trimester (5/9). It can be due to factors like suboptimal fetal position, growing body mass indices of the mothers, operator negligence which may alter the quality of fetal echocardiocardiography in early gestational age [21, 22]. It is well known that antenatal development of the heart can lead to changes of ventricular inflow and outflow and stenosis and hypoplasia can progress and might not be detectable in earlier gestation [23].

In the present study, even the malformations which can be easily detected in first and second trimester like meningomyelocoele, meningocoele were detected first during third trimester due to the lack of awareness to undergo antenatal ultrasound during first or second trimester or they were missed. The legal limit of medical termination of pregnancy (MTP) in India is 20 weeks, so MTP cannot be offered in the third trimester even if it is a lethal anomaly like achondroplasia. Achondroplasia is usually detected after 27 weeks.

When malformations are detected in the third trimester, along with extensive counselling of the parents before birth, obstetricians and neonatologists should anticipate complications related to the condition and prepare themselves and parents for it. Medico-legal implications associated with this deserve special attention. These women should be advised to undergo delivery at centres with facilities for tertiary care and neonatal intensive care units. Clinicians find it difficult to explain management issues especially in guiding the parents in decision making regarding termination of pregnancy at late gestational age [24].

Prevention is most important as most of the neonates with major congenital malformations die of prematurity inspite of corrective surgery. It is found that intake of preconceptional folic acid and/or food fortification can prevent neural tube defects and the recommendations are 0.4 to 0.8 mg of folic acid as per USPSTF recommendations [25]. Vitamin B 12 along with folic acid can be taken as per risk stratification for occurrence of neural tube defects and other folic acid sensitive congenital malformations [26]. The implications of a consanguineous marriage must be explained. The association is found to be high in the present cohort. This is consistent with other studies [27, 28]. Sozan Ameen and colleagues from Iran reported significant association of congenital malformations with medical disorders complicating pregnancy [28] and Diabetes mellitus is an established risk factor. In the present study also Diabetes was the major risk factor among medical diseases of 29% which were associated with CFM.

Conclusions

The prevalence of CFM was low in this cohort. The most common anomalies were CNS and multiple anomalies involving CNS, CVS, Gastrointestinal Systems and majority were found in primigravidae belonging to low socioeconomic status, hence it is possible that they are deficient in folic acid and vitamin B12. Nutritional counselling regarding intake of micronutrients and awareness programs to take pre-conceptional folic acid and vitamin B12 are the need of the hour for prevention. Women should be counselled regarding the need of pre-conceptional control of blood sugars and screening for diabetes in non-pregnant state in those with high risk factors before planning for pregnancy. It is also essential to look for late onset anomalies during the third trimester scan so as to plan optimum perinatal care which involves teamwork of specialists in surgical and tertiary care.

Limitations

This was a retrospective cohort study. Details of pre-conceptional care and dietary history could not be obtained.

Strengths

The study analysed the factors which can be taken care of by health education and life style interventions such as sociodemographic factors, cultural factor of consanguinity and associated medical disorders. Third trimester anomalies were analysed with respect to perinatal outcome at birth.

Availability of data

From hard copies of Medical records.

Authors Contribution Concept and data review, manuscript preparation: PD, Data collection, Data analysis, manuscript preparation: SG. Data analysis and manscript checking AMA.

Compliance with ethical standards

Conflict of interest Myself, Papa Dasari and SonalGarg, Ashraf M Ali have no conflicts of interests to declare.

Ethics approval Not applicable as it is a retrospective study; Approval taken for use of Medical records.

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