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A study on referral pattern for fetal echocardiography and identifying the various risk factors for congenital heart defects

Abstract

Background: Fetal Echocardiography is becoming an important tool for the detection of CHD but results can be unpredictable, depending on various factors like expertise, position of the baby and referral indications. Various factors are associated with detection of CHD which need further evaluation.

The present study was undertaken to study the referral pattern for Fetal Echocardiography (FE) at a tertiary Pediatric Cardiac Centre and further to identify the various risk factors associated with Congenital heart defect.

Results: The study was conducted on 200 consecutive pregnant women who were referred for fetal echocardiography at Pediatric Cardiac Unit of the hospital. The mean maternal age and the mean gestational age were 26.85 ± 4.6 years and 30.36 ± 5.14 weeks at the time of fetal screening. On evaluating the various referral indications, gestational diabetes mellitus was found in 55% of the study subjects, but CHD was detected in 3.6% of their fetuses. Hypothyroidism was the second commonest indication (16.5%) among the referrals and 3% of their foetuses were found to have CHD. The indication that accounted for the maximum number of CHD (50%) was cardiac anomaly detected on ultrasonography, followed by single umbilical artery, in which 33.3% of CHD was detected. CHD was however significantly associated only with the referral indications of cardiac anomaly on USG (p value < 0.001) and single umbilical artery (p value = 0.033). The association of the other referral indications of the subjects was not found to be significant.

Conclusion: Majority of women referred late for the fetal echocardiography screening. Extracardiac anomaly during second trimester scan warrants immediate fetal cardiac evaluation.

Keywords: fetal echocardiography, congenital heart defect(CHD), diabetes, extracardiac anomalies

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Background

A congenital heart defect [CHD] is defined as a defect in the structure of the heart or great vessels occurring during fetal development.[1] The prevalence of CHD globally is around 8 per thousand live births[2] with a mortality of 3.9 per 100,000 population.[3] Prenatal detection of CHD is of utmost importance since heart defects are associated with significant morbidity and mortality, besides antenatal detection helps in planning the further management. Fetal echocardiography is becoming an important tool for screening and can identify many structural heart diseases but it is highly variable, depending on operator expertise, gestational age, fetal position, and the type of cardiac defect but there is improvement in detection of CHD lately.[4] The yield of fetal echo in detection of CHD depends not only on the expertise of the performer but also on the indication of referral. Nevertheless its an important tool for early detection of CHD and with the availability of newer and highly sophisticated dedicated machines, CHDs can be detected in utero during second trimester or even in late first trimester with a detection rate of 85–95 % in specialized units.

There are numerous risk factors associated with development of CHD, pregestational diabetes is an important and most documented one by various authors.[5–9] American Heart Association in 2014 has provided a list of risk factors for screening the high-risk mothers leading to CHD in fetus.[6] The referral pattern for fetal echocardiography among pregnant women is a reflection of the spectrum of women visiting for fetal echocardiography, and it assists in identifying and for better understanding of congenital heart defects and the risk factors associated with it.

Methods

The aim of the study was to study the referral pattern for Fetal Echocardiography (FE) at a tertiary Pediatric Cardiac Centre and to identify the various risk factors associated with Congenital heart defect.It was a prospective observational study conducted at Pediatric Cardiac Unit of a University affiliated tertiary medical care facility.

Study population: The study was conducted on 200 consecutive pregnant women who were referred for fetal echocardiography during the study period at Pediatric Cardiac Unit of the hospital. Valid, informed and written consent was obtained from the pregnant females before including them in the study. The study was approved by the Ethical committee of the Medical College.

Sampling procedure: The information was recorded in a predesigned proforma for the profile of patients (pregnant women), indications of referral and the risk factors (if any) associated with CHD were identified.

Inclusion criteria

1. All the pregnant women referred from Obstetrics and Gynaecology Department to Pediatric Cardiac Unit for fetal echocardiography after taking informed consent.

Exclusion criteria

1. Patients not willing to be part of the study and refused to give the consent.

Data collection procedure

A pre-designed preform was used to collect demographic information i.e age, sex, height, weight and relevant history which include maternal history of any chronic disease, previous history of CHD in a child, exposure to drugs during pregnancy. The primary indications for referral for fetal echocardiography was obtained from the history, Obstetrics case records and files. A detailed structured questionnaire was used to identify various risk factors like previous obstetric history (gestational age, the gravida etc).

Description of methods used in the study

Fetal echocardiography: It was done by the trained Pediatric Cardiologist using Voluson E8 Machine (dedicated Obstetric echocardiography machine). The 2D Echo included 4-chamber, 3 vessels, short axis, arch and Ductal views, Colour Doppler and Tissue Doppler (if required) was done. The fetus was screened for any structural heart defect (shunts/ obstructive lesions) and rhythm abnormalities. Functional Echo using 2D doppler and Tissue doppler was done in mother having pregestational or gestational Diabetes and various velocities were recorded and ratios were calculated to delineate systolic and diastolic dysfunction. All the fetal echocardiographic examinations were done in a dedicated Pediatric cardiac and Fetal medicine clinic. A single fetal echo examination usually took around 15-20 mins but sometimes it was prolonged when the position of the baby was not suitable for visualisation of cardiac chambers. In these scenarios a repeat evaluation was done after mother was asked to walk for some distance in the same sitting or was called later after 48 hrs. Once a CHD was detected, parents were counselled in details to allay all the anxieties related to type of CHD and their management. In a case of significant defect, NICU was informed prior to delivery and a repeat echo was done immediately after the baby was born, diagnosis was confirmed and child was managed under Pediatric cardiac Unit.

Data analysis

Collected data was formulated in Microsoft Excel. Comparisons and analysis of data was done using the latest version of Statistical Package of Social Science (SPSS-25). Quantitative data were expressed as mean±standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent sample t-test was used to compare two means. Chi-square test or Fisher's exact test (whichever was applicable) was used to determine the association between the various risk factors and occurrence of CHD. Data comparison and analysis was made to find out the significance of the study, P value <0.05 was considered as significant.

Ethical consideration

Ethical clearance from the institutional Ethical committee was obtained prior to study. The Institutional Ethical Clearance No. was 140/FM/IEC

The nature of the study was fully explained to the participant and written informed consent was obtained from them.

Observations and results

The pregnant women were referred to Pediatric cardiac Unit from the Obstetrics and Gynaecology Unit and 200 consecutive Fetal Echocardiographic examinations on pregnant women were included for the study.

Distribution and general characteristics of study group: The majority of participants (96%) were under the age of 35 years with the mean maternal age was 26.85 ± 4.6 years (Table 1). The mean height and weight of the women was 153.52 ± 3.1 cm and 62.97 ± 8.5 kg respectively. The mean body mass index (BMI) of the women at the time of fetal screening was 26.7 ± 3.3 kg/m^2. Most of the women (67%) were multigravida.

Timing of referral: The gestational age of referrals varied from 16 weeks to more than 37 weeks and the mean gestational age was found to be 30.36±5.14 weeks (Table 1). Most of the referrals (70%) were having the Fetal Echocardiographic examination after 27 weeks of gestational age. The delay in referral for fetal echo was due to delayed presentation at our hospital which is a tertiary level care and majority of case were referred late from remote areas. Besides during the era of covid the routine evaluation of high risk mothers suffered leading to erratic visits and poor follow up.

Table 1 Baseline characteristics of study subjects

Variables	Mean ± S.D	Median	Range
Maternal age (years)	26.85 ± 4.6	26	19-40
Gestational age of presentation (weeks)	30.36 ± 5.14	32	17-39
Height (cm)	153.52 ± 3.1	153	146-160
Weight (Kg)	62.97 ± 8.5	61.0	48-92
BMI (Kg/m^2)	26.7 ± 3.3	25.9	20.8-37.8

Indications for fetal echocardiography: Various referral indications that were evaluated, maternal medical disorders (80.5%), being the most common primary indication for referral. It included pre-gestational and gestational diabetes mellitus, hypothyroidism, pregnancy-induced hypertension, Systemic Lupus Erythematosus, and Rh-incompatible pregnancy. Fetal indications were the second most common reason for referral (19.5%), which included fetal bradycardia, echogenic intracardiac foci, single umbilical artery, cardiac anomaly on ultrasonography, and polyhydramnios. Bad obstetric history accounted for 18% of the women, which included spontaneous abortions (SA), intrauterine deaths (IUDs), and unexplained early neonatal deaths. A family history of congenital heart disease contributed 7% of the total indications while 2% of the women had a history of Down syndrome in their previous child. A total 5% of the women were in miscellaneous categories of referrals, which included vitiligo and haemophilia-A (Table 2). Since multiple indications were present in a some of the participants, the total percentage of women exceeded 100%.

Fetal echocardiography findings in the study women: Out of 200 fetal echocardiography scans, 11 fetuses (5.5%) were found to have a specific congenital heart defects, while 14 fetuses (7%) were found to have functional cardiac abnormalities. Functional cardiac abnormalities were considered as transient abnormality which might later disappear but still representing an underlying defect or chromosomal abnormality, while any structural abnormality in cardiac chambers or great arteries were included in structural heart defects. A structurally normal heart was found in 175 fetuses (87.5%). Table 2 shows the categorisation of the patients based on the various referral indications and the number of CHDs detected in them. A total of 7 out of 14 women, i.e., 50% referred with an indication of cardiac

anomaly on ultrasonography screening, were found to have congenital heart defects, the maximum proportion of CHD. While one out of three women referred with an indication of single umbilical artery was found to have a congenital heart disease. There was one CHD (8.3%) in each group of 12 polyhydroamnios women and 12 women with a history of CHD in their previous child. One CHD was detected in the fetus of one of the 23 women who had a referral indication of previous unexplained early neonatal deaths. CHD was detected in the fetus of four of 110 women (3.6%) with gestational diabetes mellitus. Only 1 out of 33 women (3%) with hypothyroidism was found to have CHD in their fetuses. None of the fetuses with echogenic intracardiac foci (5), foetal bradycardia (5), and history of Down syndrome in previous child (4) had CHD. However, six women were in the miscellaneous group, four of whom had haemophilia A and two of whom had vitiligo. CHD was not detected in their foetuses.

Spectrum of congenital heart disease among fetuses: Table 3 illustrates the various types of congenital heart diseases that were found among fetuses on Fetal echocardiography. Out of 11 CHDs, AV canal defects were the most common, accounting for 36.4% of the total CHDs. Hypoplastic left heart syndrome (HLHS) was the second most common (27.3%) CHD detected. The distribution of single ventricle and isolated ventricular septal defect (VSD) was equal, i.e., 18.2%. Apart from CHDs, various other cardiac abnormalities were also found in the fetuses on echocardiography, as depicted. A significant tricuspid regurgitation (TR) was found in the fetuses of six women. Five fetuses had ventricular disproportion, of which three had more left ventricular (LV) than right ventricular (RV) disproportion. Dilated RV was found in two women, while one had ventricular hypertrophy.

Type of congenital heart disease in each group: Different types of CHDs were detected in the various categories of referral indications are depicted in Table 3. In the category of gestational diabetes mellitus, four fetuses were found to have CHDs (36.7% of all detected CHDs), which included one AV canal defect, two HLHS, and one isolated VSD. With polyhydramnios and single umbilical artery, one fetus in each group was found to have CHD, which was HLHS.

Association between various factors and congenital heart diseases: There was no significant association with the parity and age of the mother with the incidence of CHD in the fetus (Table 4). The association between the various referral indications and CHD is illustrated in Table 5. As seen in the table the association between cardiac anomaly and the presence of single umbilical artery on Ultrasonographic screening and incidence of CHD was found to be statistically significant (p value <0.05). The association of congenital heart defect with advanced maternal age was also studied by Independent samples t test but no significant difference was found between mean maternal age of the two groups. No other referral indication has the significant association with the CHD.

Table 2 Referral indications and incidence of congenital heart diseases

Referral indications	Study subjects* (N = 200) n (%)	Congenital heart diseases n (%)
Cardiac anomaly on Ultrasonography	14 (7)	7 (50)
Single umblical artey	3 (1.5)	1 (33.3)
Polyhydroamnios	12 (6)	1 (8.3)
Previous child with CHD	12 (6)	1 (8.3)
History of previous unexplained early neonatal deaths	23 (11.5)	1 (4.3)
Gestational Diabetes Mellitus	110 (55)	4 (3.6)
Hypothyroidism	33 (16.5)	1 (3)
Pregestational Diabetes Mellitus	10 (5)	0 (0)
Echogenic intracardiac foci	5 (2.5)	0 (0)
Fetal Bradycardia	5 (2.5)	0 (0)
History of SA/IUDs	13 (6.5)	0 (0)
Previous child with Down Syndrome	4 (2)	0 (0)
Systemic Lupus Erythematosus	2 (1)	0 (0)
Pregnancy Induced Hypertension	3 (1.5)	0 (0)
Mother with CHD	2 (1)	0 (0)
Rh-incompatible pregnancy	3 (1.5)	0 (0)
Miscellaneous	6 (3)	0 (0)

*Multiple referral indications were present in a single participant. Therefore total no. of subjects exceeded 100%.

Table 3 Type of CHD in each group of referrals

Referral indications	Number of congenital heart disease detected (n)	Type of congenital heart disease *	(n)
Cardiac anomaly on Ultrasonography	7	AV Canal Defect	2
		HLHS	3
		Single Ventricle	2
Gestational Diabetes Mellitus	4	AV Canal Defect	1
		HLHS	2
		VSD (isolated)	1
Hypothyroidism	1	AV Canal Defect	1
Polyhydroamnios	1	HLHS	1
History of previous unexplained early neonatal deaths	1	VSD (isolated)	1
Single umblical artey	1	HLHS	1
Previous child with CHD	1	VSD (isolated)	1

*Multiple referral indications were present in a subject. Therefore, while showing various types of CHD in various categories of referral indications, one type of CHD may be overlapped between two or more categories. As a result, the total number and type of CHD may be greater than 100%

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Table 4 Association between maternal determinants and congenital heart diseases

Maternal determinants		Study subjects n (%)	Congenital heart diseases n (%)	p value
Gravidity	Primi Gravida	62 (93.9)	4 (6.1)	0.807
	Multi Gravida	127 (94.8)	7 (5.2)	
Maternal Age	Upto 35 years	192 (96)	11 (100)	0.486
	More than 35 years	8 (4)	0	

Table 5 Association between various referral indications and CHD

Risk factors	Study subjects	Congenital heart disease n (%)	Normal structural heart n (%)	p value
Cardiac anomaly on Ultrasonography	Present	7 (50)	7 (50)	0.000
	Absent	4 (2.2)	182 (97.8)	
Single umblical artey	Present	1 (33.3)	2 (66.7)	0.033
	Absent	10 (5.1)	187 (94.7)	
Polyhydroamnios	Present	1 (8.3)	11 (91.7)	0.657
	Absent	10 (5.3)	178 (94.7)	
Previous child with CHD	Present	1 (8.3)	11 (91.7)	0.657
	Absent	10 (5.3)	178 (94.7)	
History of previous unexplained early neonatal deaths	Present	1 (4.3)	22 (95.7)	0.797
	Absent	10 (5.6)	167 (94.4)	
Gestational Diabetes Mellitus	Present	4 (3.6)	106 (96.4)	0.201
	Absent	7 (7.8)	83 (92.2)	
Hypothyroidism	Present	1 (3)	32 (97)	0.496
	Absent	10 (6)	157 (94)	

Discussion

Congenital heart defect is the commonest among the birth defects affecting millions of children world wide. One-fifth of children are likely to have significant problems that necessitate intervention in the first year of life.[10] CHD is a major and fast-growing health issue for children worldwide. Because of the severity of disease, which affects the quality of life, early detection is a important in order to implement early intervention.[11] A study conducted by Bhambani in which 1445 fetal echo were performed, of which 1183 women had no risk factor associated with CHD. A total of 76 (52.6 per 1000) fetuses were found to have some cardiac abnormality of which, 12 (8.3 per 1000) had CHD. In our study 11 fetuses (5.5%) were found to have CHD while 14 fetuses (7%) were found to have functional cardiac abnormalities. While another study from Northern India found incidence of CHD as 15 per 1000.[12,13]

In a recent study by Qiu X and coworkers[14] evaluated fetal echocardiography of 67,834 pregnant women in which 1492 fetuses were found to have CHD. Prenatal genetic examination on amniotic fluid and cord blood, revealed chromosomal abnormalities in 20.43% of foetuses with CHD. Hence, they recommended interventional prenatal genetic evaluation for fetuses with CHD, to rule out the chromosomal abnormalities.

A cross-sectional study on one hundred and one pregnant women in Egypt was done[15] to determine the clinical utility of fetal echocardiography (FE). They performed FE and detected congenital heart defects (CHDs) in 34.6%, of which complex cardiac lesions that were diagnosed, included common atrioventricular canal, cardiac masses, fetal arrhythmias and cono-truncal anomalies. Later, they performed postnatal transthoracic echocardiography on neonates and concluded that fetal echo can accurately diagnose majority of the complex lesions, but can miss few critical defects like aortic coarctation.

A retrospective analysis on fetal echocardiography of 1262 fetuses[16] studied various referral indications like abnormal anatomy scans, maternal medical disorders, family history of CHD, and fetus growth restrictions. They reported CHD in 22.7% of the fetuses. They also performed prenatal invasive testing and reported chromosomal abnormalities in 55% of the CHD-detected foetuses. In their study, they concluded that most CHDs occur during pregnancy even without any underlying prenatal risk factor, emphasising the importance of routine foetal echocardiography scans and finding the association between CHD and chromosomal abnormalities in fetuses.

In our study, the majority of referrals had a primary indication as gestational diabetes mellitus (55%). However, only 4% of them were detected to have CHD in their fetuses, and the association between gestational diabetes mellitus and CHD detection was not found to be statistically significant (p value = 0.201). Also, 5% of the referrals had pregestational DM but none of their fetuses were found to have CHD in them. Øyen et al.,[17] did a cohort study of two million births over 34 years and found a four-fold increase in the risk of CHDs in maternal pre-gestational DM (both types 1 and 2). In a systemic review, Depla et al.,[18] found that maternal diabetes (Pregestational and gestational) is associated with fetal cardiac hypertrophy, ventricular diastolic dysfunction, and overall impaired myocardial performance. This observation in our study is different from other studies where majority of CHD is diagnosed in mothers with diabetes, this might be due to small sample size and association may be detected if we had enrolled more numbers of mothers with diabetes especially with pregestational diabetes.

The second most common primary indication among referrals was hypothyroidism (16.5%) and CHD was found in 3% of their fetuses. Although the association between hypothyroidism and the detection of CHD was not found to be significant enough (p value = 0.496). However, a study by Grattanet showed CHD in 11.3% of fetuses of mothers having hypothyroidism, suggesting a significant correlation between maternal hypothyroidism and the development of CHD in the fetus.

Total of 6% of the women were referred with the indication of polyhydramnios. 8.3% of their fetuses were found to have CHD and the association was not significant (0.657). Polyhydramnios

in association with CHD suggests the presence of extracardiac or chromosomal anomalies as the increase in amniotic fluid was most likely related to defects causing difficulty in swallowing in fetuses. A study from Hungry found a significant association between CHD and Polyhydramnios.[19] The maximum proportion of CHD, i.e., 50%, was found in the women having an indication of cardiac anomaly on ultrasonography screening, and the correlation between cardiac anomaly on USG and the CHD detection was statistically significant (p value < 0.001). Our findings were similar to those of Nair et al.,[8] with a CHD detection rate of 58%, Regmi et al.,[9] with a CHD detection rate of 50%, and Li et al.,[20] with a CHD detection rate of 64%.

The second highest proportion of CHD (33.3%) was found in the referrals having an indication of single umbilical artey in the fetuses and the association was found to be significant (p value = 0.033). In a retrospective analysis of 152 fetuses with a single umbilical artery[21] reported a risk of 12.5% CHD in the fetuses. Another study[22] on 436 pregnant women having fetuses with a single umbilical artery, found a risk of 18.2% cardiac abnormalities in them.

8.3% of congenital heart diseases were found in referrals with a history of CHD in their previous child. However, the association was statistically not significant (p value = 0.657). CHD recurrence is a well-known phenomenon, and the frequency varies depending on the type of CHD in the first degree relative.[8,23] In this study, there were 12 women who had a history of CHD in their previous child, of which 8 had isolated VSD and 4 had PDA.[24]

The timing of referral was important in our study. We found that the mean gestational age of the referrals was 30 weeks, which is past the recommended time for any intervention. A possible explanation for this could be the fact that the majority of our study population was from small cities and rural locations, where there is a lack of fetal echocardiography facilities. Also, delays are more often caused by a lack of adequate knowledge of referral indications and proper timing. Another important limiting factor is the proper imaging which depends on the expertise of the operator as well as patients related factors like the lie of the baby or obese mother where the echo windows are not proper.

Conclusion

This study, though conducted on a limited sample size, had an entirely diverse profile of study women in terms of their limited knowledge and awareness and mostly belonging to rural residential areas. Out of all the referral indications, we found the maximum number of CHD in those who were referred with cardiac anomaly on screening, however it was much lower in GDM which was the commonest indication for referral. Thus, prenatal ultrasonography screening becomes of the utmost importance in the earliest detection of CHD.

Pregnant women with pregestational and gestational diabetes mellitus should be referred for a prenatal screening earliest in their 20 weeks of gestation to rule out any cardiac anomalies in their fetus.

Since there are legal as well as maternal safety restrictions beyond a specified gestational age of fetus for any decision, prompt referral for fetal echocardiography to rule out CHD is crucial.

Limitations:

a. Small sample size.

b. Functional echocardiographic parameters were not recorded.

c. Data on follow up of patients of CHD detected on fetal echo after delivery is not mentioned to know the outcome (correct/missed diagnosis).

What's the study adds: Cardiac anomaly on USG screening warrants detailed evaluation by fetal echo for CHD.

Declarations: Ethics approval and consent to participate- Ethical clearance was taken from the Instituitional ethical committee.

Consent for publication: Taken.

Availability of data and material- available from hospital records.

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Authors' contributions: SZ collected data and written the manuscript, SA reviewed the data, prepared the manuscript and made the changes.

Conflicts of interest

None.

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