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ORIGINAL ARTICLE

Referral Pattern for Fetal Echocardiography Over 10 Years in a Single Fetal Imaging Centre from Southern India

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Abstract
Aim To study the trend in referral patterns for fetal echocardiography (FE) and the outcome
Methods Retrospective study of fetuses referred to a single fetal imaging center for FE from Jan 2008 to Dec 2017. The study group was divided into group 1 (2008–2012) and group 2 (2013–2017). Indications were categorized into 'low-risk', 'maternal-risk' and 'fetal-risk'. Detection of cardiac defect (CHD) was noted as abnormal outcome and it was analysed in relation to the referral indication.
Results The study group had 32,679 cases, 11,468 in group 1 and 21,211 in group 2. Total number of referrals showed an increase of 84% between first and second half of study. 'Low-risk' referrals were the most common in both groups but high risk referrals had shown an increase of 24.5% over years. Maternal diabetes was the most common 'maternal-risk' factor and abnormal cardiac finding in obstetric scan was the common 'fetal-risk' indication. Incidence of CHD increased from 4.6 to 10.2% during the study period. CHD was seen more in 'fetal-risk' indications (65%) compared to other risk groups ($p < 0.05$). Maternal-risk indications individually did not show a significant relationship to CHD. Abnormal cardiac findings in scan, extra-cardiac anomaly, aneuploidy screen positivity, single umbilical artery, growth and liquor abnormality showed a higher risk for CHD. Among low-risk 22.5% showed CHD.
Conclusion Referral of high-risk cases for FE has increased recently. Abnormal fetal findings in scan or screening tests was significantly associated with fetal CHD. A significant percentage of CHD was detected in the low-risk group. Strengthening fetal cardiac screening is needed to optimise appropriate risk stratification as well as to increase detection of cardiac anomalies.

Keywords Fetal echocardiography · Referral pattern · Indications

Introduction

Congenital heart disease (CHD) is the commonest congenital anomaly and its prevalence is estimated to be 8–10/1000 live births [1]. Timely diagnosis is important as around 25% babies with CHD have critical lesions that present with significant morbidity and mortality in the neonatal period [2]. Fetal cardiac screening has become a part of routine obstetric scan in the second trimester. Increased availability of ultrasound, improved awareness and training has led to improvement in skill sets for fetal cardiac imaging in recent years. International guidelines mention specific indications for exclusive fetal echocardiography. This is expected to improve the prenatal detection rate, counselling and postnatal care in fetuses. Because of all these observations, referral pattern for fetal echocardiography (FE) had changed over the years. And

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any change in the trend is likely to influence the medical, socio-economic and ethical scenario in that population.

Aim

The aim of this study was to understand the trend of referral for fetal echocardiography in our center over a period of 10 years. The additional objectives were to evaluate the outcome of the fetal echocardiography in the study group and to analyze if the indication for referral had any relation to the outcome.

Materials and Methods

This was a retrospective study of fetuses referred to our centre for FE from Jan 2008 to Dec 2017 (10 year period). The major variable studied was the indication for referral. To observe the difference over the time period, the study group was divided into group 1 (2008–2012) and group 2 (2013–2017). Data was retrieved from medical records (Sonocare version 8.0.0.1). Indications were categorised into three groups: 'low risk', 'maternal risk' and 'fetal risk' based on the referral indication. Cases referred due to maternal risk factors or familial risk factors were grouped under 'maternal risk'. Those referred due to abnormal fetal findings in ultrasound or screening tests were taken under 'fetal risk' and all others without any specific risk mentioned in referral note or medical records were grouped as 'low risk'. Outcome of FE was termed as normal or abnormal report based on the cardiac findings noted in each case. All cardiac abnormalities were taken as abnormal report outcome and fetal arrhythmias were excluded from the analysis. The type of cardiac defect was not taken into account as it was beyond the scope of this study.

Statistical Analysis

Descriptive analysis of the referral indications in both groups was done. In addition, the relationship between the indications and outcome was analyzed for the whole study group, then individually for group 1 and 2. Both groups were then compared. Data was analysed using R software version of 3.5.1. All collected information on referral types and CHD cases were summarised using frequency and percentages. 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. A p value of < 0.05 was considered significant. Relative Risk were calculated among maternal and fetal risk factors with the FE report. A risk ratio > 1 suggests an increased risk of that outcome in the exposed group.

Results

32,904 fetuses were referred for fetal echocardiography during the 10 year study period (11,534 in group 1 and 21,370 in group 2). Of these 225 cases were those referred for reassessment of findings, hence these were removed from the study. Thus final study group comprised of 32,679 cases, 11,468 in group 1 and 21,211 in group 2. This included 2181 (6.6%) fetuses from twin gestations. There was an 84% increase in number of referrals from first to second group.

Average maternal age and gestational age were not different between groups. Third trimester referrals reduced from 36 to 8%. Average maternal age in group 1 was 27.7 years and in group 2, 28 years. Average gestational age in group 1 was 23.4 weeks (18–28 weeks) and in group 2, 22.6 weeks (18–27 weeks).

Referral Indications

Distribution of different types of referral indications among the two groups were as shown in Fig. 1. Majority of referrals (65%) were from the 'low risk' category. Maternal risk indications formed 19% and fetal risk indication 14.6%. A small number of cases (1.4%) had both fetal and maternal risk indications. 'Low risk' indications showed a decreasing trend over years (from 80.6% in group 1 to 57% in group 2) as referral for high risk indications increased. Referral for 'maternal risk' indications increased from 10.4 to 24% and 'fetal risk' indication increased from 8.8 to 18% between group 1 and group 2 (Fig. 1).

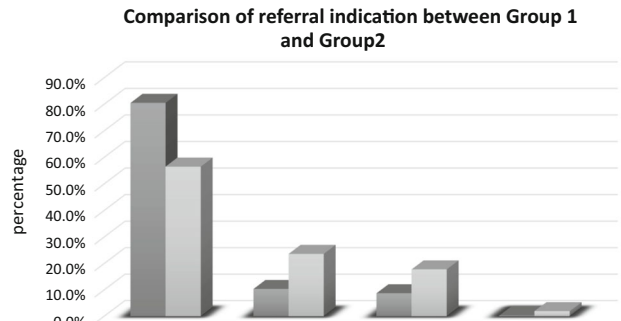

Fig. 1 Distribution of types of indications for fetal echocardiography in both time groups. Referrals for maternal and fetal risk factors showed increasing trend from group 1 to group 2

In order of commonality maternal diabetes (37%), previous offspring with CHD (15%) and family history of anomalies (12%) topped the chart among 'maternal risk' indication, and this pattern was the same in both time periods. In the 'fetal risk' category, abnormal cardiac findings in scan was the most common indication (40%) followed by echogenic intracardiac focus (17%) and referral for extra-cardiac anomaly (16%). Between the two groups, echogenic focus was more common referral than extra-cardiac anomaly in the second time period (Table 1).

Outcome

Fetal echocardiography was reported abnormal in 8.2% of cases in the total study group. The proportion had increased from 4.6% in group 1 to 10.2% in the second group which was more than double (Table 1 sup).

When the incidence of CHD under each indication category was looked at, more abnormalities were noted in the 'fetal risk' indications compared to others. Among all abnormal cases 66.6% were in the 'fetal risk' category (62% in group 1, 68% in group 2) and statistical analysis showed this association as significant with p value < 0.05. 'Low risk' indications were the second common association with CHD (22.5% of total; 31.2% in group 1 and 20% in group 2). In both time periods 'maternal risk' indications were less commonly associated with CHD in the fetus than 'low risk' indications (Fig. 2).

The commonly noted high risk indications in both maternal and fetal risk categories were analysed individually to correlate with the abnormal outcome of FE (Table 2). Maternal risk indications individually did not show a significant relationship to presence of CHD in the fetus. In maternal diabetes when gestational and pre-gestational diabetes were analysed separately 3% and 5% of them had CHD respectively. Among the fetal risk indications, abnormal cardiac findings in scan and presence of extra-cardiac anomaly were strongly associated with abnormal fetal heart. All other fetal indications except echogenic intracardiac focus also showed significant risk

Table 1 Distribution of maternal and fetal risk indications in both time periods shown in this table

High risk indications	Period		Total
	2008–2012 group 1	2013–2017 group 2	
Maternal			
Maternal diabetes	560 (41.5%)	2432 (36.5%)	2992 (37.3%)
Previous offspring with CHD	198 (14.7%)	975 (14.6%)	1173 (14.6%)
Family history of anomalies	198 (14.7%)	769 (11.5%)	967 (12.1%)
Hypothyroidism	22 (1.6%)	766 (11.5%)	788 (9.8%)
BOH/IUD	149 (11%)	351 (5.3%)	500 (6.2%)
Rh negative	44 (3.3%)	464 (7%)	508 (6.3%)
PIH	55 (4.1%)	207 (3.1%)	262 (3.3%)
Assisted conception	20 (1.5%)	230 (3.4%)	250 (3.1%)
SLE	27 (2%)	113 (1.7%)	140 (1.8%)
Advanced maternal age	25 (1.8%)	125 (1.9%)	150 (1.9%)
Family history of Chromosomal abnormalities	25 (1.8%)	109 (1.6%)	134 (1.7%)
Others	27 (2%)	128 (1.9%)	155 (1.9%)
Total	n = 1350	n = 6669	n = 8019
Fetal			
Abnormal cardiac view	480 (42.7%)	1810 (39.4%)	2290 (40%)
Echogenic cardiac foci	92 (8.2%)	877 (19.1%)	969 (16.9%)
Extra-cardiac anomaly	239 (21.3%)	651 (14.2%)	890 (15.6%)
Aneuploidy screen positive	121 (10.8%)	700 (15.2%)	821 (14.3%)
SUA	39 (3.5%)	367 (8%)	406 (7.2%)
Liquor abnormality	110 (9.7%)	104 (2.2%)	108 (1.9%)
Growth abnormality	43 (3.8%)	65 (1.4%)	214 (3.7%)
TTTS	0 (0%)	25 (0.5%)	25 (0.4%)
Total	n = 1124	n = 4599	n = 5723

BOH bad obstetric history; *IUD* intrauterine demise; *SLE* systemic lupus erythematosus; *PIH* pregnancy induced hypertension. *SUA* single umbilical artery; *TTTS* twin to twin transfusion syndrome

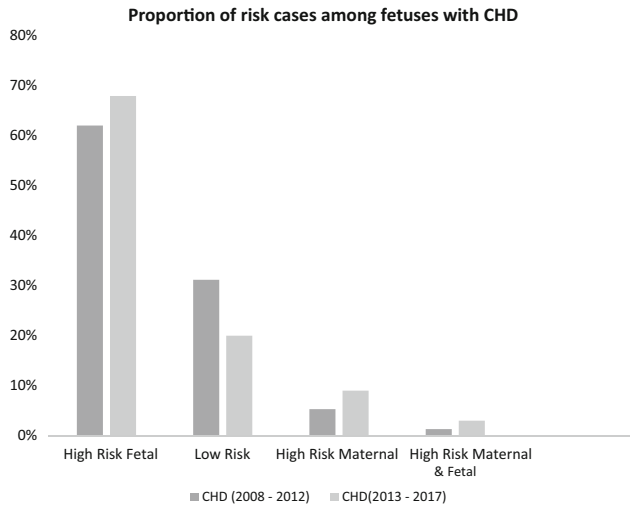

Fig. 2 Chart showing the proportion of risk group among fetuses with CHD in both time periods. In both the groups, high risk fetal indications yielded maximum number of CHD

relationship (Table 2). Fetuses who were referred for suspected extra-cardiac anomaly showed CHD in 25%. Among the twins 156 (7.2%) had shown abnormal outcome (2.3% in group 1 and 8.2% in group 2). It is worth mentioning that among cases referred as suspected cardiac abnormality, 34% were diagnosed to be normal.

Discussion

Referral for fetal echocardiography had shown a significant increase over the years. Timing of referral has also changed, with a reduction in late gestation referrals. This may be due to increased awareness on appropriate timing for prenatal detection of cardiac anomalies and its implications in neonatal life. However, the average gestation at referral was above 22 weeks in both groups which could be due to socio-economic or demographic factors, such as availability or accessibility of fetal imaging centres. A similar study on FE referral pattern from northern India also showed mean gestation at referral as 24 ± 5 weeks [3]. Addressing the factors for the delay may make the referral time more appropriate for Indian scenario as the legal limit for termination for pregnancy is 20 weeks. Kanwal et al. from Pakistan studied FE referrals beyond 33 weeks with 60% of mothers being educated; and noted that 94% of these were referred by obstetricians and 89% were booked

Table 2 Relative risk for CHD in each maternal risk and fetal risk indications

High risk	Indication	Fetal echocardiography		RR (CI)
		Normal	Abnormal	
Maternal	Maternal diabetes	2892 (96.7%)	100 (3.3%)	0.38 (0.31–0.47)
	Previous offspring with CHD	1108 (94.5%)	65 (5.5%)	0.66 (0.52–0.84)
	Family history of anomalies	922 (95.3%)	45 (4.7%)	0.56 (0.42–0.74)
	Hypothyroidism	760 (96.4%)	28 (3.6%)	0.43 (0.29–0.61)
	BOH/IUD	491 (96.7%)	17 (3.3%)	0.40 (0.25–0.64)
	Rh negative	476 (95.2%)	24 (4.8%)	0.58 (0.39–0.86)
	PIH	247 (94.3%)	15 (5.7%)	0.69 (0.42–1.14)
	Assisted conception	241 (96.4%)	9 (3.6%)	0.44 (0.23–0.83)
	SLE	144 (96%)	6 (4%)	0.69 (0.35–1.36)
	Advanced maternal age	132 (94.3%)	8 (5.7%)	0.48 (0.22–1.06)
	Family history of Chromosomal abnormality	126 (94%)	8 (6%)	0.72 (0.37–1.42)
	Others	145 (93.5%)	10 (6.5%)	0.78 (0.43–1.43)
Fetal	Abnormal cardiac view[a]	777 (33.9%)	1513 (66.1%)	17.12 (16.07–18.23)
	Echogenic cardiac foci	943 (97.3%)	26 (2.7%)	0.32 (0.22–0.47)
	Extra-cardiac anomaly[a]	660 (74.2%)	230 (25.8%)	3.34 (2.97–3.76)
	Aneuploidy screen positive[a]	747 (91%)	74 (9%)	1.09 (0.88–1.37)
	SUA[a]	333 (82%)	73 (18%)	2.22 (1.79–2.74)
	Growth abnormality[a]	84 (77.8%)	24 (22.2%)	2.72 (1.91–3.88)
	Liquor abnormality[a]	167 (78%)	47 (22%)	2.70 (2.09–3.49)
	TTTS[a]	12 (48%)	13 (52%)	6.35 (4.35–9.27)

BOH bad obstetric history; *IUD* intrauterine demise; *SLE* systemic lupus erythematosus; *PIH* pregnancy induced hypertension; *SUA* single umbilical artery; *TTTS* twin to twin transfusion syndrome

[a]Indication with significant association with CHD

from first trimester. Based on this they suggested improving awareness among obstetricians and mothers to reduce late referrals [4].

Most of the referrals were from the low risk category and 22.5% of total CHD was from this group. Though existing guidelines do not mention referral for FE in low risk mothers, we do get routine referrals. These mothers without any maternal risk factor were referred to us directly for fetal echocardiography with or without an outside obstetric scan. It is likely that they come under the fetal risk category, if they were screened prior to referral.

High risk referrals had increased in the second half of the study period. Among the high risk indications, referral for maternal risk factors was more common than fetal indications in both the time periods. Improved awareness among referring obstetricians about maternal risk factors related to CHD as well as increased detection of cardiac abnormalities during obstetric scans can explain the change observed. Studies have observed increase in frequency of suspicion for CHD during routine obstetric scan by improvement in the skills of obstetric sonographers [5]. Though referral for maternal risk factors was higher, the yield in terms of CHD detection was significant with fetal factors than maternal. None of the maternal factors showed significant relative risk for CHD by analysis.

The most frequent maternal risk indication was diabetes mellitus, similar to the observation from Northern India [3]. In a retrospective study, Roman et al. [6] demonstrated that poor glycemic control (Hb A1c $> 8.5\%$) in early pregnancy is associated with an increased risk of CHD in offspring. In an observational study, Hunter et al. demonstrated that women with gestational diabetes have a higher risk of having a baby with CHD [7]. Among the diabetics in their study population, 3.6% had fetuses with CHD but the relative risk was not significant. Donofrio et al. [8] in the American Heart Association statement had categorized mothers with gestational diabetes with HbA1c < 6 as low risk. In our study due to non-availability of information we could not segregate based on HbA1c which might have possibly influenced our analysis.

The next common maternal indications were history of a previous child with CHD and family history of anomalies. A study published in 1991 by Callan et al. mentioned family history of anomalies as one of the common reasons for referral. Anupama et al. [3] reported that a previous child with CHD formed 7% of the total indications. AHA risk class mentions only CHD in relatives and risk stratification is based on degree of relationship [8]. In our study cardiac and non-cardiac anomalies in first to 4th degree relatives were considered as risk factor as per our policy which is based on the high rate of consanguineous marriages and spectrum of abnormalities seen. Gathering a complete family history is important in risk stratification and referral. Among the other factors, referral for assisted conception has shown an increase between groups and 4% of these had CHD. This needs further scrutiny with a larger sample in terms of method and source of conception.

When we looked at the overall outcome of fetal echocardiography in the study group a significant increase in incidence of abnormal cases were noted between the two time periods (4.6–10.2%) (Table 1 supplementary). Though this could be due to the increase of high risk referrals in the second group, more specifically it was the fetal risk indications that were associated with maximum number of CHD detection in both groups.

Among the fetal risk indications, abnormal cardiac findings during routine obstetric scan was 40% of total and it was a strong risk factor for fetal CHD in this study. From our personal observation, an increase in the fetal cardiac screening skills in the surrounding localities is noted in recent years. Accurate data on prenatal detection of CHD in India is not published to our knowledge and available information is only from tertiary units catering to fetal imaging. Hence the actual outcome of cardiac screening during obstetric scan remains unknown in our population. Similar findings have been observed in various studies [3, 9–11]. We also identified a false alarm positive rate of 34% of cases where CHD was suspected but FE was normal. Standardised optimal second trimester cardiac screening seems critical in fetal CHD detection.

The second common indication was intra-cardiac echogenic focus closely followed by referral for extra-cardiac anomaly. Though isolated echogenic focus has been proven by various studies to be a benign finding there still seems a concern about this entity. We could not find a significant association of CHD with this finding, whereas presence of extra-cardiac anomaly in fetus was strongly associated with CHD. In the study by Anupam et al (3) an echogenic intracardiac focus was the most common reason for referral and cardiac abnormality was the second common. This study was from a pediatric cardiac unit whilst ours is from a fetal imaging centre, which probably explains the variation in the pattern noted. Callan, Man Li and Wright in their studies had noted extra-cardiac anomaly to be associated with CHD in the fetus [9–11]. In our study 25% of cases referred as pure extra-cardiac anomaly showed CHD in addition.

Other risk factors like aneuploidy risk, single umbilical artery, growth restriction and liquor abnormalities also showed high risk of associated fetal CHD. Association between SUA and CHD seem to vary with population. The risk for CHD after the detection of SUA in an otherwise apparently normal fetus was reported to be small in an unselected population, whereas Man Li observed CHD risk in those referred for FE [10, 12].

The major strength of our study was the large sample size. In the absence of a population study, the observations made by us cannot be ignored as our referral units belong to lower and higher socio-economic areas as well as from both private and government centres. The major observation made on the fetal risk factors seem similar to worldwide reports.

Conclusion

Referral for fetal echocardiography has increased in recent years and a change in trend with increase in high-risk referral is noted. Referral for fetal risk factors especially abnormal cardiac findings during obstetric scan was significantly associated with presence of cardiac anomaly in the fetus. Observations made in this study reflect on improved awareness and expertise in the field of prenatal imaging in the recent years and the need for detailed echocardiography when abnormality is suspected. As significant number of low risk mothers had fetuses with CHD, prospective population studies with appropriate risk categorization of mothers and optimal cardiac screening of the fetuses seem the need of the hour to improve and standardize referral indications for fetal echocardiography.

Limitations

The main limitation of our study was its 'retrospective' nature. The sample studied is a population referred to a tertiary imaging center and may not represent a local population scenario. Risk stratification done based on the information provided by the referring doctor or from the available medical records, which may or may not represent the actual status.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interests.

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