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Original Article

Role of routine fetal echocardiography in an unselected group of pregnant women for prenatal detection of cardiac malformations

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ABSTRACT

Objectives: We investigated the potential for improvement in prenatal detection of congenital heart disease (CHD) by routinely performing detailed fetal echocardiography (FE) in all pregnant women.
Methods: Following routine obstetric sonography, 1445 unselected pregnant women were prospectively subjected to FE at gestational ages between 16 and 24 weeks, or at first visit, if they presented later. Maternal or fetal factors, conventionally known to be associated with risk of CHD, were noted.
The prevalence and detection rates of cardiac abnormalities were determined, and confirmation of findings by postnatal follow-up was done to ensure accuracy of FE. Prevalence of CHD was compared in pregnancies with or without conventional risk factors.
Results: The overall prevalence of CHD was 8.3 per 1000; only 2 CHD cases belonged to the high maternal risk group, while 10 cases were observed without maternal risk factors. Cardiac malformations were suspected in 14 fetuses during obstetric scan; but, only 5 of them had CHD, remaining 9 had structurally normal hearts. 50% of CHD cases occurred in pregnancies not associate with any (fetal or maternal) risk factor. The sensitivity, and specificity for prenatal CHD detection were 91.7% and 100% respectively.
Conclusions: Our study indicates that a substantial proportion of CHD cases occur in women not having high risk of giving birth to children with CHD. FE is a highly sensitive and specific test with strong predictive values. We recommend that FE should be done in every pregnancy.

1. Introduction

According to a rough estimate, every year, nearly 240,000 children in India are born with a congenital heart defect (CHD).[1] Accurate prenatal diagnosis has a potential to improve survival in such cases,[2] especially those who require, either prostaglandin infusion to maintain flow through ductus arteriosus in the immediate postnatal period, or rarely, emergent atrial septostomy.[3,4] In the background of limited availability of centers offering advanced neonatal cardiac care in our country,[1] need for prenatal recognition of complex cardiac malformations and timely referrals of such patients to centers equipped with obstetric as well as neonatal cardiac care, are even more relevant.

Cardiac anomalies are often missed during routine sonographic scans[5–7] because detailed cardiac examination requires special skill and is time consuming. Fetal echocardiography (FE) has very high sensitivity and specificity (more than 90% each) for the detection of cardiac malformations[8] and improves the rate of prenatal detection of CHD even in reportedly normal second trimester obstetric scans.[6] Based on these observations, some investigators have advocated inclusion of detailed FE as part of the fetal anomaly screening evaluation, even in low-risk pregnancies[9]; but due to lack of robust data, this practice has not been incorporated in the guidelines or international scientific statements[10,11] and is considered cost prohibitive by some.[12] This results in inadequate expert referrals for fetal cardiac screening. Despite observations that most neonates with CHD are born to women without any previously recognized risk factor,[4,10] only those women, who are deemed to be at high risk for producing children with CHD, are referred to cardiologists for detailed FE.[11]

To the best of our information, as far as unselected pregnancies are concerned, the Indian data on FEis limited to two studies,[13,14] which did not report the comparative diagnostic yield of the test in high and low risk groups; moreover, the follow-up data

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Table 1
Group distribution of prenatally detected cardiac malformations.

Indication for fetal echocardiography	Total number of cases studied	Number of cases with CHD	Prevalence per 1000
Maternal risk factors			
Diabetes mellitus	80	2	
Autoimmune disorder	1	0	
Fever with rash during first trimester	2	0	
Teratogen exposure	1	0	
Family history of CHD in first degree relatives of fetus	20	1	
Subjects with at least 1 maternal risk factor	104	02	19.2
Subject with no maternal risk factor	1341	10	7.5
FETAL RISK FACTORS			
Extra-cardiac organ malformation/s	39	0	
Cardiac malformation suspected during obstetric scanning	14	5	
Twin pregnancy	34	0	
Oligohydramnios	3	0	
Polyhydramnios	8	0	
Intrauterine growth retardation	10	0	
Fetal hydrops	2	0	
Tachyarrhythmia	71	0	
Bradyarrhythmia	3	0	
Subjects with at least 1 fetal risk factor	174	**5**	28.7
Subjects with no fetal risk factor	1271	**7**	**5.5**
Subject with at least one conventional risk factor (fetal/maternal)	262	6	22.9
Subjects with no conventional (fetal/maternal) risk factor	1183	6	5.1

CHD – congenital heart disease.

confirming diagnostic accuracy was either not available,[14] or was available only for a few abnormal FE cases.[13]

In this study, we have investigated the potential for improvement in prenatal diagnosis of CHD by routine performance of systematic detailed FE, indiscriminately in all pregnant women. Confirmation of findings by postnatal follow-up of studied fetuses was done to ensure accuracy of FE interpretations.

2. Methods

2.1. Study design, subjects and demographic data

This was a prospective, non-randomized, cohort study, designed to perform detailed FE in all pregnant women, presenting to the antenatal clinic of our university affiliated tertiary care center, with gestational age (GA) between 16 and 24 weeks; however, those who presented later than 24 weeks, were subjected to FE at their first presentation. The GA was as determined by obstetric sonological scan. The participants were subjected to a routine second trimester ultrasound scan, following which, they were referred to us in the cardiology department for FE.

Baseline data collection included maternal age, GA, history of consanguinity, presence of maternal or fetal factors deemed to be associated with risk of CHD in the offspring, including maternal diabetes (both gestational or pre-existent), exanthematous fever in first trimester, teratogen exposure during first or early second trimester, history of CHD in first or second degree relatives on maternal or paternal side, antenatal or postnatal recognition of CHD in previous pregnancies, history of phenylketonuria or any connective tissue disorder in mother, non-cardiac abnormalities on obstetric scan (including organ malformations, intrauterine growth retardation, amniotic fluid excess or deficiency, fetal arrhythmias, fetal hydrops), number of fetuses in the current pregnancy, and cardiac abnormality suspected but not fully defined by the ultrasonologist.

Institutional ethics committee approved the project and written informed consents were obtained from the participating subjects.

2.2. Fetal echocardiography

Detailed fetal cardiac evaluations were performed by study investigators from cardiology department, well experienced in FE. Detailed imaging was performed on commercially available Philips Affinity ultrasound system (Philips Medical Systems, Andover, MA, USA) using C6-2 curvilinear transducer. Depth and sector width were optimized to obtain maximum possible frame rate. Standard recommendations from American Institute of Ultrasound in Medicine (AIUM), as endorsed in American Heart Association's scientific statement on the Diagnosis and treatment of fetal cardiac disease,[10] were followed for qualitative evaluation of fetal heart. Structural normalcy was confirmed by image interrogations in 4-chamber (4C) view, left and right ventricular outflow tract views (LVOT and RVOT respectively), 3-vessel view, ductal arch visualization and the longitudinal aorta view projecting anatomical sites of potential coarctation. Pulsed Doppler was used for assessment of valvular flow, heart rate and rhythm. Color Doppler was used to rule out small shunts across ventricular septum. Ductal flow was assessed only in cases with anatomical reasons to suspect ductal flow reversal.

All participants were offered to come after delivery for echocardiography of their new born. Postnatal qualitative echocardiographic findings were compared with the FE findings. In cases where, parents were not willing for echocardiography, pediatrician's clinical impression on cardiac evaluation, either in neonatal period, or during vaccination visit, was used for clinical follow-up; however, wherever pediatrician had even minimal suspicion of cardiac abnormality, echocardiography was done mandatorily.

The prevalence rate of cardiac abnormalities on FE, in this unselected cohort of pregnant women, was determined, and compared between women with presence or absence of high risk factors associated with occurrence of cardiac malformations in the fetus. The CHD detection rate, the accuracy of FE diagnosis, and frequency of false positives or negatives, was determined by comparing the prenatal findings with follow-up data.

2.3. Statistical analysis

The sample size was calculated by single population proportion formula using a prevalence of CHD (6.9 per 1000) from a previously conducted similar study,[15] a confidence level of 95% and a margin error of 0.0043%. The calculated sample size was 1424; we did 1445 cases.

The categorical variables are presented as percentage, and the continuous variables as mean and standard deviation.

3. Results

The mean age of participating women was 25.6 ± 4.3 years and the mean gestational age of fetus on the day of FE was 27.7 ± 7.2 weeks. Prevalence of risk factors was as mentioned in Table 1. A total of 1445 FEs were performed, of which 104 had at least one maternal risk factor, 174 had at least one fetal risk factor, and 1183 subjects had no risk factor associated conventionally with CHD. A total of 76 (52.6 per 1000) fetuses were found to have some cardiac abnormality on FE, of which, 12 (8.3 per 1000) had CHD; 2 had cardiac tumors (attached to ventricular septum in 1, and to chorda in the other); 2 had gross right ventricle (RV) dysfunction, of which one was born with patent ductus arteriosus (PDA) and normal biventricular function, and the other with RVH and asymptomatic RV dysfunction that persisted till the last available follow-up echocardiogram at 3 months' age and was suggestive of RV cardiomyopathy orRV dysplasia (cardiac MRI not yet done). Of the other cases with cardiac abnormalities, 1 had gross RV hypertrophy associated with small diameter ductus arteriosus (possibly premature ductus closure resulting from unknown cause); 1 had calcium nodule attached to anterior Mitral leaflet; 3 had isolated moderate pericardial effusion, which completely resolved by the time of birth; 2 had cardiomegaly with moderate pericardial effusion (presumably fetal myocarditis due to maternal anemia or some unrecognized viral infection); and 52 had hyperechoic spots (seen in left ventricle in 46 cases, right ventricle in 1, left atrium in 1, and in multiple chambers in 4 cases).

Of the 12 cases of CHD, 3 were tetralogy of Fallot (TOF), 2 were isolated ventricular septal defects (VSD), 2 were dextro-transposition of the great arteries (d-TGA), 1 was hypoplastic left heart syndrome (HLHS), 1 was tricuspid atresia, 1 was double outlet right ventricle (DORV) without pulmonic stenosis (PS), 1 was situs inversus-dextrocardia without any other associated defect, and 1 had aneurysm of atrial septum and was born with secundum type atrial septal defect (ASD).

In addition to the structural abnormalities, 70 (4.8%) fetuses had sinus tachycardia, and 3 (0.2%) had sinus bradycardia.

Of all the 12 fetuses with CHD, only 2 belonged to the high maternal risk group, while 10 cases were observed in pregnancies without conventional maternal risk factors. Cardiac malformations were suspected in 14 fetuses during obstetric scan; however, only 5 of them had CHD; remaining 7 had structurally normal hearts (VSDs were over-diagnosed); and one of the 5 CHD cases was misdiagnosed as TOF, which was actually DORV without PS (video). Among all the 12 CHD cases detected, 6 (50%) occurred in pregnancies not associate with any (fetal or maternal) risk factor/s (Table 1).

Supplementary video related to this article can be found at https://doi.org/10.1016/j.ihj.2020.08.010.

Of 1445 FEs done in this study, clinical or clinical + echocardiographic follow-up was available in 1255 cases. Except the ASD case, which was prenatally diagnosed as atrial septal aneurysm, no major cardiac malformation was missed on FE; however, postnatal echocardiography detected some minor defects including 2 tiny muscular VSDs, and 189PDAs. These minor defects were not included in the sensitivity and specificity analyses since; inability to detect them is a known limitation of FE. There were no false positive cases. Hence, in this series, the sensitivity, and specificity for CHD detection were 91.7% and 100% respectively.

4. Discussion

Since the first scientific publication on FE by its pioneer F. Winsberg[16] in 1972, this imaging modality has evolved significantly to its current stage of a highly specialized and elaborate structural and functional prenatal evaluation of the heart.

Prenatal diagnosis of complex CHD not only improves survival after birth by appropriate treatment planning in delivery room,[2–4] it makes it possible to manage and treat the fetus as an individual patient, with the help of already available, as well as evolving therapeutic options[17] that expand from maternal administration of medication, to minimally invasive fetoscopic guided techniques, to invasive open uterine fetal surgeries.[10]

The prenatal CHD detection rate, in our cohort of unselected pregnancies, was excellent and comparable to what has been reported by other investigators when the cardiac evaluation was performed by professionals trained for FE.[18,19] On the other hand, lower detection rates (57%) were reported in studies where the initial screening was done by personnel with basic ultrasound training,[7] despite the fact that the suspected abnormal cases were re-examined by trained physicians, in presence of pediatric cardiologist. We could achieve much higher sensitivity and specificity, probably because all the FEs were primarily done by professionals trained in pediatric echocardiography.

Like other studies investigating the role of routine FE in all pregnancies,[14,18,19] we also observed that a substantial proportion (50% in our cohort) of cardiac malformations actually occurred in fetuses recognized to be at low risk of developing CHD (Table 1); this may be due to some unknown environmental exposures of the parents to factors that are yet to be incriminated as etiologically related to fetal cardiac malformations. Although, the prevalence of CHD per thousand cases was more in high risk subjects, in absolute numbers, half the CHD cases were seen in low risk pregnancies, since the proportion of high risk pregnancies is very low.

Investigations involving routine sonological scanning, have reported low and widely varying prenatal detection rates of CHD, even from developed countries.[5,20] A study conducted about two decades back[5] observed CHD detection rate as low as19 − 48% in western European countries; however, relatively recent data[20] reports detection rate of 30−60%, which is still suboptimal. It is also observed that the prenatal diagnosis is often delayed,[20–22] a fact that affects the fetal development as well as precludes the possibility of appropriate actions, eventually resulting in traumatic psychological impact on the prospective parents, prohibiting them from taking timely decisions about pregnancy termination.

A major factor responsible for suboptimal and delayed detection of cardiac malformations on routine obstetric scans is lack of operator skill[23,24] in terms of accurate assessment of fetal heart, probably because heart assessment is different from assessment of other organs due to its small size, continuous motion, and complexities of its malformations. It is also observed that the defects that are obvious in 4C view are relatively less often missed, while abnormalities involving outflow tracts and conotruncal anomalies frequently go unnoticed.[20,25] In order to overcome these deficiencies, different strategies and technologies have been tried, which include protocol based incorporation of multiple views,[7] use of advanced image reconstruction technologies that can potentially reduce the operator dependency e.g., three- and four-dimensional echocardiography[26] with spatiotemporal image correlation (STIC), and recently evaluated processing software, the 5D-Heart,[27] which

utilizes fetal intelligent navigation echocardiography (FINE) technique. Although encouraging, these sophisticated techniques are unlikely to become the solution for the existing problems of underdiagnosis and delayed diagnosis, at least in near future because; firstly, they are still in investigational stages; secondly, the cost constraints will restrict their use in developing countries; and thirdly, further operator training will be required for their use. Therefore, offering FE by an expert, to all the pregnant women, in addition to the routine second trimester scan, appears more practical, efficient and cost-effective method to improve diagnosis and prognosis in CHD.

5. Conclusions

Our study clearly indicates that a substantial proportion of CHD cases occur in women not considered at high risk of giving birth to children with cardiac malformations. It also confirms that FE is a highly sensitive and specific test with strong predictive values. Therefore, we recommend that at least one detailed fetal echocardiographic assessment should be considered a part of routine fetal scanning.

5.1. Strengths and limitations

Adequate sample size, prospective collection of data and availability of follow-up in 87% cases ensuring accuracy of the results, are strengths of this study; however as an unavoidable limitation, we could not do autopsies in cases where, either abortions occurred, or the babies died immediately after birth, before postnatal echocardiography could be performed.

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Declaration of competing interest

None.

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