# Referral indications for foetal echocardiography in a low resource setting

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## Abstract

**Objective:** The aim of this study was to review primary indications for foetal echocardiography among pregnant women at a tertiary care center in a low resource setting.

**Methods:** A retrospective record review was conducted of all women who have had a foetal echocardiogram between January 2015 and December 2016 at The Aga Khan University Hospital, Karachi, Pakistan. Information regarding maternal clinical characteristics, anomaly scan findings, indications for echocardiography and findings on foetal echocardiogram (FE) was collected.

**Results:** The dataset included 1909 patients. Maternal comorbidities including maternal diabetes, (n=614, 47%) was the most common maternal indication, while multiple pregnancy (n=232, 38%) and intra-cardiac echogenic foci (n=168, 28%) was the most common foetal indication for referral. Major CHD was detected in 4.2% (n=81) of cases. In those with CHD, the most common indication for getting a FE was an abnormal 4-chamber (n=31, 38%) view on the screening obstetric ultrasound.

**Conclusions:** Most of our patients were referred on the basis of indications that were not warranted based on international guidelines and very few had major CHD on FE. This emphasizes the need for justifying referrals for a resource intensive procedure such as FE.

**Keywords:** Foetal echocardiography, Congenital heart disease, Low-resource setting, Indications.
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## Introduction

Congenital heart defects (CHD) are the most common of all congenital defects with a prevalence of 8-10 cases per 1000 live births.[1] In addition, these are the most common congenital cause for infant mortality.[2] It has been estimated that around 50,000 children are born with CHD every year in Pakistan, making early detection of CHD essential.[3]

Despite the importance of early detection, CHDs are one of the most frequently missed malformations on routine foetal sonography.[4] Foetal echocardiograms (FE) have proved to be a powerful tool for screening CHDs.[5] However, since it is expensive, time consuming and requires highly skilled operators, it might not always be feasible to perform this investigation especially in a developing country like Pakistan. Therefore, identification of high risk groups for referral is paramount to decrease burden on health care system.

The American Heart Association have listed common indications for foetal echocardiography (FE)[6. Common maternal indications include autoimmune (systemic lupus erthymetasosus), metabolic disease (eg, pregestational diabetes mellitus) and teratogen exposure; while common foetal indications include abnormal cardiac screening examination, foetal chromosomal or extracardiac anomaly, increased nuchal translucency and monochorionic twins.[6] Other indications include first-degree relative with CHD, maternal use of certain medications such as ACE inhibitors and abnormal foetal heart rate. Similar indications have been reported by The American Institute of Ultrasound in Medicine, as well as, the International Society of Ultrasound in Obstetrics and Gynaecology.[7,8]

In a resource constrained setting such as Pakistan, identifying the right indications to refer for FE allowing for equitable usage of resources, remains a challenge. Hence, this study aimed to look at primary indications for FE among pregnant women visiting our center.

## Materials and Methods

This study was a retrospective record review of women, who had a FE at our study site between 1st January 2015 to 31st December 2016. The FE programme at our center involves specific training of sonographers and junior faculty members (total of 100 FE supervised with a mix of normal and abnormal) prior to credentialing them to scan

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independently. Additionally the lab has 3 trained sonographers each having performed more than 500 FE. We received approval from the Ethics Review Committee at our center (5342-Ped-ERC-18). All women who had a FE during the defined time period were identified using the database in the Paediatric Echocardiography Suite. The medical records of these women were retrieved through the Hospital Information Management System (HIMS) to obtain the relevant information. The variables of interest included maternal and gestational age at the time of echocardiography, gravidity, parity, maternal co-morbids, anomaly scan findings, indications for echocardiography, findings on pre-natal echocardiogram and delivery information.

Data was entered and analyzed using SPSS version 20.0. Data was reported as means ± standard deviation for continuous variables and frequency (n) and percentages for categorical variables. Based on broad categories of CHD defined by World Bank, FE findings were categorized as (i) unremarkable (ii) minor CHD (iii) major CHD and (iv) heart rhythm issues.[9] Minor CHD is defined as septal defects, while major CHD was defined as Tetralogy of Fallot, double outlet right ventricle, hypoplastic left heart syndrome, transposition of great arteries and complete atrio-ventricular septal defects.[9]

## Results

The total number of participants during study period was 1909. The average age of mothers at the time of FE was 32.7±5.2 years, while mean gestational age was 24.1±3.7 weeks. Mean gravidity and parity were 2.8±1.7 and 1.1±1.0, respectively.

Majority of study participant, 1304(68%) were referred for FE based on maternal indications, whereas 605 (32%) were referred based on foetal indications. Maternal indications included maternal co-morbids reported in 614 (47%), advanced maternal age (>35 years) reported in 144 (11%) and past foetal demise reported in 143 (11%) participants. Two hundred and thirteen (16%) women were referred for FE "screening" and the exact reason for screening could not be ascertained. Amongst maternal co-morbids, gestational diabetes was reported in 387 (63%) women, followed by pregestational diabetes in 70 (11%), thyroid disorders in 33 (5%) and chronic hypertension in 30 (5%). Multiple pregnancy was the most common foetal indication for FE, reported in 232 (38%) women followed by intra-cardiac echogenic foci in 168 (28%), extra-cardiac abnormality in 129 (21%) and abnormal four chamber and/or outflow tract on ultrasound in 67 (11%). The maternal and foetal indications for FE have been shown in Figure-1.

Majority of the cases, 1765(92.4%) did not have any significant clinical finding on FE (Figure-2). Minor CHD was detected in 58 (3.0%) cases, while major CHD was detected in 81 (4.2%) of cases. Only 6 cases (0.3%) had heart rhythm issues.

Patients referred on indication of maternal pregestational diabetes, only 1 case had major CHD on FE, whereas remaining 69 (99%) cases were unremarkable. Similar findings were reported for mothers with gestational diabetes, where 385 (99%) FEs did not have any significant clinical finding. Although majority of foetal referral indications were on the basis of intracardiac echogenic focus, only 3 (2%) had a major CHD, while 162 (96%) had unremarkable findings. Similar pattern was seen in women with multiple pregnancies, where 227 patients (98%) had unremarkable findings followed by minor CHD in 2 cases (1%), while only 3 cases (1%) had major CHD. The highest yield for major CHD was in 31 (46%) patients referred for evaluation of an abnormal four chamber/outflow tract view on ultrasound (Figure-2).

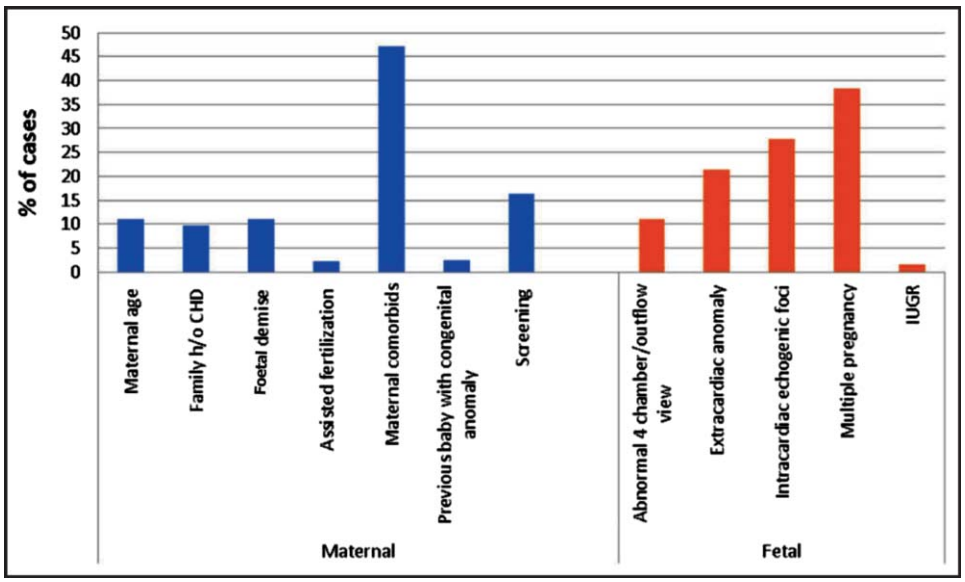


**Figure-1:** Maternal and fetal referral indications for fetal echocardiography. IUGR: Intrauterine Growth Retardation

Majority of our participants, 1136(60%) delivered at our center. The average birth

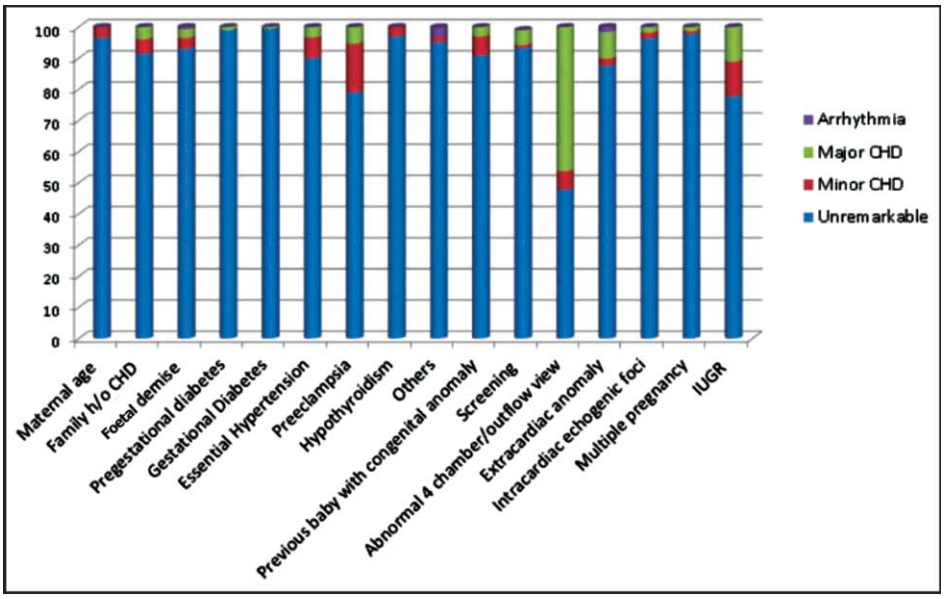


**Figure-2:** Distribution of major and minor CHD based on the indication for foetal echocardiography.IUGR: Intra Uterine Growth Retardation

**Table-1:** Maternal comorbidity and positive foetal echocardiography findings.

| Maternal Comorbids (n=614) | Findings on foetal echocardiography; n (%) |
|---|---|
| Pregestational Diabetes (n= 70) | Complete atrio-ventricular septal defect; 1 (1%) |
| Gestational Diabetes (n= 387) | Total anomalous pulmonary venous return; 1 (0.25%) |
| | Complete atrio-ventricular septal defect; 1 (0.25%) |
| Chronic Hypertension (n=30) | Complex congenital heart disease; 1 (3.3%) |
| | Ventricular septal defects; 2 (6.7%) |
| Preeclampsia (n= 19) | Double outlet right ventricle; 1 (5.3%) |
| | Ventricular septal defects; 3 (15.8%) |
| Systemic lupus erythematosus (n=14) | None |
| Hypothyroidism (n= 33) | Ventricular septal defect; 1 (3%) |
| Others (n=61)* | Aortic arch abnormality; 1 (1.6%) |
| | Ventricular septal defect; 1 (1.6%) |
| | Type 2 heart block; 1 (1.6%) |

* epilepsy, obstetric cholestasis, gestational thrombocytopenia, rheumatoid arthritis, antithrombin 3 deficiency etc.

weight was 2.7±0.6 kg. Patients with major CHD findings on FE, 15 (41.7%) had a normal delivery, while 23 (63.9%) neonates needed intensive care post-delivery.

## Discussion

A total of 1909 patients were referred for FE. The most common indications for referral were maternal comorbids such as maternal diabetes and foetal indications such as intracardiac echogenic foci and abnormal four chamber/outflow tract view on ultrasound. Majority of the findings on FE (92%) were clinically insignificant. Only 4% (n=81) patients had a major CHD on FE. This is comparatively lower than other studies, where CHD was detected in 19 - 29% of referrals.[10,11] A possible explanation for this difference might be the referral indications for suspected CHD on screening ultrasound, which lead to the highest yield of CHD, being the main source of referral (38%) in Clur et al's work as compared to 11% in our study.[12]

A higher number of maternal indications (68%) were reported, including maternal diabetes, chronic hypertension, pre-eclampsia, advanced maternal age, and family history of CHD, whereas foetal indication were only 32%. Our findings were similar to Fayyaz et al, who reported 61.4% of indications being maternal.[13] However, a 10 year audit of foetal echocardiography referrals by Clur et al, revealed fetal indications to be more frequent than maternal indications. Among these indications, increased nuchal translucency (32%) was the most common indication followed by suspected cardiac anomaly (27%). One possible reason for this might be that this unit was a specialized Foetal Medicine Unit receiving complex referrals for fetal scanning.[12]

Maternal gestational diabetes was the most frequent indicator for referral (n=380, 63%), however, this particular risk has not been specified by relevant guideline.[6] Furthermore, only 1% (n=2) of our study participants referred for this indication had major CHD. With a relatively low yield for CHD and an increasing number of women with gestational diabetes,[14] it might be important to reconsider this indication for equitable use of resources in low middle-income countries.

Tarabit et al reported that women conceived via assisted reproductive techniques (ART) had a significantly higher risk of Tetralogy of Fallot as compared to controls.[15] Although assisted fertilization is an indication for FE, none of the cases referred to our center with this indication had a major CHD. This might be due to the limited availability of ART in Pakistan and small number of cases (2%) referred to our center. A systematic review by Bahtiyar et al reported that monochorionic/diamniotic twin gestation was a significant risk factor for CHD (RR, 9.18; 95% CI, 5.51-15.29).[16] In our study, despite being the largest contributor to foetal indication (38%), multiple gestation yielded only 3 cases of major CHD.

Although advanced maternal age is not specified as an indication for FE in international guidelines,[17,18] it was a major contributor to maternal indications for FE referrals in our study (11%). However, major CHD was not reported in any of the foetuses of these mothers. Similar findings were reported by Best et al where advanced maternal age (≥ 35 years) was not a risk factor for CHD.[19] Based on their study, the authors recommended that there was no evidence that women in the United Kingdom should be referred for specialist prenatal cardiac screening based on their age.[19] We believe that a similar recommendation seems justified in Pakistan, where FE is not routinely available and is an expensive imaging modality.

Only 67(11%) patients were referred for FE on the basis of an abnormal four chamber or outflow view. Even though this indication was not the most common reason for referral for FE, it yielded most cases of major CHD (46%). In a similar study in India, the most common foetal indication was an abnormal four-chamber view (69%).[20] Another study by Wright et al, reported suspected CHD on screening ultrasound as the most common foetal indicator (39%) and had the highest CHD prevalence (60%).[21] Obtaining adequate four chamber and outflow tracts views as recommended by the American Institute of Ultrasound in Medicine guidelines for performance of standard diagnostic obstetric ultrasound examination might help in accurately identifying reason for referral.[22]

Barsoom et al, reported that 12% of their study patients were referred for intra-cardiac echogenic foci.[12,21] In contrast, one of the most common foetal indication reported in our study was echogenic foci (28%), only 1.8% had major CHD. Our findings are consistent with Shakoor et al, who also reported 95.7% of cases with uncomplicated perinatal outcome amongst those referred for intra-cardiac echogenic focus.[23] Therefore, referral on the basis of echogenic focus alone should be reconsidered especially in low risk cases.

This study had several strengths and limitations. The strengths of this study were large number of FE reports from a low middle income country like Pakistan. However, due to the retrospective nature of this study, we had some missing information in medical records. Also, we did not have postnatal echocardiogram available on all the cases, hence, postnatal follow ups of these babies were used to determine neonatal wellbeing (surrogate of missed diagnosis on FE). This might induce misclassification bias.

## Conclusion

In conclusion, the vast majority of patients referred in our study were for the indication of maternal gestational diabetes, multiple pregnancy and intra-cardiac echogenic focus. However, none of these were warranted based on existing international guidelines and very few had major CHD on FE. As FE requires highly skilled operators and is an expensive imaging modality, its use as a screening tool in resource constrained settings needs to be justified. Obstetricians working in such settings should hence be cognizant regarding referral indications. Training of obstetric sonographers for assessment of foetal heart and outflow tracts during routine ultrasound examination might be one of the approaches that have potential to improve the yield of CHD on FE.

**Disclaimer:** None to declare

**Conflict of Interest:** None to declare

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