INTRODUCTION

Cardiac defects are the commonest congenital defects in the fetus with a prevalence of 5 – 10 cases per 1000 live births. Cardiac anomalies cause significant mortality and morbidity in the newborn and thus it is important to exclude fetal cardiac malformations prenatally so that delivery in affected fetuses can be planned close to a cardiac care centre.

Fetal echocardiography is a rapidly evolving field since 1972 when it was first reported by Winsberg. This field has evolved since then and recently many advances have been made in this field with regard to Doppler studies and fetal arrhythmias. Fetal echocardiography also offers in-utero therapeutic options.

A variety of congenital cardiac defects can be identified on fetal echocardiography as early as the start of the second trimester with transvaginal sonography. On transabdominal ultrasound, scanning in early third trimester allows a sonographer to pick-up majority of cardiac anomalies. These include a variety of defects as ventricular septal defects, single atrium, valvular anomalies as atresias, regurgitant valves, anomalous arterial and venous connections, hypoplasia of right or left ventricles, double outlet right or left ventricles. Scanning a high risk population allows identification of a variety of congenital cardiac anomalies. Most cardiac defects occur in low risk population; the diagnostic yield of referral is low and many newborns with no risk factor continue to have cardiac defects on postnatal examination. This is alarming for the unprepared family.

This study was conducted to identify the factors which are significantly associated with congenital cardiac malformations found in cases referred for fetal echocardiography.

METHODOLOGY

This study was carried out in the Radiology Department of CMH, Rawalpindi, from January 2007 to November 2010. Fetal echocardiography was done on Toshiba Aplio and General Electric Logic 500 with Doppler application. The referral factors for fetal echocardiography were evaluated with the findings on fetal echocardiography. The method of induction was non-probability purposive sampling. All patients referred for fetal echocardiography with one or more risk factors as well as those with incidental discovery of anatomical cardiac defect and cardiac arrhythmias were entertained. Only those fetuses with structural cardiac anomalies were considered abnormal. The risk factors were extracardiac anatomic abnormalities including
hydrops fetalis, fetal cardiac arrhythmias, suspected cardiac anomaly on routine ultrasound, single umbilical artery, maternal metabolic disorders as insulin-dependent diabetes mellitus, maternal epilepsy on drug therapy, congenital heart disease in any parent or family, bad obstetric history, precious pregnancy, previously affected child and chromosomal abnormalities in a child.

Patients with no risk factors who were diagnosed as having a fetus with cardiac anomalies on routine ultrasound examination were also included in the study. Fetuses referred for echogenic focus in left ventricle were also considered under the same heading. Patients were not screened for phenylketonuria as routine screening test for the condition was not available. All patients included for fetal echocardiography were mentally normal.

Rhythm abnormalities as fetal bradycardia, tachycardia, dropped beats were all considered under the heading of fetal arrhythmias.

A detailed anomaly scan was carried out to rule out extra cardiac anomalies. Detailed cardiac evaluation of the fetus was then performed with four-chamber view for assessment of the cardiac chambers, base-of-the heart view for assessment of the great vessels, aortic arch view, longitudinal view of the aorta and venous connections of the heart. Doppler evaluation was performed for identification of septal defects and valvular regurgitation. In case of any doubt, patients were called for a re-scan. All fetal echocardiograms were performed by a single specially trained radiologist. In case of any doubt and in complex cases, paediatric cardiologist was involved.

Data was entered on Statistical Package for Social Sciences (SPSS) version 15. Univariate logistic regression analysis was carried out for each variable. Variables with statistical significance of less than 0.05 were subjected to multivariate logistic regression analysis. Fetal echocardiographic diagnosis was taken as the dependent variable and all other variables were the independent variables.

RESULTS

Three hundred patients were registered for fetal echocardiography during the study period. Out of them 36 were excluded due to inadequate data. Two hundred and sixty four patients were subsequently included. The age of the mothers ranged from 19 – 42 years with mean age of 28.11 ± 4.49 years. Fetal echocardiography was done at a mean fetal age of 29.4 ± 4.8 weeks. Out of them 183 cases had a single risk factor for referral (69.3%) for fetal echocardiography and 67 cases (25.4%) had more than one risk factor for referral. There were 14 patients (6.4%) with no risk factors. Those 14 patients were referred after detection of congenital heart disease on routine antenatal examination. Ten out of these were referred for congenital cardiac defects while 3 were referred for echogenic focus in left ventricle.

Fetal echocardiography showed congenital heart disease in 8 cases referred for congenital cardiac defects. Three cases with echogenic focus in the left ventricle had structurally normal heart. One patient was investigated for abnormal uterine artery Doppler and fetal echocardiography finding was normal in this patient.

Extra cardiac anomalies were found in 15 patients. Out of these, one fetus had extra cardiac anomaly of gastroschisis, hydrops fetalis (n = 2), hydrops fetalis with small limb bones (n = 2), polyhydramnios without hydrops (n = 1), polyhydramnios with hydronephrosis (n = 1), diaphragmatic hernia (n = 2), omphalocele (n = 1), abdominal mass (n=1), renal agenesis (n = 1), sequestered lung segment (n = 1) and small femur length (n = 1). Association of extracardiac anomalies with congenital heart disease was not statistically significant.

One hundred and fourteen patients (43.2%) were referred for screening for congenital heart disease for a previously affected child with congenital cardiac defect. Out of them, 08 fetuses (7%) had congenital cardiac defect (p = 0.3). There were 10 referrals for multiple congenital anomalies in a previous child. The anomalies included cleft lip and palate, omphalocele, anencephaly, myelomeningocele, tracheo esophageal fistula, galactosemia, cataract and atrial septal defect (p = 0.999).

There were 162 (61.4%) patients with maternal risk factors. Five (2.3%) had maternal congenital heart disease (left ventricular outflow tract obstruction, ventricular septal defect, patent ductus arteriosus and mitral leaflet prolapse). Fourteen patients (5.3%) had Insulin dependent diabetes; 146 patients had precious pregnancy which included 129 patients with death of one or more children including intra uterine deaths and 17 patients with missed abortions. Three patients (1.1%) were epileptic on medication. This factor was significant on univariate regression analysis but not on multivariate analysis.

One (0.4%) patient was referred for paternal congenital heart disease. In this case, father had Hypertrophic Obstructive Cardiomyopathy (HOCM). The fetus was normal on echocardiography.

There were 12 fetuses referred for arrhythmias. Three cases had bradyarrhythmias which was not due to a structural cardiac defect in 02 fetuses. The first fetus had complete congenital heart block (CCHB) along with pericardial and pleural effusions and died in utero. The second fetus with brady arrhythmia had 2:1 block initially which later changed to complete heart block. No structural abnormality of the heart was seen. The fetus was delivered normally and so far has not required
pacing. The third fetus with brady arrhythmia had complete atrio-ventricular septal defect (AVSD) and died after birth. Eight fetuses were referred for drop beats. One referral was due to episodes of fetal bradycardia on routine examination.

Out of all the risk factors, statistical significance with p-value of less than 0.05 was seen in patients whose cardiac anomaly was picked-up on routine ultrasound examination, and those with maternal factors on univariate analysis (Table I). The other risk factors were not significant statistically.

Multivariate analysis of the risk factors, as given in Table-II, shows that the only risk factor of significance was congenital heart disease seen on routine obstetric ultrasound examination.

**DISCUSSION**

In this study, detection of congenital heart disease on antenatal ultrasound was the most significant factor producing positive fetal echocardiography findings. The most important views in fetal echocardiography are the four-chamber view and the base of the heart view. These two views help in excluding 70 – 80% of the anomalies. It is important to exclude extracardiac anomalies before scanning for cardiac anomalies as many extracardiac anomalies involving skeletal, nervous system, gastrointestinal, respiratory and urogenital system may be associated. In one study, it was observed that ventricular septal defect (VSD) was associated with the highest incidence and transposition of great arteries (TGA) was associated with the lowest incidence of extracardiac malformations. Another study showed that patients with congenital heart disease had a 22% frequency of associated extra cardiac anomalies, syndromic association, or chromosomal abnormalities. A detailed scan for extracardiac anomalies was carried out in each case. Gastrointestinal anomalies such as omphalocele (more frequently), Gastroschisis (less frequently), and congenital diaphragmatic hernia may be associated with congenital cardiac defects. Omphalocele may be associated with ventricular septal defects, tetralogy of fallot, pulmonary stenosis and coarctation of aorta in 17 – 47%. Cardiac defects are the most common defects in fetuses with omphalocele. One of the patients with omphalocele had complete AVSD with pulmonary atresia.

There is a 10.6% association of congenital heart disease with congenital diaphragmatic hernia. In the 3 patients with congenital diaphragmatic hernia, no cardiac anomaly was seen on fetal echocardiographic examination.

Fetal arrhythmias account for 1 – 2% of cases. Out of these tachyarrhythmias are the commonest accounting for 95% and brady arrhythmias account for 5% of the cases. In this study, only brady arrhythmia was seen. Brady arrhythmia may occur due to sick sinus syndrome, blocked atrial beats, congenital complete AV block, or long QT syndrome.

Congenital complete heart block (CCHB) is associated with a worse prognosis and this in association with congenital heart disease carries mortality of 90%. In this study, 02 fetuses had CCHB, born to the same mother. The first fetus had a fixed heart rate of 58 bpm. The fetus had hydrops fetalis with pleural effusion and died in utero at 08 months of gestation. The second fetus had CCHB which was initially diagnosed as 2:1 heart block and later on changed to CCHB. This time there was no hydrops and other than the CCHB, there was no other cardiac or extracardiac abnormality. This time the mother delivered a full term baby with slow heart rate and complete heart block. The child is 03 years of age and is active. Presently, the placement of permanent pacemaker is deferred till the child becomes symptomatic. The mother was positive for anti-Ro antibodies. Five percent of children born to mothers with

**Table I: Univariate analysis of risk factors with p-value and Odds ratio.**

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Total number of cases</th>
<th>Normal on fetal echo</th>
<th>Abnormal on fetal echo</th>
<th>p-value</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal factors</td>
<td>162 (61.4%)</td>
<td>150 (63%)</td>
<td>12 (42%)</td>
<td>0.037</td>
<td>2.3</td>
</tr>
<tr>
<td>Paternal factors</td>
<td>1 (0.4%)</td>
<td>1 (4.8%)</td>
<td>0 (0%)</td>
<td>1</td>
<td>0.000</td>
</tr>
<tr>
<td>Congenital heart detected disease on routine examination</td>
<td>14 (5.3%)</td>
<td>8 (28%)</td>
<td>6 (2.5%)</td>
<td>&lt; 0.001</td>
<td>0.046</td>
</tr>
<tr>
<td>Family history of congenital heart disease</td>
<td>114 (43.2%)</td>
<td>11 (39%)</td>
<td>100 (42%)</td>
<td>0.304</td>
<td>1.5</td>
</tr>
<tr>
<td>Extracardiac fetal anomaly</td>
<td>15 (5.7%)</td>
<td>Nil (0%)</td>
<td>15 (6.3%)</td>
<td>0.999</td>
<td>2E+008</td>
</tr>
<tr>
<td>Two-vessel cord</td>
<td>5 (1.9%)</td>
<td>4 (1.6%)</td>
<td>1 (3.5%)</td>
<td>0.999</td>
<td>2E+008</td>
</tr>
<tr>
<td>Multiple congenital anomalies in a previous child</td>
<td>11 (4.2%)</td>
<td>Nil (0%)</td>
<td>11 (4.6%)</td>
<td>0.999</td>
<td>2E+008</td>
</tr>
<tr>
<td>Fetal arrhythmias</td>
<td>12 (4.5%)</td>
<td>11 (4.6%)</td>
<td>1 (3.5%)</td>
<td>0.490</td>
<td>0.575</td>
</tr>
</tbody>
</table>

**Table II: Multivariate analysis of cases with p-value less than 0.05 on univariate.**

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Number of cases</th>
<th>Normal on fetal echo</th>
<th>Abnormal on fetal echo</th>
<th>p-value</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal factors</td>
<td>162</td>
<td>150 (63%)</td>
<td>12 (42%)</td>
<td>0.670</td>
<td>1.2</td>
</tr>
<tr>
<td>Congenital heart disease on routine examination</td>
<td>14</td>
<td>6 (2.5%)</td>
<td>8 (25%)</td>
<td>&lt; 0.001</td>
<td>0.05</td>
</tr>
</tbody>
</table>
The majority of patients with maternal factors were those with previous pregnancy with either missed abortions /IUD or demise of one or more child after birth. The risk of congenital heart disease in a fetus with a father with congenital heart defect is 1.5 – 3%. Another common indication in this study was a previously affected child with congenital heart disease. This was not significant. A low diagnostic yield of this finding has been reported in other studies as well. The limitations of the study was the small number of patients for certain risk factors. No case of chromosomal anomalies was seen. Certain risk factors as phenylketonuria in the mother was not studied as screening test for this was not routinely available.

CONCLUSION

Cardiac examination should be routinely done as part of anomaly scan as the most important referral indication for fetal echocardiography is fetal cardiac anomaly detected on routine scanning. Four chamber view and base of the heart view help in excluding a majority of the anomalies. Fetal brady arrhythmias are not necessarily due to structural defects.

REFERENCES


