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ORIGINAL ARTICLE

Trends and Outcomes After Prenatal Diagnosis of Congenital Cardiac Defects: Experience of a Dedicated Fetal Medicine Centre from South India

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Abstract The primary objective of the study was to present a 5-year data on the outcomes after prenatal diagnosis of CHD. This is a retrospective descriptive study, conducted in the fetal medicine unit of an academic tertiary care referral centre in South India. The details of all cases with a prenatal diagnosis of fetal cardiac lesions from January 2012 through December 2016 were collected. All cases were systematically analyzed for type of lesion, associated malformations, chromosomal abnormalities, prognosis of the lesion, the decision taken by the couples and the information regarding post natal outcome, wherever available. Prenatally diagnosed fetal cardiac lesions were identified in 310 cases. In 220 (76.1%) cases, the couple opted for termination of pregnancy. In this group, 52% of them had an isolated cardiac defect with good prognosis. In the rest of the 69 cases who decided to continue, 7 cases had an IUD. In the 62 cases that culminated in a live birth, 46 cases opted for postnatal cardiac care. Corrective surgery was attempted in 18 neonates with 2 resulting in neonatal death. Prenatal diagnosis of isolated CHD provides an opportunity for an improved immediate neonatal outcome. A thorough evaluation for extracardiac and genetic abnormality will facilitate better utilization of health care resources by triaging patients with isolated CHD having good prognosis for targeted postnatal care. Also, antenatal pediatric cardiology counselling will enable the couple to make decisions regarding postnatal management options.

Keywords Congenital heart defect · Echocardiography · Conotruncal anomalies · Perinatal outcomes · Ventricular septal defect · Conotruncal abnormality · Karyotypic abnormality · Extra-cardiac malformation

Background

Congenital heart defects (CHD) account for 1% human malformations and are the most common congenital anomaly in the fetus, with an approximate prevelance of 6–8 per 1000 live births [1]. Despite continuous efforts to improve cardiac sonography over the last few decades [2], cardiac anomalies are still the most overlooked lesions during prenatal sonographic scanning [3, 4]. Majority of neonates with CHD are born to mothers with no known risk factors. In spite of advances in palliative and corrective surgeries, CHD are the most common cause of neonatal mortality due to a congenital malformation, with 25% of them being critical cardiac lesions, detectable prenatally [5, 6]. Hence, fetal cardiac evaluation aims at early diagnosis of CHD which allows parental counseling and timely postnatal management, thereby reducing morbidity and improving perinatal outcomes.

Materials and Methods

This was a retrospective, observational study, conducted in the Fetal medicine unit of Centre for Infertility Management and Assisted Reproduction (CIMAR) hospital, Edappal, Malappuram, Kerala, India. The centre is an

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academic tertiary level referral unit providing fetal medicine services to a wide range of antenatal women in north Kerala. After approval from the institutional ethics board, the details pertaining to all cases of prenatally diagnosed fetal cardiac lesions from January 2012 through December 2016 were collected irrespective of gestational age, and systematically analyzed. The variables recorded on a computer database included patient demographics, gestational age and indication for referral, type of lesion, associated malformations, chromosomal abnormalities, prognosis of the lesion, the decision taken by the couples and the information regarding post natal outcome, wherever available. The follow up of each case was taken by direct telephonic contact.

Ultrasound scans during this period were performed using GE Voluson E8 and GE Voluson E6, using transabdominal curvilinear trandsducers with frequency 2–5 MHz (C1-5-D) and trans-vaginal transducers with frequency 5–7.5 MHz (RIC5-9-D) (GE-General Electrics, Vienna, Austria). The cardiac screening protocol was adapted from the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines [7]. In indicated cases, amniocentesis or chorionic villous sampling was performed for fetal karyotyping. Upon diagnosis, as per our institutional protocols, we gave a non-directive counseling to the families regarding the nature of the anomaly and expected outcome as per the current literature. We also advised paediatric cardiology counseling especially in cases with critical lesions, to discuss options for management and expected peri-operative outcomes.

The heart defects were classified as major, minor or soft markers. A major cardiac defect was defined as a malformation of the heart and/or the great arteries that were potentially lethal requiring postnatal interventions either corrective or palliative or were severe enough to warrant termination of pregnancy. Cases were grouped under the major defects according to whether they could have been diagnosed based on findings in four chamber view alone, outflow tract views, arch abnormality, valvular abnormalities, tumors, heterotaxy syndromes and multiple cardiac lesions. Heart defects were classified as minor when they were variants of the normal anatomy that required no intervention or follow up postnatally, e.g. right aortic arch, persistent left superior vena cava (SVC). Soft markers were those ultrasound findings which had an increased likelihood for aneuploidies, such as isolated ARSA (aberrant right subclavian artery). Lesions with a favorable prognosis were those with a normal four chamber view, having good biventricular function, without any extracardiac malformation or karyotypic abnormality and arrythmias. This provides important information to supplement the antenatal counseling. Pregnancy outcomes were categorized as: pregnancies terminated after diagnosis, intra-uterine death and pregnancies that culminated in a live birth. In babies delivered alive, the immediate neonatal outcomes were assigned as those babies that received cardiac evaluation and those that did not. Cases were followed up from the time of prenatal diagnosis into the postnatal period wherever available to obtain a better understanding of the outcome of the lesion.

The primary objective of the study was to describe the outcomes after prenatal diagnosis of congenital heart diseases of a 5 year data from our fetal medicine center. The secondary objective was to elaborate and study the cases that were subjected to postnatal cardiac care.

The collected data was analyzed using the statistical software SPSS version 15.0 (Statistical Package for the Social Sciences, Chicago, II, USA). Descriptive statistics was carried out with continuous variables expressed as median and categorical data as percentages. Standard deviation was taken for quantitative variable.

Results

During the period January 2012 through December 2016, 310 cases of prenatally diagnosed fetal cardiac lesions were identified, out of which, 227 (73.2%) cases were referred to our centre. Of these 227 cases, 167 (73.6%) had an abnormal fetal sonogram but a cardiac lesion was suspected only in 83 of these 167 cases. In the rest of the 84 cases which were referred in view of a non cardiac fetal anomaly, 90% of the lesions had an abnormal four chamber view defect. The other indications included, referral for a routine antenatal scan (47/227, 20.7%), biochemical screening positive (7/227, 3%), maternal illness (2/227, 0.9%), monochorionicity (2, 0.9%) and previous adverse obstetric history (2, 0.9%).

The mean gestational age at diagnosis of the cardiac defect was 22 weeks (± 5.52). The year-wise distribution of cases according to the trimester of diagnosis is shown in Fig. 1. Only 26 (8%) cases had a risk factor for occurrence of a cardiac malformation, e.g. maternal heart disease, maternal systemic illness, history of previous baby with aneuploidy, heart anomaly or extracardiac anomaly.

In the entire cohort of antenatally diagnosed cases, there was a clear predominance of major cardiac defects (290/310, 93.5%). Though lesions detectable by abnormal four-chamber views predominated these cases (116/290, 40%), an almost equal number of conotruncal anomalies were also detected over the years (103/290, 35.5%). Major cases are enumerated in Fig. 2 according to the fetal diagnosis regardless of its accuracy.

Fetal genetic analysis was obtained in 133 cases, of which chromosomal aberrations were detected in 37/133 (27.8%). The most common abnormality was trisomy 18 in

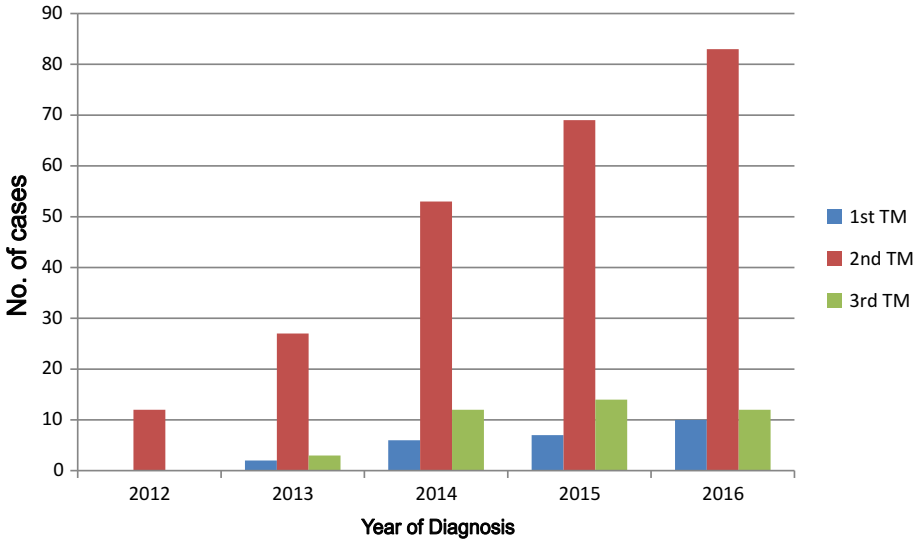

Fig. 1 Annual trends in diagnosis of cases according to trimester (TM)

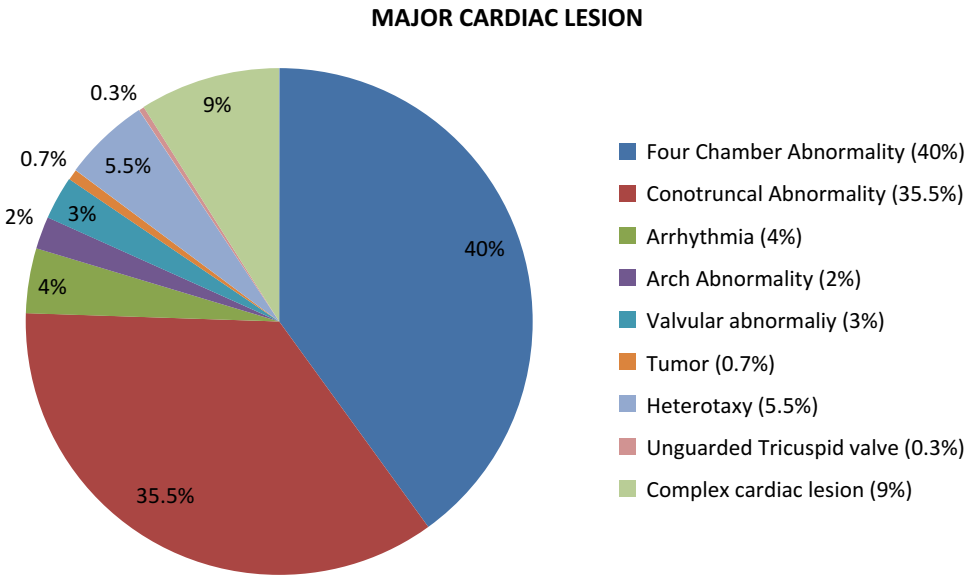

Fig. 2 Types of major cardiac lesions

11 cases. Atrioventricular septal defect (AVSD) was the commonest type of congenital heart defect in cases with abnormal karyotype; four of these cases were associated with trisomy 18 and three with trisomy 21. The two cases of 22q11.1 microdeletion were associated with Tetrology of Fallot (TOF). Table 1 depicts the types of cardiac defects present in cases who had chromosomal abnormalities.

Extracardiac malformations were present in 148 (47.7%) of 310 cases. Of them, 68 patients opted for fetal genetic analysis and 22 cases had an abnormal karyotype. Table 2 indicates the frequency of the extra-cardiac malformations.

Twenty one cases were lost to follow up. The overall termination rate for the fetal cardiac lesions was 76% (220/289), of which the lesions which had a favorable prognosis at the time of diagnosis accounted for 50.9% (112/220) of the cases. Of the remaining 69 cases in which the pregnancy was continued, 7 cases died in utero and 62 culminated in a live birth. Table 3 provides details on the outcomes of the fetal cardiac defects.

No cardiac evaluation was sought for 16 of the cases that delivered live. Among them, 3 cases had a complex congenital heart defect and ended in a neonatal death. In the rest of the 13 cases that are alive at a follow up of 1.5 years, only one case had an associated malformation i.e. agenesis of corpus callosum. The rest of the 12 heart defects were minor.

Among the 46 cases of live birth that had undergone an antenatal or postnatal cardiac evaluation, 18 cases were subjected to cardiac surgery, of which only 2 deaths occurred due to post-operative infection. Sixteen cases are doing well at an average follow up period of 1.5 years. No

Table 1 Types of cardiac defects in chromosomal abnormalities

Chromosomal abnormality	Total cases (n)	Associated extracardiac anomalies (n)	Type of CHD (number of cases)
Trisomy 21	7	2	AVSD (3), VSD (1), ARSA (1), Ebstein's anomaly (1), HLHS (1)
Trisomy 18	11	10	AVSD (4), VSD (3), ARSA(1), HLHS (1), DORV (1), Co Ao (1)
Trisomy 13	3	3	LSVC (1), TGA (1), PTA(1)
Triploidy	3	2	TOF (1), DORV (1), PTA (1)
Turner's syndrome	3	0	HLHS (3)
Klinefilter's syndrome	2	0	VSD (1), APVS (1)
22 q 11 microdeletion	2	1	TOF (2)
Others	6	2	DORV (1), TGA (1), HLHS (1), MS (1), Ta-VSD (2)
Total	37	20	37

Table 2 Distribution of extracardiac anomalies

Extracardiac anomaly	Total number of cases (n)
Central nervous system	27
Skeletal	5
Renal	14
Facial	5
Gastrointestinal tract	2
Respiratory	2
Liquor abnormality	7
Umblical Arterio-Venous fistula	1
Aneuploidy markers	51
Multiple anomalies	34
Total	148

surgical intervention was done in 28 liveborn babies, among which 14 neonatal deaths occurred due to complexity of the heart defect and the other 14 cases were minor defects or sort markers. The survival rate for live born cases until the end of 1 year of age was 69.34% (43/62). Figure 3 depicts the neonatal outcomes of 62 live born cases.

Discussion

There have been limited studies to examine the impact of prenatal diagnosis of CHD on pregnancy outcomes in the developing world [8]. CHDs are six times more common than chromosomal abnormalities and four times more common than neural tube defects [9]. However, due to the wide spectrum of defects in the evolving fetal heart, majority of CHDs go undetected. In the present study conducted on 310 pregnant patients, mean gestational age at diagnosis of the cardiac defect was 22 weeks. However, the number of cases picked up, especially in the first trimester, has steadily increased over the 5 years as shown in few population based studies also [10].

Ours being an academic tertiary referral hospital, 73% of prenatally diagnosed cases were referred to us. Although, the most common indication for referral was an abnormal fetal sonogram (73.6%), only 83 of these 167 cases was for an abnormal cardiac view. This was in accordance with other studies that highlight the importance of training opportunities for sonographers performing fetal imaging, for detection of conotruncal and more complex lesions [11–13]. Also, the need for a detailed fetal cardiac examination as a part of routine antenatal scans has been emphasized as a high proportion of prenatally detectable cases of CHD (284/310) occurred in pregnant women with no identifiable risk factors [14, 15].

Of the 290 cases diagnosed, 93.5% were major cardiac defects, of which 40% (116/290) had an abnormal four chamber view. This is in accordance with a large population study which found that the four chamber view abnormalities are the most common prenatally diagnosed fetal heart lesion [16]. Surprisingly, when individual lesions were taken into account, double outlet right ventricle (DORV) was the most frequently detected fetal cardiac abnormality (43 cases). This was followed by AVSD (26 cases) and Hypoplastic left heart syndrome (HLHS) (24 cases). It has been shown that prenatal detection of conotruncal abnormalities (CTA) significantly improves the postnatal mortality [17], thus it is important to antenatally diagnose these cases. The difficulty in visualization of the spatial relationship of great arteries is a limiting factor in the diagnosis of such lesions. Although previous studies [18, 19] showed the prevalence of CTA in reported fetal series to range from 2.5–21%, in the present study, CTA accounted for 35.5% of cases.

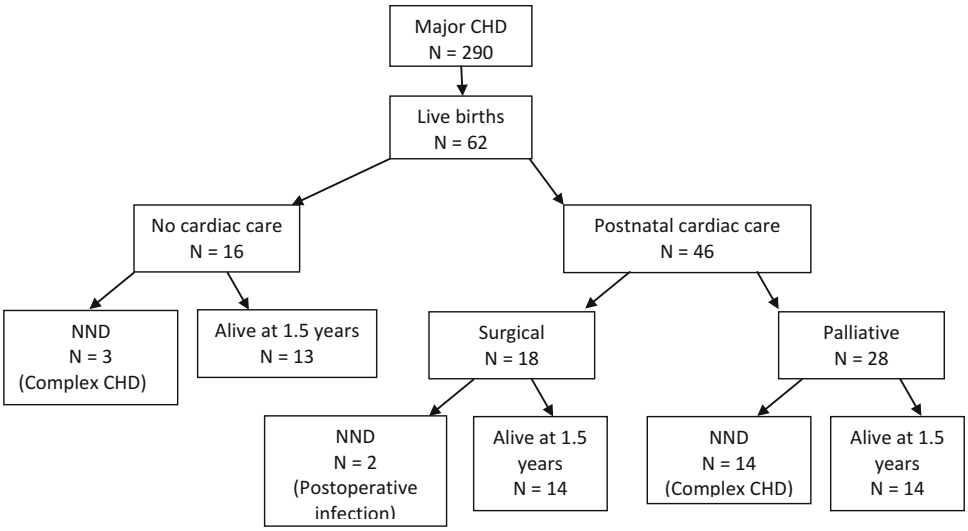

Fig. 3 Neonatal outcomes of live births. *CHD* congenital heart disease, *NND* neonatal death)

Extracardiac malformations and genetic abnormalities are a common association and have a major impact on the prognosis of the fetus [20, 21]. Hence, it is very important to have a complete evaluation of the fetus after the initial diagnosis before parental counseling for prognosis. In the present study, 48% of the cases had extra cardiac anomalies, most frequent of which was of central nervous system. This is similar to other studies [22]. Also, this suggests that the extracardiac malformations triggered the detection of the CHDs, as observed by other investigators [18, 23, 24]. Despite extensive counseling, genetic testing was attempted in only 133 cases and chromosomal aberrations was detected in 43% of them. This is much higher than in the studies by Chaoui et al. [25] and Gembruch et al. [26].

Studies demonstrate a decrease in postnatal detection of conditions, such as the HLHS, as a result of parental choice for termination after early diagnosis [27]. As the expertise of the sonologist extends and improves, and if parental choice continues in the same trend as before, there will be a decrease in the number of children with complex cardiac

Table 3 Outcomes of cases with abnormal karyotype and associated malformations of fetal cardiac defects

Type of Cardiac lesion	Total n (%)	Abnormal karyotype n (of 133 cases)	Associated malformation n (%)	TOP n (%)	Continued and IUD n (%)	Continued and NND n (%)	Continued and alive n (%)	Lost to Follow up n
Four chamber abnormality	116 (40%)	22	59	94	3	5	9	5
Conotruncal abnormality	103 (35.5%)	10	53	71	1	7	12	12
Arch abnormality	6 (2%)	1	4	4	0	0	2	0
Valvular abnormality	8 (3%)	1	5	6	1	1	0	0
Arrhythmia	12 (4%)	0	0	4	1	0	7	0
Tumor	2 (0.7%)	0	0	0	0	0	1	1
Heterotaxy	16 (5.5%)	0	7	14	0	2	0	0
Unguarded Tricuspid valve	1 (0.3%)	0	0	1	0	0	0	0
Complex heart disease	26 (9%)	0	11	19	1	3	0	3
Minor/soft markers	20 (6.45%)	3	1	7	0	0	13	0
Total	310 (100%)	37	148 (47.7%)	220 (71%)	7 (2.2%)	18 (5.8%)	44 (14.1%)	21 (6.7%)

TOP termination of pregnancy, *NND* neonatal death, *IUD* intrauterine death

malformations. This shall significantly reduce the economic burden on the health care systems. The overall termination rate in the present study was 76.1%.

Prenatal diagnosis of major CHD has shown to improve newborn peri-operative status with treatment starting soon after birth, prior to a planned cardiac surgery, thereby, reducing morbidity [28]. But the results in this study show utilization of post-natal tertiary cardiac care only in a limited number of neonates, even in those with isolated reparable lesions. Out of the 76% patients who opted for termination of pregnancy without a formal paediatric cardiology consultation, a significant 50.9% had lesions warranting a favorable prognosis. Hence, fetuses with isolated surgically correctable heart disease with a normal karyotype should be thoroughly counseled regarding the opportunity of a planned birth in tertiary cardiac centres and the reduction in morbidity due to a diagnostic delay after birth.

There are some limitations in the present study. It may have underestimated the total frequency of conditions such as ventricular septal defects (VSD) and pulmonary stenosis (PS) as they are a component of various complex heart diseases. Diagnostic precision was not possible in terminated cases due to poor acceptance of fetal autopsy. Follow-up of all cases could not be obtained. As this was a single centre study, the survival benefit from prenatal diagnosis on the population as a whole may actually be greater than it was seen. A long-term follow up will give a more robust data on the impact of prenatal diagnosis on the eventual outcomes for these patients.

Conclusions

Detailed cardiac evaluation should be an indispensable part of fetal sonography. This will ensure earlier detection of malformations, thus giving the couple more pregnancy management options, including termination. A thorough evaluation for extracardiac and genetic abnormalities will facilitate a better utilization of health care resources by triaging those patients with isolated surgically correctable CHD for targeted postnatal care. Thus, lesion-specific parental counseling and prognostication of each heart defect at diagnosis is essential. Pediatric cardiology counseling will further enable the couple to make decisions regarding postnatal management options.

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