ISSN 2321 -9017
Volume 5, No.2, February – March 2017
International Journal of Bio-Medical Informatics and e-Health
Available Online at http://www.warse.org/IJBMIeH/static/pdf/file/ijbmieh01522017.pdf

Prenatal Detection of Congenital Heart Defects: Study & Comparative Analysis of Existing Techniques

Jitendra Chourasia[1], Vijay Chourasia[2], A. K. Mittra[3]
1Research Scholar, Bapurao Deshmukh College of Engineering, Wardha. (jitchourasia@gmail.com)
2Assistant Professor, M.I.E.T., Gondia. (chourasiav@gmail.com)
3Professor & Head, Electronics Engineering. M.I.E.T., Gondia. (akmittra@gmail.com)

ABSTRACT

Congenital Heart defects (CHD) are one of the most common birth defects and is the foremost reason of the birth-defect associated deaths. A CHD is a structural or functional abnormality developed during pregnancy of the heart before birth. Over last few decades a lot of technological advancement took place for prenatal detection of CHD. We reviewed and analysed the performance of currently used techniques with the goal of determining a non-invasive, cost-effective alternative for computer-aided diagnostic system. The distinguishing capabilities of different existing techniques are explored and compared. The outcome of that comparison is represented and discussed concretely. The comparison results confirm the prospects of Fetal Phonocardiography as a supporting tool which can be used for prenatal detection of CHD.

KEYWORDS: Congenital Heart Defects, Echocardiography, Phonocardiography, Nuchal-fold scan, Fetal MRI, Amniocentesis.

1. INTRODUCTION

The vast majority of babies born in the world is healthy, but the babies born with some kind of abnormalities in the structure of the heart are also enormous and are of great concern to human beings. “A gross structural abnormality of the heart or intra-thoracic great vessels that is actually or potentially of functional significance” is described as congenital heart defect or disease (CHD) [1]. This definition excludes the abnormality in left superior cava and the branches of the aortic arch, though they play a role in blood circulation of the fetal. In a broad sense the structural or functional abnormality developed in the heart and its great vessels during the antenatal period and remains present after birth is referred as CHD [2]. It is the most common congenital anomaly and is one of the major causes of morbidity and mortality all over the world [3,4].

According to World Health Organization (WHO) in 2005, heart disease caused 17.5 million (30%) of the 58 million deaths that occurred worldwide. The incidence rate of CHD in INDIA is 8/1000 babies. With this rate nearly 1, 80,000 children are born with CHD each year in INDIA; About 50% suffer from critical CHD requiring early attention and about 10 % of present infants’ mortality in INDIA [5]. Every year a large number of children are added to this group of CHD. In a latest study [6] accomplished between August 2013 and September 2014 out of 5984 persons examined, 100 were identified with CHDs in MGM hospital, Warangal (India), giving a prevalence of 16.7 per 1000 (i.e. 1.67 %). In another study [7] carried out in Pakistan, between 150 cardiac patients, 55.3% were male and 44.7% were female. Congenital heart diseases seen in 89.3% and 10.7% had acquired heart disease. Thus the demographic statics show the high impact of CHD in developing countries like India and Pakistan.

It is still a big challenge for the medical professionals to identify it at an early stage and the necessary steps to initiate for reducing the CHD birth rate. During the last decade, with the advancement in medical technology, several techniques are developed diagnosis of congenital defects in the fetus. In this paper, a comprehensive study of these techniques is presented along with the physiology of the fetal heart, causes of CHD, and their different types recognized after birth. The comparison and conclusions are also presented in subsequent sections.

2. PHYSIOLOGY AND BLOOD CIRCULATION OF FETAL HEART

The structure and circulatory system of a fetal heart are quite different from that of a baby after birth. The fetal heart begins to develop soon after conception, but it becomes able to pump blood throughout the body by the end of the fifth week. The lungs of fetal do not function until birth when it takes its first breath. During development in the womb fetus receives oxygen and other life supplements from the mother through the umbilical cord from the placenta [8].

In normal prenatal circulation, the oxygenated blood from the placenta and deoxygenated blood from the fetus body enters to the right atrium simultaneously. Most of this mixed blood is pushed into the left atrium directly through a special opening called a foramen ovale thus bypass the pulmonary circulation system. From there it moves into the aorta through left ventricles in the similar manner as it moves in heart after birth. The aorta delivers the blood to the fetus for fulfillment of nourishment required for development of the fetus. The leftover blood in the right atrium moves into

right ventricles, which pumps it into the pulmonary artery. The blood is directed from the pulmonary artery through the ductus arteriosus into the aorta. Ductus arteriosus shunt lungs. Again, the aorta delivers the blood to the body of the fetus.

The foramen ovale and Ductus arteriosus are special openings in the fetal circulatory system, which closes with a few days after birth [9,10]. When baby takes the first breath after clamping of the cord and detachment from the placenta; lungs fill with air; the blood pressure in the lung arteries goes down. Foramen ovale closed by one -way flap on the left side of the foramen ovale and effectively separates the two atria. This causes due to increased pressure in the left atrium because of blood flow into and out of the lungs. Similarly, the ductus arteriosus closes to form separate left pulmonary artery and aorta [8].

Circulation after Birth: After birth, only deoxygenated blood enters to the right atrium and from here it moves to right ventricles and through the pulmonary artery to the lungs. The blood gets oxygenated through the lungs and this oxygenated blood enters the left atrium and then enters two left ventricles and then to the aorta. The aorta transfers this oxygenated blood to the rest of the body for nourishment. The blood circulation in the heart before and after birth are shown in figure 1 (a) and (b).

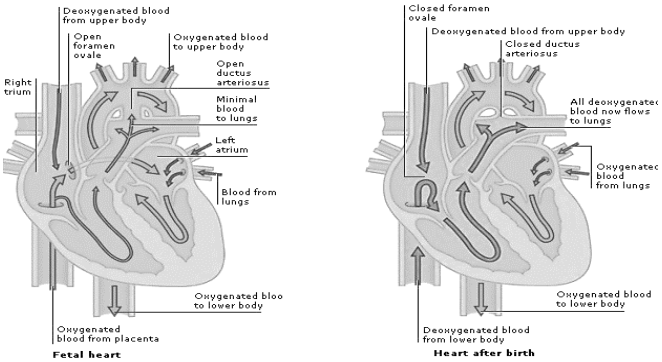

Figure 1: Blood circulation in (a) fetal heart (b) neonatal heart

3. CAUSES OF CONGENITAL HEART DEFECTS

In most cases, medical experts do not know the actual cause of abnormal development of the heart but there are few factors which play a vital role in the development of CHD [11]. They are classified in two groups; Environmental and Genetic.

a) Environmental factors: The risk of development of heart defect in fetal increases when a pregnant lady contact with rubella virus in first trimester of pregnancy. Centers for Disease Control and Prevention (CDC) also suggested not to conceive pregnancy within a month after receiving the MMR vaccine to avoid any abnormality in fetal. Also, some medications like ACE (angiotensin converting enzyme) inhibitors, Acne medication, and illegal drugs like cocaine, heroin or alcohol are dangerous those increase the risk of abnormality development if taken by the mother during pregnancy. Apart from these if a pregnant lady smokes actively or passively, the carbon monoxide from cigarettes, passes easily from the mother's bloodstream into her baby's blood and increase the risk of heart defect.

b) Genetic factors: The probable chance of heart defect increases in case when siblings or offspring are having CHD. Mutations are another factor which develops heart defect. More than 1/3rd of neonates born with Down syndrome and 1/4th of girl child born with Turner syndrome have heart defects.

4. SIGNS AND SYMPTOMS OF CONGENITAL HEART DEFECTS

No symptoms of heart defects transfer from fetal to the mother during pregnancy. Heart defects generally become evident in newborns within a few weeks or months after birth. Heart murmurs heard during the examination, a bluish tint to skin, lips and fingernails, Fast breathing/shortness of breath, Poor weight gain in infants are the primary signs of the CHD that can be observed in newborns. These signs and symptoms of CHD may vary case to case and also depends on the severity of defects.

5. TYPES OF HEART DEFECTS

Most CHD either obstructs blood flow in the heart or vessels near it or blood flows in an anomalous pattern. Rarely, defects occur in which only one ventricle is present or both pulmonary artery and aorta arise from the same ventricles. These defects developed during pregnancy and recognized after birth classified into two groups: Cyanotic (blue) Heart defect and Acyanotic (pink) Heart defect.

a) Cyanotic Defect: In Cyanotic Heart defect the lips, fingers, and toes of a child appears blue, due to abnormal flow of blood. Normally, blood from the whole body enters into the right side of the heart. This right side of the heart push the blood to the lungs for oxygenation. The oxygen–rich blood moves on the left side of heart. The left side of the heart pumps the blood to the whole body through the aorta. Due to Cyanotic defect deoxygenated blood from the right part of heart mixed with oxygenated blood to the left part of the heart. This reduced the level of oxygen in the blood ready to flow in the rest of the body. The low oxygen level blood turns lips, fingers and toes bluish. The brief of cyanotic defects is presented below. Commonly developed defect in prenatal is Tetralogy of fallot. This defect develops due to a combination of four defects: a lessening of pulmonary valve; an enlarged right ventricle; a hole between the right and left ventricles; and an aorta connected to both left and right ventricles. Transposition of the great arteries (TGA) is another cyanotic defect observed in neonatal; pulmonary artery from the left ventricle change the position with aorta from the right ventricle. Tricuspid atresia (absence or closed

tricuspid valve), Pulmonary atresia (absence or closed pulmonary valve), Truncus arteriosus (a common artery arises from right and left ventricles), total anomalous pulmonary venous connection – TAPVC (malposition of all four pulmonary veins), Hypoplastic left heart syndrome (severely underdeveloped left ventricle, aortic valve ,mitral valve and aorta) are some another form of cyanotic defects.

b) Acyanotic Defect: In acyanotic defect the oxygenated blood shunts from left side of the heart to right side, thus body does not turn bluish, but exercise and exertion difficulty may be observed. Ductus Arteriousus is an opening between the pulmonary artery and the aorta; normally present during fetal life and closes after birth. If it does not close some bloods returns to the lungs. DA is frequently seen in premature babies. Septal defect caused by an opening between the wall of the ventricles known as Ventricle Septal Defect and opening between the wall of atria known as Atrial Septal Defect. Other septal defects are Eisenmenger's syndrome and Atrioventricular septal defect. Obstruction defects also come under acyanotic defects. Pulmonary stenosis (PS) is caused by a narrowing of the valve between the right ventricle and the pulmonary artery and Aortic stenosis (AS) is caused due to narrowing of aortic valve which lies between left ventricles and aorta. Coarctation of the aorta is due to narrowing of the aorta that supplies blood to the entire body. Other obstruction defects are Bicuspid aortic valve (Aortic valve develops with only three flaps in place of normally three flaps), Sub-aortic stenosis (narrow left ventricle just below the aortic valve) and Ebstein's anomaly (downward displacement of the tricuspid valve into the right ventricle).

6. EXISTING TECHNIQUES FOR PRENATAL DETECTION OF CHD

In this section, an attempt has been made to review and analyses the performance of currently used CHD detection techniques. The most popular diagnostic techniques used for detection of heart defects in fetal during the antepartum period are fetal echocardiography (fECG), fetal magnetic resonance imaging (fMRI), Amniocentesis, Nuchal-fold scan and fetal phonocardiography (fPCG).

A] Fetal Echocardiography (fECG) Technique

Fetal echocardiography is a non-invasive ultrasound technique done during pregnancy to evaluate the heart of the unborn baby. It is used for thorough study of the structure and functioning of the fetus's heart and to confirm the presence or absence of cardiac abnormalities [12]. In this technique, the ultrasonic sound waves of 5 to 7 MHz frequency is applied through a sensor by applying gel to the abdominal surface. The ultrasonic sound waves move through the mother's and baby's skin and other body tissues to the baby's heart tissues, from where the waves bounce (or "echo") off and create an image of the fetal heart structures. There are two ways a fetal echocardiogram is performed; abdominal ultrasound and transvaginal ultrasound. The abdominal ultrasound is the most common form of ultrasound to evaluate the baby's heart, but transvaginal ultrasound is typically used early in pregnancy. A small ultrasound transducer is inserted through the vagina and rests against the back of the vagina. The fetal echocardiography equipment with a typical scanned image is shown in figure 2.

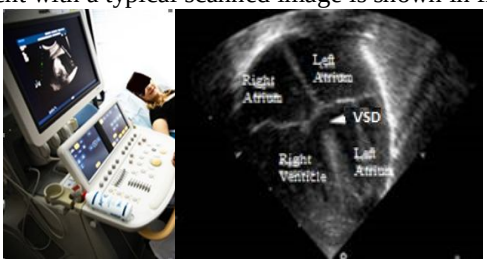

Figure 2: Fetal Echocardiography and typical image

Fetal echocardiograms can be performed any time after 17–18 weeks of gestation [13] but has a chance of missed or misinterpretation. Hence, International Society of Ultrasound in Obstetrics and Gynecology, suggested to go for second scan between weeks 18 to 22; it is the ideal period to identify cardiac malformation as fetal's heart adequately developed by this time and does not require any additional scan for identification of CHD [14].

Various studies are done to observe the efficiency of fECG. Rasiah et al, 2006 [15] included 10 studied, 4 transabdominal ultrasonography, 4 transvaginal and 2 a combination of both, included in his research studies of fetal echocardiography and concluded that an echocardiography examination of the fetus is feasible for accurately detecting major CHD in the first trimester and may be suggested to women at high risk of having children with CHD. In a study Smrcek, 2006 [16] observed in-utero detection rate of fetal echocardiography was 86.96%. Hornberger et al., 2012 [17] reviewed the current state of the art of fetal/perinatal cardiology and the advances that have occurred in the field largely over the past decade. They concluded that despite the many advances in this field, there is an ongoing need to recognize the unique challenges faced in prenatal diagnosis. They suggested that there is a critical need to improve prenatal detection at routine obstetrical ultrasound or through the development of more objective screening tools that will ultimately allow fetal and perinatal cardiology to achieve its full impact. In another study Ventriglia et al. 2016 [18] concluded that overall, fECG may be considered feasible, highly sensitive and specific when performed by experienced fetal cardiologists. He also statically discussed that most of the major cardiac abnormalities can be diagnosed from 12-16 weeks of gestation. Furthermore, the combined fECG with Nuchal translucency scan approach gives 60-70% increase in detection rate. Combined analysis is also justified in the case of the high CHD frequency due to genetic syndromes in the first and second trimester.

The advantages of fECG are that it is still the gold standard for the evaluation of the fetal heart after heart

auscultation through a stethoscope. It allows the parents to understand the heart problems in unborn babies and prepares them psychologically at the time of delivery. 3D – 4D echo are also available for fetal heart abnormality evaluation which makes it more reliable. But there are also few limitations this technique. Some abnormalities cannot be detected prenatally due to its poor resolution. Maternal obesity, prone fetal position, and late gestation) can make a detailed heart evaluation very difficult due to acoustic shadowing, especially during the third trimester. Exposures of ultrasound waves elevate temperature by 4°C above normal in fetal tissues [19]. This may develop other congenital defects. Hence frequent use is avoided by experts. Due to cost of equipment, the benefits of echocardiography are rarely available in rural places.

B] Fetal Magnetic Resonance Imaging (fMRI) Technique

Fetal MRI is another non-invasive imaging test that offers detailed information about anatomic structures of the fetus. It is now a well-established imaging modality for the diagnostic evaluation of the fetus with congenital anomalies. This technique supplements the information obtained from high-resolution fetal ultrasound and provides additional information about the fetus. Fetal magnetic resonance imaging was first described in the 1990s, but image degradation by fetal motion and the relatively long acquisition time discouraged the use of MRI for the examination of fetal anatomy [20]. The introduction of ultra-fast techniques made successively use of MRI by minimizing fetal movement and improved visualization of fetal images [21].

In this non-invasive diagnostic test about 1.5 Tesla superconducting magnet using a phased-array surface coil is used. MRI scanning is executed by laying down the pregnant woman in a supine position or left lateral decubitus position inside a very large magnet, which creates a magnetic field around her. This magnetic field causes all water molecules to line up the same way and then operator applies it in different ways and measures the way water molecules go back to their normal position, which allows to create a variety of images. A variety of rapid MRI sequences are used to obtain T1-weighted (longitudinal magnetization is recovered) and T2-weighted (transverse magnetization) images. However, the most widely used sequence in fetal imaging is the single-shot fast spin-echo to overcome the complication due to movement of fetal. In this technique, data from data from all of k-space is obtained after a single 90º-excitation pulse. The MRI equipment and a typical MRI of the fetus is shown in figure 3.

The results of the fMRI are highly affected by the motion of the fetus and poor resolution at an early gestational age. Therefore, it is usually done after 18 weeks of gestation. The ventricles are observed larger with MRI compared to USG between weeks 20–24. It decreases between weeks 24–28. The ventricles seem narrower than normal between weeks 34–36 [22]. Thus the best evaluation of cardiac abnormality in the fetus is after week 24.

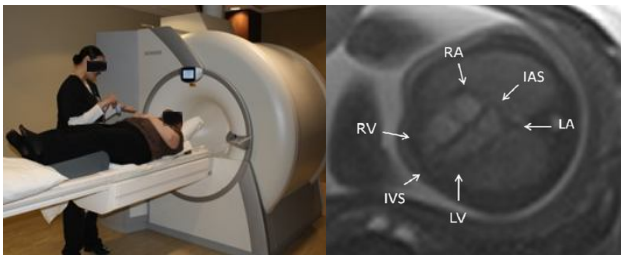

Figure 3: MRI Equipment and fMRI image

A lot of research is carried out to identify the efficiency and accuracy of fMRI. Manganaro et al., 2008 [23] in their study of fetal MRI for identifying cardiac abnormality, reviewed 31 MRI of fetal and concluded that it has a potential to visualize the fetal heart and this makes it a second tool to fetal echocardiography in the prenatal study of congenital heart malformations. In another study Ming Zhu, 2015 [24] reviewed 280 cases of fetal CHD in which fetal MRI was performed at 17 to 39 weeks of gestation and concluded that though fetal echo still was the first choice method in the CHD detection of fetal. MRI can become an alternative imaging modality for CHD detection of fetal. He also concluded by comparing the result of fetal MRI with the echocardiography's result, it has some limitations. Fetal MRI sometimes missed small VSD and mild valvular stenosis, still believe MRI really can provide some additional important information about fetal CHD. Mlczoch et al. 2016 [25] used fMRI with an aim to assess the frequency of placental abnormalities in fetuses with CHD. They used 1.5 tesla MRI data of 245 fetuses (aged 18–35 gestational weeks - GW) with CHD were retrospectively for this study and evaluated placenta on T1, T2, echo planar. They concluded that fMRI detects placental abnormalities in up to 1/3 of CHD fetuses.

The primary advantages of MRI include its high spatial resolution. It has excellent soft tissue contrast which provides the distinction of maternal and fetal organs. It is Non-invasive and does not contain ionizing radiation. It shows the potential value in detecting cardiac abnormalities. Fetal MRI can identify positional anomalies of the heart; different sizes of the heart chambers and malformations of the great vessels and atrioventricular canal defects can be visualized by fetal MRI. But even with rapid image acquisition, motion can still affect the quality of the fetal MRI. Fast beating of the fetal heart is another obstacle in MRI. It requires large access time, on an average it takes 40-50 minutes to perform. It is costly. The expert is required to interpret the result of fetal MRI. Fetal MRI sometimes missed small VSD and mild valvular stenosis.

C] Nuchal Translucency (NT) Scan Technique

A nuchal translucency screening, is a routine ultrasound performed to measure increased fluid at the base of their necks; a spot known as the nuchal fold. The increase

thickness indicates the presence of an extra chromosome. At the early stage, every fetus carries some kind of fluids in the soft part of its back neck. So using ultrasound scanning this area is measured. The nuchal fold thickness exceeds a set threshold of 3.5mm point out a greater risk of CHD and can detect 85% of birth defects accurately [26,27]. The normal and increased nuchal fold thickness is shown in figure 4. This fluid can be measured with ultrasound when the base of the neck is still transparent. Because the nuchal fold becomes less clear as the baby grows, timing is crucial; the best assessment time with this technique is between 11th to 14th weeks.

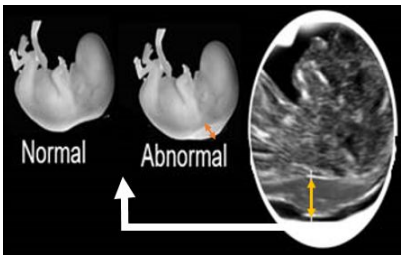

Figure 4: Normal and Increased Nuchal Fold Thickness

The efficiency and reliability of the test are studied through various studies. Mavrides et al., 2001[28] observed the low sensitivity of NT for serious CHD in the general population and concluded that NT cannot be relied on as the sole or a major screening tool. Malone, 2003 [29] observed that the accuracy of NT screening in detecting DS ranges from 29% to 100%, at false-positive rates of 0.3% to 11.6%. He pointed out that some studies have demonstrated a 100% success rate at obtaining an NT measurement. However, none of them provides information on the adequacy of these images once obtained. On the contrary, a strong association between webbed neck and coarctation of the aorta in infants with Turner syndrome was observed by Clark, 2005. In Makrydimas et al, 2005 [30] published their results from a pooled database in which the nuchal translucency was measured during the first-trimester in 637 fetuses with congenital heart defects. The fetuses were divided into two groups, with abnormal chromosomes and with normal chromosomes. When the nuchal translucency was 3.5 mm or greater, 59% of fetuses with heart defects and abnormal chromosomes were identified. Similarly, 23% of fetuses with normal chromosomes and heart defects were identified because of an increased nuchal translucency measurement. Bas-Budecka, 2010 [31] suggested nuchal translucency screening and ductus venosus blood flow has been useful methods of identifying cardiac anomalies in chromosomally normal fetuses. Guraya, 2013 [27] concluded that an NT of 3.5 mm or more should be considered significant and warrants further investigations by serum markers, depending upon the gestational age. Also for accurate measurements of NT, quality guidelines follow up; training and supervision of the sonologist are of utmost importance. Borelli et al., 2016 [32] examined the association between maternal characteristics, routinely collected first- and second-trimester bio markers and the risk of having an infant with a critical congenital heart defect (CCHD). Poisson regression analyses were used to estimate the relative risk and found an interval of a CCHD. Despite the increased risk, performance of the testing demonstrated low sensitivity and specificity for screening.

The advantages of the NT technique for cardiac abnormality detection are it is non- invasive. If the risk is high, it is done at an early stage of pregnancy, which gives plenty of time to decide your next steps. It can supports to the result observed by other techniques, when combined. The limitation of NT technique is an ultrasound examination of the fetus is a subjective process that is highly dependent on operator skills and the quality of the sonographic equipment. Like other screening tests, an NT scan won't give a diagnosis; it only assesses baby's risk for certain problems. Individually, it is not reliable technique.

D] Amniocentesis Technique

Amniocentesis is the only invasive medical procedure used in prenatal diagnosis and it is used to look for certain types of birth defects, such as Down syndrome, a chromosomal abnormality [33]. During pregnancy, the fetus is surrounded by amniotic fluid, a substance much like water. The amniotic fluid contains live fetal cells and other substances, such as alpha-fetoprotein (AFP). These substances provide important information about your baby's health before birth. A thin needle is inserted into the uterus to take out a sample of amniotic fluid as shown in figure 5. The amniotic fluid is surrounded in the uterus and protects the fetus. It contains fetus cells, which is used to test anomalies. A special care is required to protect the fetus from any injury with a needle. Hence ultrasound is used to find the position and movement of the baby in the uterus while inserting the needle. The procedure takes about 45 minutes, although the collection of fluid takes less than 5 minutes.

This test is specially used to identify chromosomal and genetic abnormalities by amniotic fluid, which contain the fetal cells. It does not identify CHD directly, but establish suspected cardiac malformation relation with the underlying syndrome like Down syndrome, Marfan syndrome, and Turner's syndrome [34].

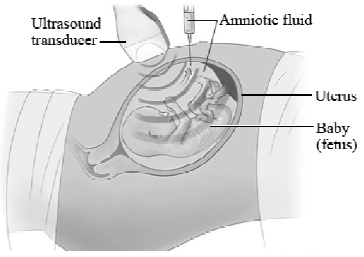

Figure 5: Extraction of Amniotic Fluid using needle

Prenatal examination using amniocentesis technique should be done during 16 – 20 weeks of gestation to avoid the risk of miscarriage due to needle used for extracting a sample. It can also perform in later stage if necessary.

Amniotic fluid cells are the primary means of prenatal chromosomal diagnosis [35]. It offers an opportunity to obtain important information about the pregnancy. It seems that second trimester amniocentesis is a relatively safe and reliable method for prenatal diagnosis. However, it is recommended to be done by well-trained and experienced hands [36]. The presence of extra chromosome trisomy 21 is associated with heart defects. The advantages of amniocentesis are it identifies several genetic disorders and disorder related with congenital defects. It confirms, if an abnormality is present in a fetus and may have been detected from other tests.

The drawbacks are: it is invasive technique. It is recommended to be done by well-trained and experienced hands. Especially used to identify chromosomal and genetic abnormalities not heart defects directly. Because it carries a slightly increased risk of miscarriage amniocentesis is usually reserved for those women considered at higher risk.

E] Fetal Phonocardiography (fPCG) Technique

Fetal phonocardiography (fPCG) is another important non-invasive technique of detecting cardiac abnormality in fetal. The fPCG is a graphical recording of fetal heart sounds picked up from the maternal abdomen by a sensitive microphone. This recording is normally performed in a noiseless room with the pregnant woman in the supine position with her head resting on a pillow.

The recording of the sound which is a linear summation of vibrations produced by the fetal heart, maternal organs and external sources [37]. This signal carries valuable information about physiological conditions of the fetal health [38]. In this technique, the fetal heart sound is recorded from the abdomen of a pregnant woman by means of a sensitive microphone. This recording is normally performed in a silent room with the pregnant woman in the supine position. The fPCG transducer is placed firmly at the desired position on the abdomen using a suction ring and a rubber strap. The fetal phonocardiogram presents heart sounds and murmurs most precisely [39]. Timings, relative intensities pertaining to murmur, and other details of fetal heart sound can be seen easily from graphics of the recordings. The typical phonocardiogram is shown in figure 6.

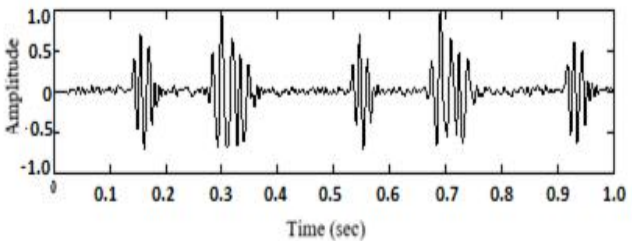

Figure 6: Typical Phonocardiography Signal

Since the heart of fetal fully developed by the 10th week of pregnancy, the acquisition and recording of heart sound may start from the end of the first trimester to start of delivery pain. So the assessment period is too long. However, the best assessment period of fPCG for detection of CHD may be after the first-trimester, i.e. the 12th week of pregnancy when the developed heart defect plays the significant role in circulation and may appear in terms of pathological murmurs.

Many researchers used fPCG signal as a source for assessment of fetal well-being's through FHR estimation and Baseline FHR, Baseline Variability, Acceleration and Deceleration of the FHR, but a very limited work is done for detection of CHD through fPCG. The idea of detecting CHD through fPCG does not strike to most of the researchers.

Maeda et al., 2013 [40] made an effort of murmur detection through heart sound oscilloscopic image recorded on a photographic film and concluded that heart sound auscultation should not be applied for the fetal monitoring due its poor ability to detect FHR abnormalities. However, 16.8% physiologic systolic murmur of frequency 100-200 Hz was detected in the diagnosis of 105 fPCG signals, but no abnormality detected in neonatal after birth. The other research groups Kovack et al., 2011 [41], with the study of fetal phonocardiography-Past and future possibilities; they started work on detection of abnormalities through fPCG signal. A. T. Balogh, 2012 [42] under the guidance of Kovack, presented the work of analysis of the Heart Sounds and Murmurs of fetuses and preterm infants. They observed fetal heart murmurs in the case of certain congenital heart diseases and established that murmur detection and analysis can contribute to the widespread screening of cardiac abnormalities, especially in the low-risk population. They concluded that all these findings could assist in the development of a fetal expert system for automated surveillance or clinical decision support. They also resolved that, in order to estimate the contribution of fetal heart murmur detected during the screening for congenital heart diseases a large number of fetuses with and without CHD have to be examined, and they left this work for the future. In progress, to above work Kovacs et al. 2015, presented another work on detection of cardiac abnormality through fPCG. They considered fPCG signals of 1000 pregnant women being in the 28th – 40th week of gestation, recorded with the telemedicine fetal monitor at home, combined with the prescribed 20-minute CTG test during the last eight years. They used the combination of the Wavelet transform, the auto correlation, and the Matching Pursuit methods for detection of S1 and S2 as primary step and FHR is computed based on S1 timing. In this work, they predicted murmur based on identifying the unwanted shape exists in the systolic or diastolic intervals. It was demonstrated that with the nine-parameter (type, volume, dominant frequency, bandwidth, position, duration, shape, splits time if, any in S1 and S2) identified from fetal heart murmur would be possible to determine the relationship of these to the different heart defects, in order to indicate probable postnatal difficulties.

The advantages of fPCG technique are, it is a non-invasive (passive) technique. It contains valuable information about fetal well-being and heart structure abnormality. Signal acquisition equipment is portable & cheap, hence can be made available everywhere. No expert is required; a simple training can be given to the operator. The disadvantages are, fPCG signals are sensitive to internal and external noise and signal is non-stationary.

7. COMPARATIVE ANALYSIS OF CHD DIAGNOSTIC TECHNIQUES

In the previous sections, an attempted was made to describe and elaborate review of various techniques for prenatal detection of CHD. A comparative analysis of these techniques is done in this section to find out a simple, non-invasive yet efficient diagnostic tool for detection of heart abnormality during the intrauterine period. The analysis was carried out using different parameters such as simplicity, assessment period, safety, economy, etc. The outcomes of comparative analysis of diagnostic techniques for CHD are depicted in Table 1.

It is observed that all techniques except fPCG requires operator for its handing and interpretation. Through fPCG technique no energy is penetrated inside the womb hence it is safe. All techniques make use of bulky and costly instruments for diagnosis while the acquisition, recording and analysis of fetal heart sound instruments required are cheaper. Hence fPCG technique is cost effective and home or distance monitoring is possible with it. The amniocentesis and NT do not identify the CHD directly, but link the result with developing CHD. It along with fECG and fMRI provides the maximum assessment time in comparison to amniocentesis, which has a risk of miscarriage in later stages of pregnancy and NT can be done in the early stage till the fold back is transparent.

8. CONCLUSION

We have presented a review of various techniques for prenatal detection of CHD. On the basis of published literature, it can be concluded that the congenital heart defects are one of the major causes of deaths worldwide. In order to minimize the mortalities due to CHD, their diagnosis should be more effective, precise and should start as early as possible. It should be cost-effective and safe. We have attempted to describe and elaborate review of various techniques used for prenatal detection of CHD. These techniques are fECG, fMRI, NT, Amniocentesis and fPCG. Their working principles, advantages and limitations were reviewed. From the descriptions and findings, clearly fECG, fMRI, NT and Amniocentesis can only be performed properly in a clinical environment under the supervision of an experienced physician. Experts are required for interpreting their results and moreover; these techniques are complicated. The NT and Amniocentesis do not identify the CHD directly, but link the development of CHD with chromosomal abnormality, which is identified through these techniques. The Amniocentesis is the only invasive technique, while all other techniques are non-invasive and among them, fPCG is simply passive. The fPCG is the advancement of the very primary diagnosis process through a stethoscope. The fPCG signals carry valuable information about the anatomical and physiological states of the fetal heart. It can be used to identify different established abnormalities through murmurs. It is recognized as an efficient and safe method for early detection and long-term monitoring heart defects in fetus heart. It can be broadly utilized because it is inexpensive, non-invasive, safe, and easy for medical professionals to perform. The major limitation of this technique is the poor signal to noise ratio. If the signal is acquired in a silent room with many trials to get in with minimum noise from the best position on the abdomen surface, the segment of fPCG may also be useful for identification of CHD murmur. The fPCG is the only technique which can be used at home and distant monitoring as well.

Table 1: Result of Comparative Analysis of Diagnostic Techniques

Techniques / Parameters	fECG	fMRI	Nuchal Translucency	Amniocentesis	fPCG
Simplicity/ minimal expertise	Expert is required	Expert is required	Expert is required	Expert is required	**Simplest**
Safety	Safe	Safe	Safe	Risk of Miscarriage is highest	**Safest**
Economy	Expensive	Most Expensive	Expensive	Moderate cost	**Most cost effective**
Accuracy in identifying CHD	**Accurate**	**Accurate**	Does not detect CHD directly	Does not detect CHD directly	**Accurate**
Home/distant monitoring	Not Possible	Not Possible	Not possible	Not possible	**Possible**
Long term monitoring	Possible	Possible	Not possible	Possible	**Possible**
Best Assessment period (in weeks)	18 to 22	24 to 28	11 to 14	16 to 20	12 to 36 **(Max)**
Handling of diagnosis unit	Difficult to handle	Most difficult to handle	Difficult to handle	Most difficult to handle	**Most convenient**

REFERENCES

1. Mitchell S., Korones S., Berendes H. **Congenital heart disease in 56,109 births Incidence and natural history**, *Circulation*, Vol.43, pp. 323–32, 1971.
2. **What Are Congenital Heart Defects?**, *National Heart, Lung, and Blood Institut*e, 2011, Retrieved 20 December 2014.
3. Hoffman J. **The global burden of congenital heart disease**, *Cardiovasc Journal of Africa*, Vol. 24(4), pp. 141–5, 2013.
4. Thangaratinam S., Brown K. and Zamora J. et al. **Pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies: a systematic review and meta-analysis**, *Lancet*, Vol. 379(9835), pp. 2459–64, 2012.

5. Saxena A. **Congenital Heart Disease in India: A status Report**, *Indian journal of paediatrics*, Vol.72, pp. 595-8, 2005.
6. Yogi M., Vasudev K., Venkatramana. **Clinical study of extracardiac malformations associated with congenital heart disease**, *Journal of Evidence based Medicine and Healthcare*, Vol. 2(53), pp. 8724 – 30, 2015.
7. Mohammad N., Shaikh S., Memon S. and Das H. **Spectrum of heart disease in children under 5 years of age at Liaquat University Hospital, Hyderabad, Pakistan**, *Indian Heart Journal*, Vol. 66(1), pp. 145-9, 2014.
8. Murphy P. **The fetal circulation**, *Oxford Journals Medicine BJA: Contin Educ Anaesth Crit Care Pain*, Vol. 5(4), pp. 107-112, 2005.
9. Christie A. **Normal closing time of the foramen ovale and ductus arteriosus; an anatomic and statistical study**, *Am J Dis Child*, Vol. 40(2), pp. 323-6, 1930.
10. Moss AJ, Emmanouilides GC, Duffie ER Jr. **Closure of the ductus arteriosus in the newborn infant**, *Pediatrics*, Vol.32, pp. 25–30, 1963.
11. **Congenital Heart Disease: Causes**, *Health line* April 6 2012, Retrieved on 20 December 2014.
12. Lee W., Allan L., Carvalho J., Chaoui R., Copel J., Devore G., Hecher K., Munoz H., Nelson T., Paladini D. and Yagel S. **ISUOG consensus statement: what constitutes a fetal echocardio-gram?**, *Ultrasound Obstet Gynecol*, Vol. 32, pp. 239–242, 2008.
13. Garne E., Stoll C. and Clementi M., **Evaluation of prenatal diagnosis of congenital heart diseases by ultrasound: experience from 20 European registries** *Ultrasound Obstet Gynecol*., Vol. 17(5), pp. 386-91, 2001.
14. Carvalho J., Moscoso G., Tekay A., Campbell S., Thilaganathan B. and Shinebourne E. **Clinical impact of first and early second trimester fetal echocardiography on high-risk pregnancies**, *Heart*, Vol. 90(8), pp. 921–6, 2004.
15. Rasiah S., Publicover M. and Ewer A. et al. **A systematic review of the accuracy of first-trimester ultrasound examination for detecting major congenital heart disease**, *Ultrasound Obstet Gynecol*., Vol. 28(1), pp. 110-6, 2006.
16. Smrcek J., Christoph B. and Annegret G. et al. **Detection Rate of Early Fetal Echocardiography and In Utero Development of Congenital Heart Defects**, *Journal Ultrasound Med* , Vol. 25 (2), pp. 187-96, 2006.
17. Hornberger L., Moon-Grady A. and Tworetzky W. **Fetal Echocardiography and Prenatal Cardiovascular Interventions – An Update**, *Journal of Clinical & Experimental Cardiology*, 2012, doi:10.4172/2155-9880.S8-009.
18. Ventriglia F., Caiaro A. and Giancotti A. et al. **Reliability of Early Fetal Echocardiography for Congenital Heart Disease Detection: A Preliminary Experience and Outcome Analysis of 102 Fetuses to Demonstrate the Value of a Clinical Flow-Chart Designed for At-Risk Pregnancy Management**, *Pediat Therapeut*, 2016. doi:10.4172/2161-0665.1000270.
19. Colin Deane. **Safety of Diagnostic Ultrasound in Fetal Scanning**, 2002. https://sonoworld.com/Client/Fetus/html/doppler/capitulos-html /chapter_02.htm, Retrieved 20 December 2014.
20. Rossi A and Prefumo F. **Additional value of fetal magnetic resonance imaging in the prenatal diagnosis of central nervous system anomalies: a systematic review of the literature**, *Ultrasound Obstet Gynecol* , Vol. 44 (4), pp. 388–93, 2014.
21. Levine D., Barnes P., Sher S., Semelka R., Li W., McArdle C., Worawattanakul S., Edelman R. **Fetal fast MR imaging: reproducibility, technical quality, and conspicuity of anatomy**, *Radiology*, Vol. 206, pp. 549–54, 1998.
22. Lan L., Yamashita Y., Tang Y., Sugahara T., Takahashi M., Ohba T. and Okamura H. **Normal fetal brain development: MR imaging with a half-Fourier rapid acquisition with relaxation enhancement sequence**, *Radiology*, Vol. 215(1), pp. 205-10, 2000.
23. Manganaro L., Savelli S., Di Maurizio M. and Perrone A. et al. **Assessment of congenital heart disease (CHD): is there a role for fetal magnetic resonance imaging (MRI)?**, *Eur J Radiol*., Vol. 72(1), pp.172-80, 2009.
24. Ming Zhu. **Fetal cardiac MRI**, *Journal of Cardiovascular Magnetic Resonance*, Vol. 17(1), pp.220, 2015.
25. Mlczoch E., Gruber G. and Dekan S. et al. **Congenital heart disease and the placenta – preliminary results from a fetal MRI program**, *Ultrasound Obstet Gynecol*, Vol 48, 2016. doi:10.1002/uog.16479.
26. Malhotra N., Malhotra J., Tomar S. and Malhotra Bora N. et al. **Ultrasonography and Birth Defects - Review Articles**, *Donald School Journal of Ultrasound in Obstetrics and Gynecology*, Vol. 7(2), pp. 149-59, 2013.
27. Guraya S. **The Associations of Nuchal Translucency and Fetal Abnormalities; Significance and Implications**, *Journal of Clinical Diagnostic Research*, Vol. 7, pp. 936–41, 2013.
28. Mavrides E., Cobian-Sanchez F. and Tekay A. et al. **Limitations of using first-trimester nuchal translucency measurement in routine screening for major congenital heart defects**, *Ultrasound Obstet Gynecol*., Vol. 17(2), pp. 106-10, 2001.
29. Malone F. and D'Alton M. **First-trimester sonographic screening for Down syndrome**, *Obstetrics & Gynecology*, Vol. 102(5), pp. 1066–79, 2003.
30. Makrydimas G., Sotiriadis A. and Huggon C. et al. **Nuchal translucency and fetal cardiac defects: a pooled analysis of major fetal echocardiography centers**, *Am J Obstet Gynecol*, Vol. 192(1), pp.89-95, 2005.
31. Bas-Budecka E., Perenc M. and Sieroszewski P. **The role of fetal nuchal translucency (NT) and ductus venosus blood flow (DV) in the detection of congenital heart defects**, *Ginekol Pol*., Vol. 81(4), pp. 272-6, 2010.

32. Borelli M., Baer R., and Chambers C. et al. **Critical congenital heart defects and abnormal levels of routinely collected first- and second-trimester biomarkers**, *Am J Med Genet A*, 2016. doi: 10.1002/ajmg.a.38013.
33. Neagos D., Cretu R., Sfetea R. and Bohiltea L. **The importance of screening and prenatal diagnosis in the identification of the numerical chromosomal abnormalities**, *Journal of Clinical Medicine* Maedica (Buchar), Vol. 6, pp. 179-84, 2011.
34. Kalogiannidis I., Prapa S., Dagklis T., Karkanaki A., Petousis S., Prapas Y. and Prapas N. Amniocentesis-related adverse outcomes according to placent**al location and risk factors for fetal loss after midtrimester amniocentesis**, *Clin Exp Obstet Gynecol*., Vol. 38(3), pp. 239-42, 2011.
35. Pierpont M., Basson C., Benson D., et al. **Genetic basis for congenital heart defects: current knowledge**, *Circulation*, Vol. 115(23), pp. 3015–38, 2007.
36. Simin T., Sharareh B. and Hossein A. et al. **Outcome of Pregnancies Presenting for Diagnostic Evaluation of Fetal Trisom**, *Life Sci Journa*l Vol. 10(2), pp.1682-87, 2013.
37. Chourasia V. and Tiwari, A., **Fetal heart rate variability analysis from phonocardiographic recordings**, *Journal of mechanics in medicine and biology*, Vol. 11 (05), pp.1315-31, 2011.
38. Chourasia J., Chourasia V. and Mittra A. **Prenatal identification of CHD murmur using four segment phonocardiographic signal analysis**, *Journal of Medical Engineering & Technology*, Vol. 41(2), pp. 122-30, 2017.
39. Kovacs F., Kadar K., Hosszu G., Balogh A., Zsedrovits T., Kersner N., Nagy A. and Jeney G. **Screening of Congenital Heart Diseases with Fetal Phonocardiography**, *International Journal of Medical, Health, Biomedical, Bioengineering and Pharmaceutical Engineering*, Vol. 9(6), pp. 497-501, 2015.
40. Maeda K. and Nakano H. **Systolic foetal heart murmur detected in foetal phonocardiography**, *Occup Med Health Aff*., 2013 doi: 10.4172/2329- 6879.1000102.
41. Kovacs F., Horvath C., Balogh A., Hosszu G. **Fetal phonocardiography--past and future possibilities**, *Computer Methods and Programs in Biomedicine*, Vol. 104(1), pp. 19-25, 2011.
42. Balogh A., **Analysis of the heart sounds and murmurs of fetuses and preterm infants**, Ph.D. dissertation, Pazmany Peter Catholic University, 2012.