Tissue Doppler, Pulsed Wave Doppler and M-mode Ultrasonography to Measure Fetal PR-interval in Second Trimester in Normal Pregnant Egyptian Ladies

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Background: Autoimmune associated complete heart block is irreversible. However, several cases reports have suggested that less severe forms of heart block might be reversible with maternal steroid therapy. To identify fetuses with prolonged AV time intervals, normal values first have to be obtained.

Aim: The aim of the present study was to establish an Egyptian normal reference values for human fetal mechanical PR interval using M-mode, PWD, and TDI as well as to compare ease of recording and reliability of ultrasonographic approaches used to measure fetal mechanical PR interval and detect the different factors affecting on the normal values.

Design: Prospective observational study.

Methods: From (August 2008 to August 2009) sixty normal pregnant Egyptian ladies with uncomplicated pregnancies were enrolled in the study with mean age of (27.8±5.3). Those ladies were between 14-26 weeks gestation. All of them had measured fetal mechanical PR interval by M-mode, PWD and TDI.

Results: Measurement of mechanical PR interval was done using 5 different methods, M-mode (Ao valve and post. wall of LA) method was performed on 6 of the pregnant female (10%), PWD (LV in/out) method was performed on the whole study group (100%), PWD (SVC/Ao) method was performed on 11 pregnant female (18.3%),while the application of TDI (Aa-IV) method was performed on 59 pregnant female (98.3%) and TDI (Aa-Sa) method could be performed in 59 pregnant female(98.3%).We excluded M-mode method and PWD (SVC/Ao) method from further analysis. According to gestational age the study population was divided into three groups: group (I) <18 weeks, group (II) 18-22 weeks and group (III)>22 weeks. The present study revealed that mechanical PR interval values using PWD (LV in/out) in the three groups were 115±7,120±17 and125±8 ms respectively with no statistical difference between those groups. Using TDI (Aa-IV) in all three groups normal values were 87±7, 90±7 and 93±7 ms respectively with statistical significant difference where (P- value 0.002). Mechanical

PR interval values using TDI (Aa-Sa) in all three groups were125±7,126±7 and 135±10 ms respectively with statistical significance difference where (P- value 0.002). There was significant positive correlation between gestational age and different methods used to measure fetal mechanical PR interval. There was no significant correlation between fetal heart rate and different methods when measuring fetal mechanical PR interval.

Conclusion: As comparing the different methods we found that using PWD (LV in/out) is the most applicable method in the assessment of the mechanical PR interval and also both methods of TDI. There are differences in normal PR interval values measured by the 5 methods. The present study showed that there was correlation between mechanical PR interval and gestational age, there is increase in mechanical PR interval with increase the gestational age and there is no change of mechanical PR interval with increase of heart rate.

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AE	atrial ectopic
Ao	ascending aorta
ASD	atrial septum defect
AV	atrioventricular
AVRT	atrioventricular reentry
AVNRT	atrioventricular nodal reentry
Bpm	beat per minute
CCAVB	congential complete atrioventricular block
CHD	Congenital heart disease
ECG	electrocardiogram
FE	Fetal echocardiography
HR	heart rate
IDDM	insulin dependent diabetes
IV	isovolumic contraction
LQTS	long QT syndrome
LV	left ventricle
Mm	millimeter
Ms	milliseconds
NLE	neonatal lupus erythematosus
PDA	patent ductus arteriosus
PJRT	paroxysmal junctional reciprocating tachycardia
PRIDE	PR interval dexamethasone evaluation
PWD	pulsed wave Doppler
Sa	ventricular systole
SLE	systemic lupus erythematosus
SS	Sjögren syndrome
SVC	superior venous cava
SVT	supraventricular tachycardia
TDI	tissue Doppler imaging
VA	ventriculo-atrial
VSD	ventricular septum defect

Introduction

Fetal cardiac dysrhythmias are potentially life-threatening conditions. However, intermittent extrasystoles, which are frequently encountered in clinical practice, do not require treatment. Sustained forms of brady- and tachyarrhythmias might require fetal intervention. Fetal echocardiography (FE) is essential not only to establish the diagnosis but also to monitor fetal response to therapy. **(Api and Carvalho; 2008)**

In the last decade, improvements in ultrasound methodology and new diagnostic tools have contributed to better diagnostic accuracy and to a greater understanding of the electrophysiological mechanisms involved in fetal cardiac dysrhythmias. **(Api and Carvalho; 2008)**

AV dissociation can occur in association with structural heart defects, such as ventricular inversion or L- transposition of the great vessels, or as an isolated lesion: congential complete atrioventricular block (CCAVB). **(Friedman et al; 2001)**

Isolated CCAVB in the fetus is generally associated with the presence of maternal SS-A/RO and SS-B/LA antibodies, and its substrate is inflammatory injury of the fetal conduction system resulting in permanent damage of the AV node. **(Friedman et al; 2001)**

However, only 1-5%of all women with SS-A/RO and SS-B/LA antibodies give birth to the affected children, and recurrence occurs in less than 20% of consecutive pregnancies .**(Brucato et al;2001)**

Congential complete atrioventricular block, once diagnosed in utero, is associated a high morbidity and mortality, and more than 60% of the children surviving in the fetal and neonatal period eventually require permanent pacemaker therapy. (**Breur et al; 2002)**

These are serious implications for the management of any fetus and pregnancy in which AV block is encountered.

The fetus in which third degree block is the presenting marker of injury may not benefit from treatment. The critical times to intervene would be when PR interval is prolonged but atrial signals continue to reach the ventricles (first- or second- degree block).

From a clinical prespective, there is a clear need to identify a marker of CCAVB. **(Nii et al; 2006)**

Accordingly, an observational study of pregnant women was initiated to determine the earliest non invasive echocardiographic marker of AV nodal injury.

The parameter was measurement of PR interval.

Aim of the work

The aim of the present study was to establish an Egyptian normal reference values for human fetal mechanical PR interval using M-mode, PWD, TDI as well as comparing these methods and detect the different factors affecting on the normal values.

Fetal Echocardiography

Congenital heart disease (CHD) is, by definition, cardiovascular disease present at birth. Most CHD is due to gross structural developmental cardiovascular anomalies such as septal defects, stenosis or atresia of valves, hypoplasia or absence of one or other ventricle, or abnormal connections between great vessels and the heart. **(Simpson, 2009)**

A few children are born with arrhythmias (mainly conduction defects), and hypertrophic or dilated cardiomyopathy, although these usually present later in childhood or adulthood.**(Lopes et al, 2008)**

Even though asphyxial heart disease is present at birth, it is not included as CHD. As defined, CHD is one of the most common serious congenital anomalies, occurring inup to 2 % of live born children, and in an even higher percentage of fetuses. **(Makikallio et al, 2006)**

Technical advances in ultrasound technology over the past decade and the introduction of fetal echocardiography into the prenatal ultrasound examination have further improved the antenatal detection of congenital heart disease (CHD). **(Tegnander et al, 2006)**

Nevertheless, cardiac anomalies are the most frequently overlooked lesions during prenatal ultrasound evaluation, and this has profound medical, psychological, socioeconomic, and medicolegal consequences. There are several controversial issues in this field, and the usefulness of fetal echocardiography as a screening instrument in unselected populations has remained a matter of debate.**(Vida et al, 2007)**

Congenital heart defects constitute a major segment of birth malformations, the reported incidence rate per 1000 live born infants increases from 3.3 at birth to 4.0 at the end of the first week of neonatal life,

5.2 by the end of the first month, and 7.8 by the end of the first year. **(Mulholland et al, 2007)**

The likelihood of detecting a fetal cardiac defect is closely related to the experience of the ultrasonographer, the timing of the examination, and the equipment used. **(Mulholland et al, 2007)**

To perform a complete and accurate examination, high resolution ultrasound with pulsed and color Doppler imaging capabilities are required. **(Sifa et al, 2009)**

However, most children are born to mothers who have no known risk features during pregnancy. Screening in the low-risk population has been reported to have lower accuracy than in the high-risk population. **(Breathnach et al, 2007)**

Fetuses with lesions that require intervention early in the neonatal period might especially benefit from closer care and the planning of delivery. Furthermore, the possibility of intrauterine cardiac intervention, which is established for antiarrhythmic treatment but is still in the experimental stage for others, might further improve fetal outcome. **(Kohl et al, 2007)**

Indications for fetal echocardiography

Although only approximately 10 % of fetuses with cardiac anomalies have known risk factors, detailed fetal echocardiography, including first trimester evaluation, should be offered to this high-risk population.

Fetal factors*:*

Persistent fetal arrhythmia occurs in approximately 1-2% of all pregnancies, the development of a fetal arrhythmia may be the mode of presentation of certain heart defects, such as tachy-arrhythmias with Ebstein's anomaly, complete heart block with atrioventricular septal defects,

L-transposition of the great arteries and heterotaxy syndromes. **(Hayashi et al, 2009)**

Isolated extrasystoles account for almost 50 to 80% of all fetal arrhythmias; they are mostly benign with a small (0.05%) risk of sustained SVT later.

Structural defects are much more common with the sustained brady-and tachy-arrhythmias. **(Yasuki et al, 2009)**

Fetal bradycardia may be due to blocked ectopics, sinus slowing or complete heart block. It is essential to have a proper diagnosis as the prognosis and management vary with the cause. The prognosis is extremely poor in patients with heart block and complex CHD with mortality rate approaching 90% .Sustained tachy-arrhythmias may be secondary to sinus tachycardia, supraventricular tachycardia or rarely, ventricular in origin. **(Aburawi et al; 2006)**

Fetal echocardiography now has a well-established role in the diagnosis, follow up and management of fetal arrhythmias. **(Yasuki et al, 2009)**

The association of extra-cardiac congenital malformations with CHD has been well established and varies with the organ system involved.

Chronic hypoxia and cardiac failure from congenital heart disease may present with abnormal fetal growth and fetal distress. Cardiac failure may be the result of high output states such as anemia or arteriovenous fistulae, myocardial dysfuntion, with primary or secondary valve regurgitation, severe structural defects or sustained arrhythmias. Fetal Doppler studies have provided further insights into the fetal adaptive mechanisms. CHD is one of the major causes of non-immune fetal hydrops accounting for nearly half of the cases and is associated with a high mortality. Early indicators include abnormal chamber size, cardiomegaly, abnormal M- mode and Doppler indices. **(Hayashi et al, 2009)**

Maternal factors:

Risk factors include environmental factors and maternal diseases, maternal insulin dependent diabetes (IDDM) results in a three to four fold increase in CHD in fetuses and cardiac anomalies (predominantly transposition of great arteries and VSD) account for one third of the fetal structural anomalies in this group. **(Macintosh et al, 2006)**

Hypertrophic cardiomyopathy associated with chronic hyperinsulinemia may develop in about 16% of the fetuses.

The association of maternal connective tissue disorders such as lupus with complete heart block is well established, accounting for almost 40% of the cases, Thus, the presence of fetal heart block should prompt testing for the presence of anti-Ro and anti La antibodies in the mother. The recurrence risk for complete heart block in subsequent pregnancies is estimated to be about 10%, and hence warrants close monitoring of subsequent pregnancies.**(Goncalves et al,2006)**

Familial factors:

A positive family of congenital heart disease is a common indication with a relatively low yield.

However, the reassurance provided by a normal fetal echo is most important for these families. The recurrence risk varies for different lesions and with the family members involved. For example, with one previously affected sibling the recurrence risk is around 2%, but varies with the type of CHD, ranging from 5-10% for left heart obstructive lesions, complex CHD and truncus arteriosus. With maternal CHD, the risk of recurrence varies from 2-15%, with congenital aortic stenosis, coarctation, tetralogy of Fallot, atrioventricular septal defects and truncus arteriosus showing a higher recurrence risk. The average risk is around 3% with paternal CHD. Similarly, certain genetic and familial syndromes are associated with heart diseases. **(Tzifa et al, 2007)**

Timing of Examination

Fetal echocardiography can be performed at any time during the second trimester when cardiac anatomical details can be satisfactorily visualized. For example, a mother who is at a slightly increased risk for CHD should be electively scheduled for a detailed cardiac scan at some time between 18 and 22 weeks' menstrual age. These include mothers with a family history of CHD, maternal diabetes or exposure to teratogenic drugs, and fetuses that have had an increased nuchal translucency thickness measurement. **(International Society of Ultrasound in Obstetrics and Gynecology, 2006)**

Fetal cardiac abnormalities may occur in association with extracardiac anomalies and therefore a detailed cardiac scan may be indicated when such anomalies are detected. **(Parra-Cordero et al, 2007)**

A mother who is particularly anxious because of a family history, perhaps loss of a previous child for example, or where the nuchal translucency measurement is ≥3.5 mm, may be offered a scan at or before 14 weeks gestation, with a follow-up scan at 20–22 weeks. If a fetus is suspected of having CHD at any scan, it should be seen as soon as possible, regardless of menstrual age others have suggested using a fetal echocardiogram as a component of the genetic sonogram, to evaluate fetuses at risk for chromosome abnormalities. (**Lee et al, 2008)**