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Morphometrical estimation of fetal heart growth at different gestational ages by In vivo and In vitro techniques

KEYWORDS: Fetal heart dimensions, Ultrasonography, Gestational ages, Growth of fetal heart.

Dr. Haritha Kumari Nimmagadda
Lecturer in Anatomy, MGM Medical College, Sec-18, Kamothe, Navi Mumbai-410216.

Ms. Pooja Pant
Post Graduate, Anatomy, MGM Medical College, Sec-18, Kamothe, Navi Mumbai-410216.

Mr. Rajeev Mukhia
Post Graduate, Anatomy, MGM Medical College, Sec-18, Kamothe, Navi Mumbai-410216.

Dr. Aruna Mukherjee
Professor and Head, Anatomy, MGM Medical College, Sec-18, Kamothe, Navi Mumbai-410216.

ABSTRACT *A significant benefit of the cardiovascular assessment of anatomico-pathological studies is that the cause of death can be more rapidly clarified during the perinatal period when death is due to gross malformations. However, difficulties increase when the events are mainly related to microscopic structures. Thus, the present study was conducted to establish the normograms of fetal cardiac dimensions so as to find out the development of fetal heart in size during various gestational ages using conventional sonography and morphological dissection. The fetal heart shows a linear growth along with the gestational age. The ventricular growth contributes higher than the atrial growth at all gestational ages. The right ventricle had shown a significant growth which is higher than left ventricle before 16 weeks of gestation but after 16 weeks there was no significance found in the growth pattern of both ventricles.*

Introduction:

There is a complex sequence of events that result in a well formed heart at birth and disruption of any portion may result in a defect.[1] The orderly timing of cell growth, cell migration, and programmed cell death (apoptosis) has been studied extensively and the genes that control the process are being elucidated.[1] Although reasonable knowledge about intrauterine cardiovascular development currently exists, certain aspects of this process are still causing much scientific discussion. Some details of intrauterine cardiovascular development in the human and other species have been clarified recently[2-12], but these still have yet to be confirmed. It is also important to assess interspecific differences to avoid rough interpretational errors in the results obtained.[11-13] Even though the idea that differences exist between myocardial structures in the same individual during development is controversial, few studies have focused on this subject.[14-15] A significant benefit of the cardiovascular assessment of anatomico-pathological studies is that the cause of death can be more rapidly clarified during the perinatal period when death is due to gross malformations. The knowledge of cardiac dimensions in utero plays an important role in the assessment of the fetuses with congenital heart disease, once these conditions can progress during the prenatal period and lead to severe cardiac decompensation. Although there are reports presented about fetal cardiovascular dimensions, the information in this field is still limited. Thus, the present study was conducted to establish the normograms of fetal cardiac dimensions so as to find out the development of fetal heart in size during various gestational ages using conventional sonographic technique as well as morphological dissection.

Materials and Methods:

Depending upon the gestational age of the fetus, the sample from both techniques were divided into three groups i.e., 1-16 weeks, 16-24 weeks and 24-40 weeks of gestation.

Sonographical study

The present study was conducted in the pregnant women in the region of Maharashtra, in the Mahatma Gandhi Mission's University of health sciences, along with the help of various institutes associated with hospitals. For this purpose a minimum of 1000 pregnant women coming for routine clinical checkup were included in the study. The criteria for the selection process of individuals were of age group 18-35 years with normal menstrual history, with singleton, normal growth and uncomplicated pregnancy during routine clinical examinations as well as normal ultrasonography. The study was done according to the PNDT (Pre Natal Diagnosis Technique) Act where the sex of the fetus was not determined. Fetal ultrasonography was conducted in two dimensional view of the fetus. Once the Fetal position is acquired, the Length and Antero-posterior diameter of the entire heart and dimensions of each chamber were measured in various fetuses. Total observations were tabulated, statistically analyzed and correlated clinically.

Morphological Study:

Fetuses during various gestational ages were collected from various health science centers after spontaneous abortions. The sex of the fetus was not considered. The cause of the abortion was taken into notice. Fetuses at different gestational ages were collected with informed consent by the parents. Only those fetuses with mothers free of gestational diabetes or hypertension were included for the study. The heart was dissected and washed thoroughly with running tap water and then with 90% alcohol to remove any impurities. Anteroposterior and transverse measurements were taken. An oblique section through the heart opened all chambers. The length and width of individual chambers were measured. All measurements were tabulated and statistically analyzed.

Results:

A total number of 863 cases were taken for sonography (fig.1) .Out of which, 138 (16%) cases belong to Ist group i.e., below 16 weeks of gestation, 198 (23%) belong to IInd group i.e., 16-24 weeks of gestation and 527 (61%) cases belong to IIIrd group i.e., 24-40 weeks of gestation. Below 13 weeks of gestation, only cardiac area was noted. Hence only antero-posterior and transverse dimensions of entire cardiac area were noted. The individual chamber size was measurable from 13 weeks onwards.

All dimensions increased significantly from Ist group of gestational age to IIIrd group of gestational age showing the growth of the heart in a linear fashion during prenatal period (table-1).

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The rise in growth of antero-posterior diameter is comparatively higher than the transverse diameter in all gestational age groups (table-1). The left atrium grows by width than length before 16 weeks (table-3). After 16 weeks the length increases more than width. Even the left ventricle also grows by width before 16 weeks (table-3). These results correlate with those of morphological results after 16 weeks of gestation (table-5). Before 16 weeks, morphological results cannot be collected because individual chambers cannot be distinguished as the size of the heart is too small.

The right atrium length is comparatively higher than the width in all gestational ages (table-2). But the ventricle is showing a peculiar growth of width compared to the height of the chamber below 16 weeks and in later gestational ages, the length of the right ventricle rises high compared to the width. These results were similar to the morphological results collected from aborted fetuses (table-5).

Compared to both the atria, the growth is higher in the ventricles at all gestational age groups. The right atrium showed a higher growth pattern in comparision with left atrium at all gestational age groups in length but the width of two atria at all age groups remained all most same. These values had shown difference with the values obtained morphologically. This variation in results was obtained due to great difference in the sample size taken for two different techniques. In aborted fetuses, the ventricles had shown increase in the length, but width was almost same as that of atria.

The right ventricle had shown a significant growth which is higher than left ventricle below 16 weeks of gestation. But left ventricle had shown rise in the growth, in both length and width, which is comparatively higher than right ventricle after 16 weeks of gestation.

In all the chambers, there is a significant rise in the growth of size during last age group i.e., 24-40 weeks of gestation which correlated with morphological results.

Below 16 weeks of gestation, there was no statistical difference in the total dimensions obtained by sonography and morphological dissection (table-6). But after 16 weeks, there were few statistically significant differences in the dimensions of individual chambers obtained by two different methods (table-7, 8). This can be basically because of great difference in the sample size and tissue changes occurring after death of the fetus and preservation in the formalin.

By plotting all the values measured by sonography (fig.3, 4), the growth of fetal heart at almost every gestational age was noted. By above mentioned graphs, the Anteroposterior dimension showed a linear growth from lowest gestational age till the end of gestation.

A growth spurt can be specifically seen at around 16 weeks of gestation, 21-22 weeks of gestation and finally at around 36 weeks of gestation. The transverse diameter had almost shown a constant linearity in the growth from lowest to highest gestational age.

Discussion:
The cardiac screening in prenatal period can reduce the fetal deaths with cardiac defects at later stages of life. The fetal heart shows a linear growth along with the gestational age. The ventricular growth contributes higher than the atrial growth at all gestational ages. The right ventricle had shown a significant growth which is higher than left ventricle before 16 weeks of gestation but after 16 weeks there was no significance found in the growth pattern of both ventricles. During entire gestation, three growth spurts were noticed in the Anteroposterior dimensions i.e., at around 16.2 weeks, 21-22 weeks and at around 32 weeks of gestation, while transverse dimensions had shown a constant linearity in the growth. This study has provided fundamental information about the morphometry of the fetal heart and its myocardium in the developing fetal heart. Until now, the lack of such data has precluded an appraisal of the role of structural factors in the functional changes occurring during cardiac development within human species. In addition, although morphometric studies of the developing heart have been performed in other experimental animals cardiac structure-function comparisons in these species have been constrained by a lack of corresponding progressive data spanning fetal life. An important methodological aspect of our study was following the growth of hearts by in vivo and in vitro techniques.

Conclusions:
A normal range of fetal cardiac measurements is a basic need for the sonographer performing fetal sonography. In many cardiac malformations, fetal chambers or great vessels may be either large or abnormally small. When only the four chamber view is examined, asymmetry of sides may be the only hint of certain defects such as total anomalous pulmonary drainage or Coarctation of Aorta. Therefore, not only is the absolute size of a chamber or a vessel important but also the ratio between the dimensions of both sides.

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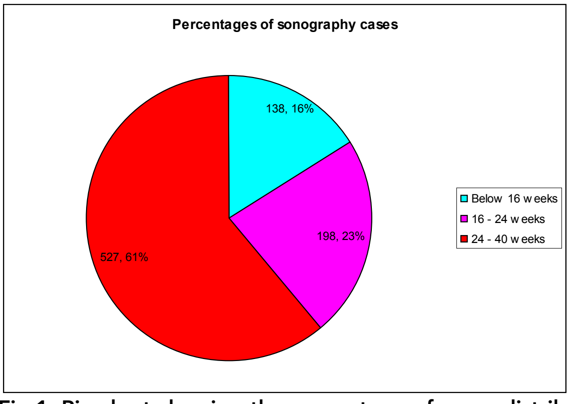

Fig.1:-Pie chart showing the percentage of cases distributed in three age groups.

Age GroupWise Comparisons of parameters											
Parameters		AP	TR	LA (L)	LA (W)	LV (L)	LV (W)	RA (L)	RA (W)	RV (L)	RV (W)
Mean	Below 16 weeks	0.6261	0.429	0.1291	0.1817	0.1633	0.2305	0.2238	0.1871	0.2226	0.2694
	16 - 24 weeks	1.8576	1.1753	0.4584	0.3846	0.631	0.4449	0.4895	0.4103	0.5902	0.3947
	24 - 40 weeks	3.555	2.6715	1.112	0.9613	1.4737	1.0036	1.1917	0.973	1.4137	0.9787

Table: 1- Age group wise comparison of mean of all parameters

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Table-2 Comparision of parameters between Right atrium and Right ventricle

Gestational Age		Right Atrium Length	Right Atrium Width	Right Ventricle Length	Right Ventricle Width
Below 16 weeks	Mean	.2238	.1871	.2226	.2694
	Std. Deviation	.05880	.05409	.07816	.06007
16 to 24 weeks	Mean	.4895	.4103	.5902	.3947
	Std. Deviation	.10823	.10055	.16132	.10741
24 to 40 weeks	Mean	1.1917	.9730	1.4137	.9787
	Std. Deviation	.31664	.36012	.32327	.30278

Table-3 Comparision of parameters between Left atrium and Left ventricle

Gestational Age	Statistic	Left Atrium Length	Left Atrium Width	Left Ventricle Length	Left Ventricle Width
Below 16 weeks	Mean	.1291	.1817	.1633	.2305
	Std. Deviation	.02435	.08074	.07818	.07293
16 to 24 weeks	Mean	.4584	.3846	.6310	.4449
	Std. Deviation	.13320	.11301	.22959	.09124
24 to 40 weeks	Mean	1.1120	.9613	1.4737	1.0036
	Std. Deviation	.32110	.27163	.32758	.32080

Table-4 Multiple Comparisons done to assess the growth

Dependent Variable	Gestational Age		Mean Difference	Significance
Left Atrium Length	Below 16 weeks	16 to 24 weeks	0.3293	.000
	16 to 24 weeks	24 to 40 weeks	0.6536	.000
Left Atrium Width	Below 16 weeks	16 to 24 weeks	0.2029	.000
	16 to 24 weeks	24 to 40 weeks	0.5767	.000
Left Ventricle Length	Below 16 weeks	16 to 24 weeks	0.4676	.000
	16 to 24 weeks	24 to 40 weeks	0.8428	.000
Left Ventricle Width	Below 16 weeks	16 to 24 weeks	0.2144	.000
	16 to 24 weeks	24 to 40 weeks	0.5587	.000
Right Atrium Length	Below 16 weeks	16 to 24 weeks	0.2658	.000
	16 to 24 weeks	24 to 40 weeks	0.7021	.000
Right Atrium Width	Below 16 weeks	16 to 24 weeks	0.2231	.000
	16 to 24 weeks	24 to 40 weeks	0.5628	.000
Right Ventricle Length	Below 16 weeks	16 to 24 weeks	0.3676	.000
	16 to 24 weeks	24 to 40 weeks	0.8235	.000
Right Ventricle Width	Below 16 weeks	16 to 24 weeks	0.1253	.002
	16 to 24 weeks	24 to 40 weeks	0.5841	.000

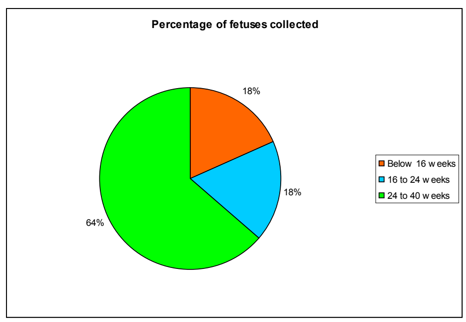

Fig.2: Pie chart showing percentages of fetuses obtained in each group.

Table-5: Mean of all parameters obtained in all gestational ages in aborted fetuses

	AP	TR	LA (L)	LA (W)	LV (L)	LV (W)	RA (L)	RA (W)	RV (L)	RV (W)
Overall	2.548	1.949	0.946	0.777	1.446	0.769	0.946	0.835	1.369	0.815
Below 16 weeks	0.717	0.567	-	-	-	-	-	-	-	-
16 - 24 weeks	1.767	1.300	0.580	0.500	0.980	0.420	0.804	0.664	0.940	0.480
24 - 40 weeks	3.295	2.529	1.033	0.843	1.557	0.851	0.980	0.876	1.471	0.895

(Dimensions of individual chambers below 16 weeks were not possible to collect from aborted fetalhearts)

Table-6:Comparision of dimensions in sonography and morphological techniques

Group Statistics (Below 16 weeks)

	Group	Mean	Std. Deviation	p-value
AnteroPosterior Diameter	Sonographical	.6261	.12974	0.521
	Morphological	.7167	.16021	
Transverse Diameter	Sonographical	.4290	.11153	0.118
	Morphological	.5667	.16330	

Table-7:Comparision of dimensions in sonography and morphological techniques Group Statistics (16-24 weeks)

	Group	Mean	Std. Deviation	P-Value
Antero Posterior Diameter	Sonographical	1.8576	.34717	0.5810
	Morphological	1.7667	.42740	
Transverse Diameter	Sonographical	1.1753	.29669	0.4810
	Morphological	1.3000	.36332	
Left Atrium Length	Sonographical	.4584	.13320	0.0038
	Morphological	.5800	.30332	
Left Atrium Width	Sonographical	.3846	.11301	0.0000
	Morphological	.5000	.34641	
Left Ventricle Length	Sonographical	.6310	.22959	0.0537
	Morphological	.9800	.35637	
Left Ventricle Width	Sonographical	.4449	.09124	0.0034
	Morphological	.4200	.17889	
Right Atrium Length	Sonographical	.4895	.10823	0.0000
	Morphological	.8040	.50703	
Right Atrium Width	Sonographical	.4103	.10055	0.0000
	Morphological	.6640	.62568	
Right Ventricle Length	Sonographical	.5902	.16132	0.1583
	Morphological	.9400	.26077	
Right Ventricle Width	Sonographical	.3947	.10741	0.0934
	Morphological	.4800	.19235	

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Table-8: Comparision of dimensions in sonography and morphological techniques Group Statistics (24-40 weeks)

	Group	Mean	Std. Deviation	P-Value
Antero Posterior Diameter	Sonographical	3.5550	.84172	.439
	Morphological	3.2948	.79396	
Transverse Diameter	Sonographical	2.6715	.63245	.675
	Morphological	2.5286	.68055	
Left Atrium Length	Sonographical	1.1120	.32110	.901
	Morphological	1.0333	.33516	
Left Atrium Width	Sonographical	.9613	.27163	.956
	Morphological	.8429	.28909	
Left Ventricle Length	Sonographical	1.4737	.32758	.634
	Morphological	1.5571	.35295	
Left Ventricle Width	Sonographical	1.0036	.32080	.000
	Morphological	.8514	.21666	
Right Atrium Length	Sonographical	1.1917	.31664	.776
	Morphological	.9795	.27478	
Right Atrium Width	Sonographical	.9730	.36012	.025
	Morphological	.8762	.27551	
Right Ventricle Length	Sonographical	1.4137	.32327	.540
	Morphological	1.4714	.34949	
Right Ventricle Width	Sonographical	.9787	.30278	.043
	Morphological	.8952	.28014	

Fig.3- A plot of Antero-posterior diameter of all Sonographical cases at different gestational ages

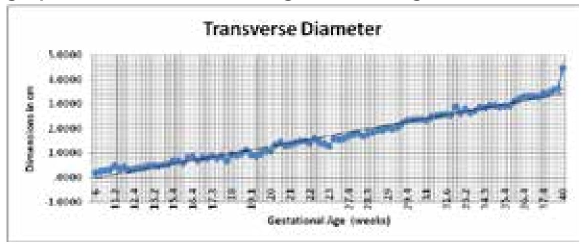

Fig. 4- A plot of Transverse diameter of all Sonographical cases at different gestational ages

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