Original Article

Reference Values of Echocardiographic Measurements of Cardiac Structures and Function among Healthy Infants in Enugu, Nigeria: A Prospective Observational Study

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Abstract

Background: There are varying results in reference values of cardiac structures and function in healthy infants in every locality. It is expedient to develop reference values among infants in this locale. **Aims:** This study sought to evaluate the reference values of echocardiographic measurements of cardiac structures and function in healthy Igbo infants in Enugu, Nigeria. **Materials and Methods:** This is a prospective study which involved 105 healthy infants who had echocardiographic measurement of cardiac structure and function over a four-year period. **Results:** The mean weight of the subjects was 3.8286 ± 0.498 kg at 95% confidence interval. The mean gestational age at birth was 38.5 ± 1.265 weeks at 95% confidence interval. Scatter diagram showed the relationship between cardiac structures and body surface area (BSA). There was a positive association between BSA and mitral valve (MV), tricuspid valve (TV), aortic valve (AV), and pulmonary valve (PV). The association between MV and BSA is as in the equation, MV = 200 × BSA-38. The relationship between BSA and other indexed cardiac structures is as in the following equations: TV = 166.7 × BSA-30.7, AV = 116.7 × BSA–21.7, PV = 116.7 × BSA–21.7, right pulmonary artery = 116.7 × BSA-22.7, left pulmonary artery = 133.3 × BSA–26.3, and main pulmonary artery = 200 × BSA-42. There was a significant positive correlation between the age of participants and most indexed cardiac structures, but no significant correlation was seen for gender. **Conclusion:** Normative reference values among Igbo infants derived from echocardiographic assessment of cardiac structural dimension and function are elicited in this study. These reference values could be a guide and could help the paediatric cardiologist and cardiothoracic surgeon in some clinical and surgical decisions.

Keywords: Cardiac structure, echocardiography, Enugu, infants, normative

INTRODUCTION

Echocardiography is a very important tool used to evaluate the anatomy and function of the cardiac valves over the past six decades.[1,2] Echocardiography is also a very vital tool for the diagnosis and evaluation of valvular disease and can be used primarily as an imaging method in assessment of valve stenosis.[3,4] The importance of the normative base values of cardiac valve dimensions in paediatric cardiology practice cannot be overemphasised. The normative values in the infants help the clinician assess the degree of deviation from the standard reference range. Besides, it will also help in delineating the difference between the normal dimension and the altered values in the correction of congenital heart defect and also to forecast the outcome of surgical correction after surgical intervention as in the case of transannular patch operation.[3-5] Furthermore, it will also help to ascertain the prognosis and efficacy of surgical correction during routine follow-up and postoperative echocardiography.

Echocardiographic assessment of normative values of cardiac dimension in infants is very uncommon in this setting. Majority

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of works done are mainly by the use of preparations of nonfixed paediatric hearts and cadavers.[5-7] Furthermore, the equations by some authors[5,7] are not congruent with that of standard reference range, because they provide a wide range of standard deviations (SDs) that depends on the type of valve and age group.

It is interesting to note that the values obtained in the above studies are different and varying. One of the authors has suggested eight equations for calculation of the normative dimensions of each valve.[7] It is therefore very pertinent to have values specific to a particular location, race, and country. It is obvious that knowledge of normal cardiac structural dimensions is often expedient in the planning of open-heart surgery in infants with congenital heart defects. In fact, efforts to define what is actually "normal" have generated controversial results. The best option is therefore to use what is generated locally for people in that geographic region.

Deviation from the normal structural and functional correlates of the heart is best elicited by means of nomograms.[8-10] The nomograms are deducted among the Caucasian population and cited in the recent American Society of Echocardiography and the European Association of Echocardiography guidelines.[8-12]

The heart of children of Igbo extract has not been evaluated by *Z*-scores and has not been included in any guideline. Caucasian anthropometric data are not representative of Indian children; this also applies to Igbo children of South East Nigeria.[12] European nomograms have been used for all surgical procedures among children with congenital heart disease in South East Nigeria. This may not be devoid of errors, especially when taking critical decision in the surgical technique. Thus, there is an urgent need for nomograms of z-scores of echocardiographic data, especially prepared for Nigerian children. This study is aimed to determine the normal values for various cardiac structures in healthy Igbo infants in Enugu city. It is also aimed to determine the range and mean (SD) of aortic valve, mitral valve, tricuspid valve, and pulmonary valve (PV) and right pulmonary artery (RPA), left pulmonary artery (LPA), and main pulmonary artery (MPA) (all in mm) of healthy Igbo infants indexed with body surface area (BSA). The work also determines the correlation between gender and mean (SD) of aortic valve, mitral valve, tricuspid valve, and PV and RPA, LPA, and MPA of healthy Igbo infants indexed with BSA. Formulae were also generated to help the clinician calculate the cardiac valve dimension of infants indexed with BSA.

MATERIALS AND METHODS

Study area

This study was carried out in a private paediatric hospital in Enugu city. This hospital provides neonatal services and receives referrals from other private obstetric hospitals where neonatal services are not available.

Study population

Infants who have not completed two months and who had no obvious congenital heart disease were recruited by convenience sampling over a four-year period from 2018 to 2021.

Ethical consideration

Ethical clearance for the study was obtained from the Research and Ethical Committee of the University of Nigeria Teaching Hospital, Ituku-Ozalla, and ESUT Teaching Hospital, Enugu.

Consent

Informed consent was sought from parents or caregivers in the course of echocardiography procedure.

Criteria for selection of subjects

Inclusion criteria

Infants who were < 2 completed months and whose parents gave consent and who had no structural abnormalities were included in the study. Infants who were born at term with normal birth weight were included in the study. Infants with normal clinical history and normal findings at physical examination were also included in the study.

Exclusion criteria

Subjects more than two completed months, preterm babies, those with congenital or acquired cardiac anomaly, infants whose mother presented with any systemic disease such as diabetic mellitus, chronic kidney disease, or congenital heart defect, and those on any cardiac medications were excluded from the study.

Echocardiographic measurements

Measurements of cardiac structures and function were evaluated with Versana Premier 2019 cardiac ultrasound imaging using the appropriate neonatal probes (12–S4) frequency transducers. The M-mode values, cardiac structures, and dimension

Table 1: Methods used in evaluating the cardiac structure and dimension in the study

Parameters (mm)	View	Phase
MV	Apical four chamber	Diastole
TV	Apical four chamber	Diastole
PV	Parasternal long axis	Systole
AV	Parasternal long axis	Systole
Intersinus distance	Parasternal long axis	Systole
Sinotubular junction	Parasternal long axis	Systole
IVS thickness diastole	M-mode (LV function)	Diastole
IVS thickness systole	M-mode (LV function)	Systole
LVID diastole	M-mode (LV function)	Diastole
LVID systole	M-mode (LV function)	Systole
LVPW thickness diastole	M-mode (LV function)	Diastole
LVPW thickness systole	M-mode (LV function)	Systole
RPA	Parasternal short axis	Maximum diameter
LPA	Parasternal short axis	Maximum diameter

LV: Left ventricular, IVS: Interventricular septum, LVID: LV internal diameter, LVPW: LV posterior wall, MV: Mitral valve, TV: Pulmonary valve, AV: Aortic valve, RPA: Right pulmonary artery, LPA: Left pulmonary artery were elicited using different views for all cardiac valves and structures, as elicited in Table 1.[8,9,12] These views were undertaken by a paediatric cardiologist. All echocardiogram views were undertaken by quantitative protocol.[8]

Bias was reduced via a quality control where another paediatric cardiologist also documented his finding. For each examination, the infant was laid supine or on the left lateral decubitus position. For each infant, intracardiac anatomy was studied using the standard two-dimensional and Doppler echocardiographic views. Infants who were not cooperative received a very mild sedative after seeking consent from their parents. The images of some of the views are shown in Figure 1.

Measurements of mitral valve and tricuspid valve (TV) were done in end-diastole. Similarly, aortic valve and PV were measured in mid-systole. Measurements of Left ventricular (LV) diameter are typically performed using M-mode. This was done with parasternal long-axis view where the cursor was placed such that it cuts through the right ventricle, the interventricular septum, the left ventricular cavity, and the posterolateral walls. The exact position of the M-mode was adjusted so as to cut across the ventricle between the papillary muscle and the mitral valve (MV).[10] The aortic diameter was measured in parasternal long-axis view. This view affords the best way of assessing the aortic root diameters by taking cognisance of the superior axial image resolution. Aortic measurements were done in end-diastole. The MPA and branch pulmonary arteries were measured in the left parasternal short-axis view in end-systole as per ASE recommendation.[11]

Sample size estimation

Statistical analysis

Data were analysed with SPSS for Windows software, Chicago version 20. Means and SD were used to describe discrete variables. Discrete, normally distributed variables were compared using Student's *t*-test or Kruskal–Wallis test for nonparametric variables. The association between discrete parametric variables was determined with Pearson correlation coefficient and Spearman correlation for nonparametric variables. Multiple regression analysis was used to show the association between dependent and independent variables. The significant probability (p) value was set at $P < 0.05$.

RESULTS

Table 1 shows the methods of evaluating the cardiac structure and dimension of the infant child.

Demographic characteristics

A total of 105 children had their cardiac valvular structures measured with echocardiography. They comprised 63.8% (67/105) of females as in Table 2. The mean age of the participants was 3.23 ± 2.79 weeks, with minimum age of one day and maximum age of 16 weeks.

Tabe 3-5 showed comparison of mean/median indexed cardiac structures between males and females, multiple regression analysis showing association between the dependent variable body surface area and independent variables and multiple

Table 2: Age and sex distribution of participants

	***n* (%)**
Gender	
Female	67 (63.8)
Male	38 (36.2)
Mean age (weeks)	
Female	3.38±2.62
Male	3.15±2.90
P	0.68

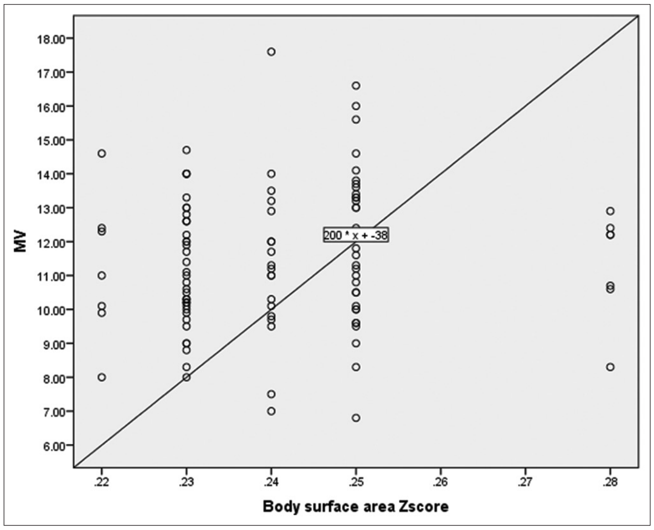

Figure 1: Linear regression between MV and body surface area. MV: Mitral valve

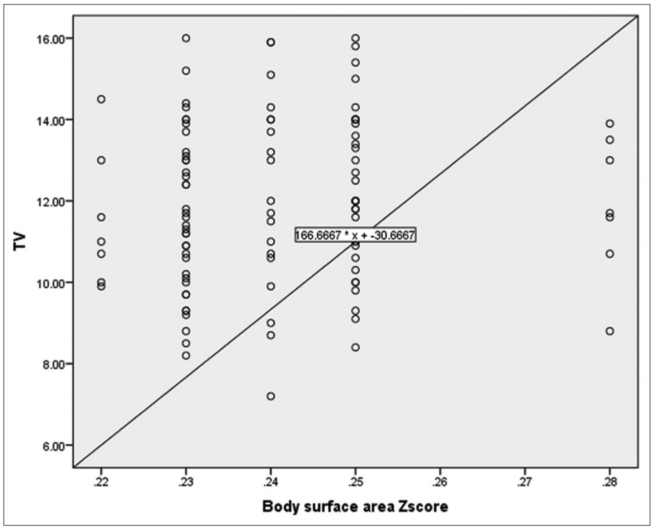

Figure 2: Linear regression between TV and body surface area. TV: Tricuspid valve

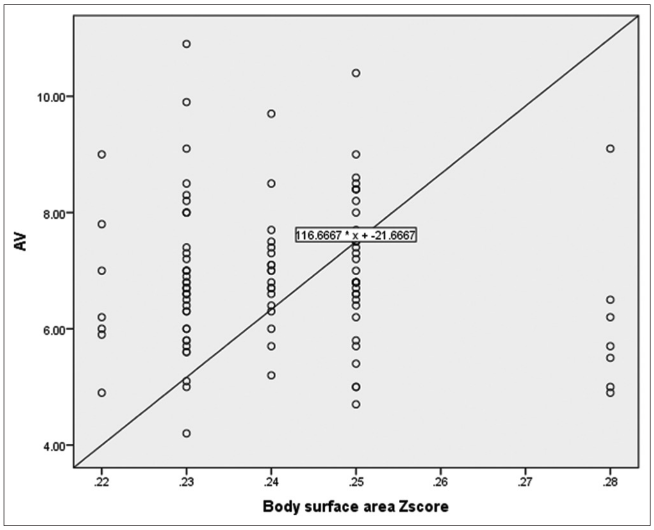

Figure 3: Linear regression between AV and body surface area. AV: Aortic vale

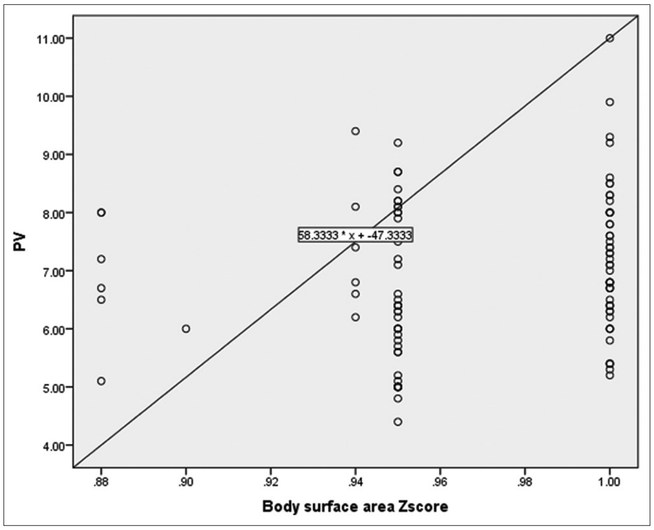

Figure 4: Linear regression between PV and body surface area. PV: Pulmonary valve

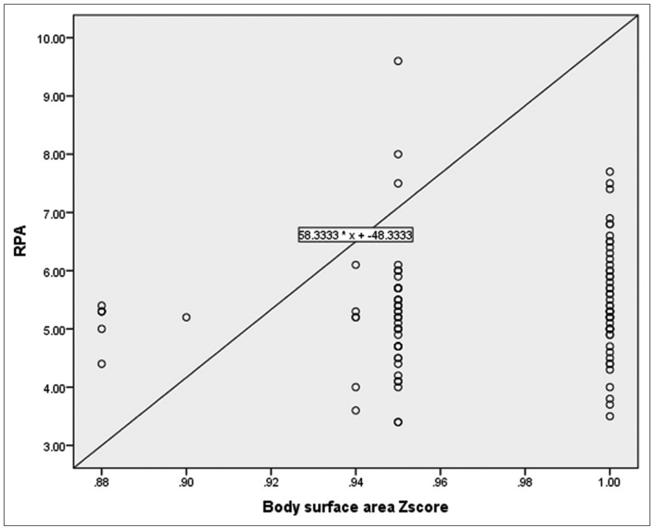

Figure 5: Linear regression between RPA and body surface area. RPA: Right pulmonary artery

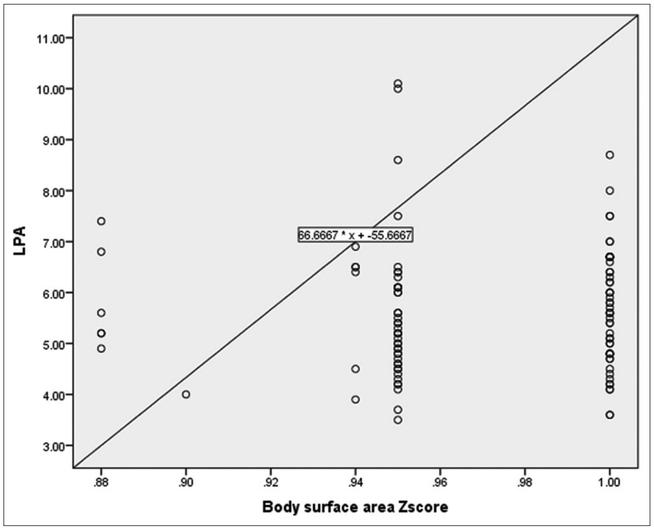

Figure 6: Linear regression between LPA and body surface area. LPA: Left pulmonary artery

regression analysis showing the association between the dependent variable (age) and independent variables respectively.

Relationship between cardiac structures and body surface area

Scatter diagrams [Figures 1-7] show the relationship between cardiac structures and BSA. There was a positive association between BSA and MV, TV, aortic valve (AV), and PV. Figure 8 showed different echo windows taken during the study and during echocardiography.[13] The association between MV and BSA is as in the equation, MV = 200 × BSA-38. The relationship between BSA and other indexed cardiac structures is as in the following equations: TV = 166.7 × BSA-30.7, AV = 16.7 × BSA–21.7, PV = 58.3 × BSA-47.3, RPA = 58.3 × BSA-48.3, LPA = 66.7 × BSA-55.7, and MPA = 100 × BSA-86.

The normality of data on cardiac structure dimensions was tested with Shapiro–Wilk test, and it showed normal distribution for the valvular dimensions: MV, TV, AV, and PV ($P = 0.63$, 0.44, 0.07, and 0.44, respectively), but RPA, LPA, interventricular septum diameter in diastole, left ventricular internal diameter in diastole, left ventricular posterior wall (LVPW), and LVPW diameter in diastole were not normally distributed ($P = 0.002$, 0.006, 0.000, 0.001, 0.000, and 0.000, respectively).

DISCUSSION

Ascertaining the dimensions and values of cardiac structures and function of infants in this locale is very vital for preoperative assessment and to monitor prognosis postoperatively in infants who present with congenital heart defects.[13-17] It could also help to monitor treatment outcome in infants who had acquired heart disease such as cardiac rhabdomyomas. Most centres

Table 3: Comparison of mean/median indexed cardiac structures between males and females

	Sex	Mean/mean rank	*P*
MV	Female	11.55±2.01	0.6
	Male	11.33±2.10	
TV	Female	12.06±2.04	0.5
	Male	11.77±2.01	
AV	Female	7.05±1.28	0.2
	Male	6.70±1.19	
PV	Female	7.04±1.31	0.2
	Male	6.74±1.19	
RPA	Female	+55.60	0.2
	Male	+48.41	
LPA	Female	+55.31	0.3
	Male	+48.92	
MPA	Female	8.08±1.90	0.06
	Male	7.33±1.90	
IVSd	Female	+51.56	0.3
	Male	+45.96	
LVIDd	Female	+47.25	0.2
	Male	+54.61	
IVSs	Female	+50.98	0.7
	Male	+48.36	
LVIDs	Female	+49.44	0.8
	Male	+50.95	
EF	Female	64.18±18.85	0.6
	Male	66.37±19.39	
FS	Female	33.95±12.43	0.2
	Male	37.54±12.70	
LVPWs	Female	+47.20	0.7
	Male	+49.44	
LVPWd	Female	+48.32	0.5
	Male	+44.81	

+ Mean rank sum, comparison done with Kruskal–Wallis test.
MV: Mitral valve, TV: Tricuspid valve, AV: Aortic valve, PV: Pulmonary valve, RPA: Right pulmonary artery, LPA: Left pulmonary artery, MPA: Main pulmonary artery, IVSd: Interventricular septum diameter in diastole, LVIDd: Left ventricular internal diameter in diastole, IVSs: Interventricular septum diameter in systole, LVIDs: Left ventricular internal diameter in systole, EF: Ejection fraction, FS: Fractionating shortening, LVPWd: Left ventricular posterior wall diameter in diastole, LVPWs: Left ventricular posterior wall diameter in systole

in the world where neonatal service is prime have developed their normative values.[18] However, none has been developed in sub-Saharan West Africa and Nigeria in particular.

Although this study though showed no gender variation of cardiac dimension in infants, however the use of correlation matrix showed a significant increase of cardiac size with age. The linear increase of cardiac dimension in infants with their age may be explained by the fact that after birth, mitotic division of cells ensues, especially in the ventricularis and spongiosa. With age and maturation, the matrix shows an increasing amount of collagen and collagen cross-links and a reduction in glycosaminoglycans.[19]

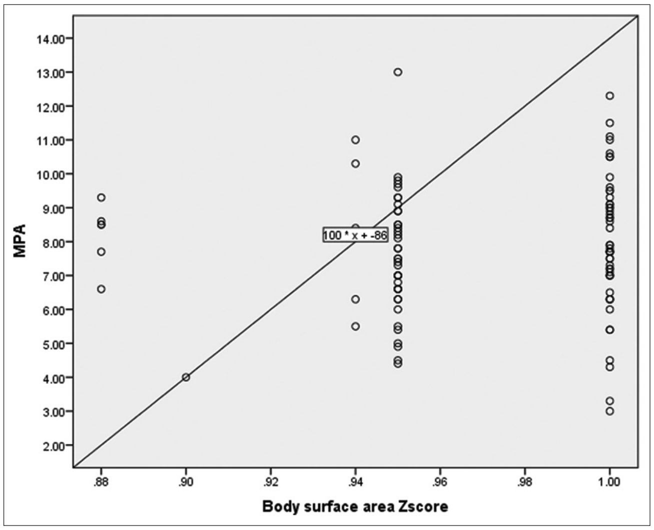

Figure 7: Linear regression between MPA and body surface area. MPA: Main pulmonary artery

Many echocardiographic measurements vary according to age and race. It will therefore be expedient to factor these variables as this will help the clinician to predict treatment measures and surgical intervention which might be influenced by the age or gender.[20] Our sample size and sociodemographic variables are similar to studies on cardiac dimension and valvular measurements in infants. For instance, Tacy *et al*.[21] included 129 infants in their study with major reports on atrioventricular valve annulus sizes. Similarly, Walther *et al*.[22] used 2010 preterm and term infants with few percentages been contributed by term infants.

Furthermore, the 105 term infants used in this study are higher than the 82 infants who were < three months used in the Detroit study.[23]

We used regression and correlation matrix in indexing our cardiac structures and dimension to surface area in this study. It is very important to note that paediatric nomograms for cardiac structures are derived from regression formulae which are unique to each study's demographic profiles in the location of the study.[24,25] The use of correlation matrix and regression for indexing cardiac structure has been corroborated by Rogé *et al*.[24] It is important to apply these findings to our locale because cardiac structures and function may vary from one country to another. For instance, Trivedi *et al*.[12] have shown that Western nomograms tend to underestimate the Z-score of children with overestimation of the severity of certain anomalies of the heart such as arch hypoplasia, which often times does not tally with intraoperative findings.

It is important to note that there are some pitfalls in the use of Z-scores or indexing with BSA, though there is a standard method of estimating cardiac structural dimension , but this standard methods may be inappropriate in obese children, or infants with foetal macrosomia. In obese children, caution should be taken when interpreting indexed values, especially the NORRE database, which excluded individuals with a body mass index >30 kg/m^2.[24,25] This can simply be explained by the fact that the calorie demand of fatty

Table 4: Multiple regression analysis showing association between the dependent variable body surface area and independent variables

Model	Unstandardized coefficients		Standardized coefficients (β)	*t*-statistic	*P*
	β	SE			
Constant	0.885	0.029		30.170	0.000
MV	0.004	0.003	0.217	1.128	0.263
TV	−0.003	0.003	−0.201	−1.004	0.318
AV	0.003	0.004	0.102	0.679	0.499
PV	0.001	0.004	0.034	0.205	0.838
RPA	0.007	0.008	0.210	0.922	0.360
LPA	−0.007	0.007	−0.244	−1.057	0.294
MPA	0.003	0.003	0.151	0.896	0.373
IVSd	0.002	0.002	0.189	1.078	0.284
LVIDd	0.002	0.001	0.216	1.294	0.200
IVSs	0.002	0.004	0.058	0.434	0.665
LVIDs	0.000	0.002	−0.013	−0.086	0.931
LVPWs	0.000	0.001	0.187	0.365	0.716
LVPWd	−0.001	0.002	−0.294	−0.632	0.529

Dependent variable: BSA. MV: Mitral valve, TV: Tricuspid valve, AV: Aortic valve, PV: Pulmonary valve, RPA: Right pulmonary artery, LPA: Left pulmonary artery, MPA: Main pulmonary artery, IVSd: Interventricular septum diameter in diastole, LVIDd: Left ventricular internal diameter in diastole, IVSs: Interventricular septum diameter in systole, LVIDs: Left ventricular internal diameter in systole, EF: Ejection fraction, FS: Fractionating shortening, LVPWd: Left ventricular posterior wall diameter in diastole, BSA: Body surface area, SE: Standard error, LVPWs: Left ventricular posterior wall diameter in systole

Table 5: Multiple regression analysis showing the association between the dependent variable (age) and independent variables

Model	Unstandardized coefficients		Standardized coefficients (β)	*t*-statistic	*P*
	β	SE			
Constant	−5.624	1.780		−3.160	0.002
MV	0.486	0.190	0.427	2.558	0.013*
TV	−0.452	0.206	−0.381	−2.197	0.031*
AV	0.157	0.244	0.084	0.643	0.522
PV	0.310	0.265	0.167	1.167	0.247
RPA	0.518	0.464	0.221	1.118	0.267
LPA	−0.016	0.412	−0.008	−0.038	0.969
MPA	0.026	0.197	0.019	0.130	0.897
IVSd	0.097	0.121	0.122	0.800	0.426
LVIDd	0.180	0.071	0.367	2.534	0.013*
IVSs	0.040	0.216	0.021	0.186	0.853
LVIDs	−0.104	0.106	−0.134	−0.989	0.326
LVPWs	−0.017	0.061	−0.127	−0.286	0.776
LVPWd	−0.027	0.106	−0.104	−0.257	0.798

*Significant *P* value. Dependent variable: Age in weeks. MV: Mitral valve, TV: Tricuspid valve, AV: Aortic valve, PV: Pulmonary valve, RPA: Right pulmonary artery, LPA: Left pulmonary artery, MPA: Main pulmonary artery, IVSd: Interventricular septum diameter in diastole, LVIDd: Left ventricular internal diameter in diastole, IVSs: Interventricular septum diameter in systole, LVIDs: Left ventricular internal diameter in systole, EF: Ejection fraction, FS: Fractionating shortening, LVPWd: Left ventricular posterior wall diameter in diastole, SE: Standard error, LVPWs: Left ventricular posterior wall diameter in systole

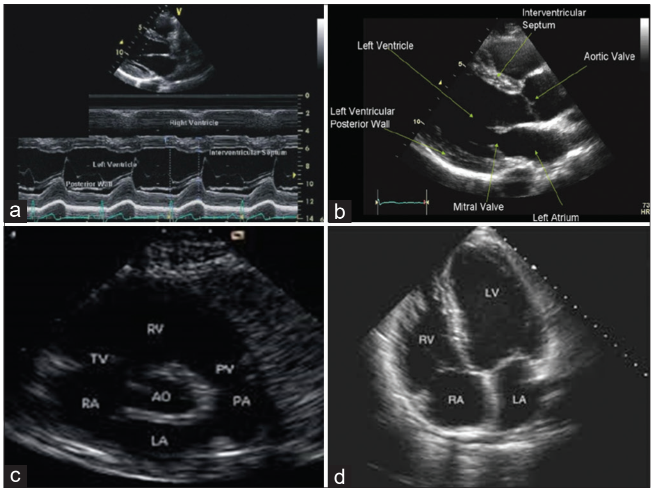

Figure 8: Echocardiographic windows of cardiac structures and function: (a) Upper left quadrant = M-mode showing ventricular function and dimension, (b) Upper right quadrant = Parasternal long-axis view, (c) Lower left quadrant = Parasternal short-axis view, (d) Lower right quadrant = Four-chamber apical view

tissue is considerably lower than muscular fibres in obsess children. Obesity is thus less likely to drive changes in chamber size or wall thickness. Lower values will therefore be derived when indexing for BSA in foetal macrosomia or obese children.[25]

Besides, the use of normal limits should not be a rubber stamp in classifying infants as having an abnormality when this parameter falls outside of the reference. It is documented in some studies that 4.6% of all normal patients had their left ventricular cavity dimension either above the upper reference limit or below the lower reference limit. It is therefore very pertinent to always consider the clinical scenario, which involve a thorough history taking and physical examination before interpreting any value that falls outside of the reference range, rather than considering them as abnormal.[26] In the corollary, some parameters may fall within normal reference range and may not actually be "normal." For instance, a patient may be noted to have a LV ejection fraction (LVEF) that dropped 75%–50% on serial M-mode echocardiography. Although both of these LVEF values are within the "normal reference limit," in this case, it is quite possible that there is an underlying pathological process and incipient LV systolic dysfunction. It is therefore advisable that echocardiographic reference ranges whether they are within, below, or above normal reference values, to be interpreted in the clinical context.[27]

CONCLUSION

Normative reference values among Igbo infants derived from echocardiographic assessment of cardiac structural dimension and function are elicited in this study. These reference values could be a guide and could help the paediatric cardiologist and cardiothoracic surgeon in some clinical and surgical decisions.

Limitation to the study

The sample size in this study is small and the use of convenience sampling technique may not give an elaborate picture. Future studies with a larger sample size will help make the study worthwhile.

Declaration

Ethical approval was obtained from the Ethics and Research Committee of the University of Nigeria Teaching Hospital, Enugu.

Availability of data and materials

The data will not be shared in order to protect the participants' anonymity.

Author contributions

JMC conceived and designed this study while JMC, ATC, BFC and ENO helped in critical revision of the article. JMC and ENO also did the data analysis/interpretation. All authors have read and approved the manuscript.

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Conflicts of interest

There are no conflicts of interest.

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