Original Article

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Radiology Section

Correlative Evaluation of Abdominal Aorta (aIMT) and Carotid Arteries (cIMT) Intima Media Thickness in Small for Gestational-Age (SGA) and Appropriate for Gestational Age (AGA) Term Newborns

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ABSTRACT

Introduction: Small for gestation newborns displays prenatal circulatory adaptations (including thickening of vessel wall) to the suboptimal intra uterine environment. These adaptations thought to lead to an altered development of the cardiovascular system and "program" the fetus for lifelong cardiovascular morbidities.

Aim: To measure and compare the Intima Media Thickness of abdominal aorta (aIMT) and Carotid Arteries (cIMT) in Small-for-Gestational-Age (SGA) term newborns with appropriate for gestation age (AGA or normal sized) term newborns using non-invasive high resolution Ultrasonography.

Material and Methods: The aIMT and cIMT by high resolution Ultrasonography of 100 SGA and 100-AGA term newborns were measured. The mean and maximum IMT of abdominal aorta and carotid artery were calculated. The Mann-Whitney test was applied to know the distribution of variables. For univariate analysis, the Pearson correlation coefficients was used. Stepwise backward multivariate linear regression was used to establish the independent risk factors for cIMT and aIMT. Correlations were analysed by using Spearman test (Significant correlation considered at 0.01 levels). Software SPSS version 18.0 for statistical analysis was used.

Results: Mean cIMT and aIMT were significantly increased in SGA term newborns (0.41±0.047 mm, 0.5±0.058 mm) than in AGA term newborns (0.35±0.032 mm, 0.45±0.041 mm). Maximum cIMT and aIMT were also significantly increased in SGA term newborns (0.45±0.05 mm, 0.58±0.05 mm) as compared to AGA term newborns (0.40±0.05 mm 0.52±0.05 mm). Both maximum and Mean aIMT and cIMT were negatively correlated (<0.001) with birth weight, length, and head circumference.

Conclusion: Screening of all SGA babies is necessary, as there has been an increasing emphasis on the early identification of those at an increased risk of developing disease so that we may provide them with early preventive and treatment options, thereby arresting or delaying the onset of morbidity and mortality.

Keywords: Atherosclerosis, Cardio vascular, High resolution Ultrasound

INTRODUCTION

Atherosclerosis is a leading cause of mortality and morbidity in the world. It is the main aetiological factor for cardiovascular and cerebrovascular disease [1]. The clinical complications of atherosclerosis occur in adult life, the process of atherogenesis begins in early life [2]. Neonates whose birth weight is less than the 10th percentile for the population based on LUBCHENCO chart are considered as small for gestation newborns [3].

Small for gestation newborns display prenatal circulatory adaptations like thickening of vessel walls and impairment of arterial vasodilatory function to the suboptimal intra uterine environment. Chronic intrauterine hypoxia and prenatal haemodynamics disturbances appear to cause structural and functional changes in the cerebral circulation. These intrauterine adaptations appear to persist postnatally and the cerebral circulation of IUGR neonates is thus different from their AGA peers during at least the first few days of life. These adaptations thought to lead to an altered development of the cardiovascular system and "program" the foetus for lifelong cardiovascular morbidities, glucose intolerance and dyslipidaemia later in life [4,5].

Recent improvements in Ultrasound (increased accuracy and resolution) have identified early vascular changes that can be assessed noninvasively [6]. The measurement of cIMT serves as an excellent marker of subclinical atherosclerosis, as shown in the studies conducted in adults [7,8]. Autopsy studies, have shown that the first atherosclerotic lesions actually begin to develop in the abdominal aorta [9,10], hence measuring aIMT might provide a better index of preclinical atherosclerosis in high-risk children than cIMT. The present study was planned at "comparative ultrasound evaluation of intima media thickness of common carotid arteries and abdominal aorta in normal term newborns and small for gestational age term newborns".

MATERIALS AND METHODS

A prospective study was conducted between November 2016 to May 2018 after obtaining Institutional ethical committee approval and written informed consent from parents/guardian in which 100-SGA and 100-AGA term newborns were included. Newborns underwent high resolution ultrasonography for the measurement of aIMT and cIMT according to the set protocols within first five days of life.

Sample Size

Based on correlation between cIMT and birth weight, r= -0.329 derived from previous literature [10] (r=Correlation coefficient), 90% statistical power and 5% statistical significance, the sample size of 100 was selected [11].

Hence, we have selected sample size of 100 for each study and control group and a total of 200 samples.

Inclusion Criteria

1. Newborns born between 37 weeks to 42 weeks of gestation, Newborns of singleton pregnancy.
2. AGA normal term newborn with birth weight of 50-90th centile and SGA term newborns with birth weight less than 10th centile as per Lubchenco's growth charts [3].

Exclusion Criteria

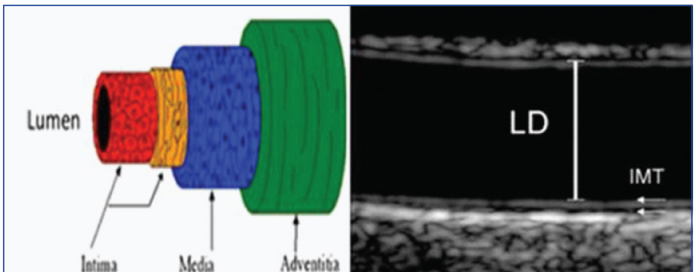
1. Newborns born less than 37 weeks and more than 42 weeks of gestation.
2. All Newborns whose mother had known diabetes, hypercholesterolemia, shock, major congenital anomalies and infections.
3. Appropriate for gestational age normal term newborn with birth weight less than 50th centile and more than 90th centile and Small for gestational age term newborns with birth weight more than 10th centile.

In the present study the newborns were divided into 2 groups: Group I included 100 AGA normal term newborns with birth weight between 50-90th centile and Group II includes 100 SGA term newborns with birth weight less than 10th centile. We recorded birth weight, gestational age, maternal age, parity of the mother. Birth weight is obtained by a labour room weighing machine (SAMSO-ELECRONIC BABY WEIGHING SCALE), accurate to five grams. All measurements were performed by a single observer. Gestational age is assessed by mother's last menstrual date, obstetric ultrasound performed before 20th weeks of gestation and the new Ballard score (i.e., "a score of gestational maturity") obtained at the time of birth.

All relevant data of mothers were obtained from records of the department of Obstetrics and Gynaecology of the institute. All high–resolution ultrasound B-mode measurements were performed on a USG machine (Philips affinity 50 G) using 5-12 MHz Linear array and 2-6 MHz convex transducers for Common carotid artery and abdominal Aorta intima media thickness, which is defined as the distance measured from the leading border of the first echogenic line to the leading border of the second echogenic line.

Imaging Protocol

1. Abdominal Aortic IMT measurement- Aorta is measured in distal abdominal portion initially identified with 2-6 MHz convex transducer then IMT is measured in the posterior vessel wall using 5-12 MHz linear array transducer after proper vessel orientation, adjusting gain and magnification in supine position.
2. Common Carotid arteries IMT measurements- Measurements are obtained on each sides just 1cm proximal to its bifurcation by using 5-12 MHz linear array transducer after proper vessel orientation, gain adjustment and magnification as shown in [Table/Fig-1].



[Table/Fig-1]: aIMT and cIMT measurement.
(Adapted from: McCloskey K et al., Cardiovascular Ultrasound. 2014) [12].

STATISTICAL ANALYSIS

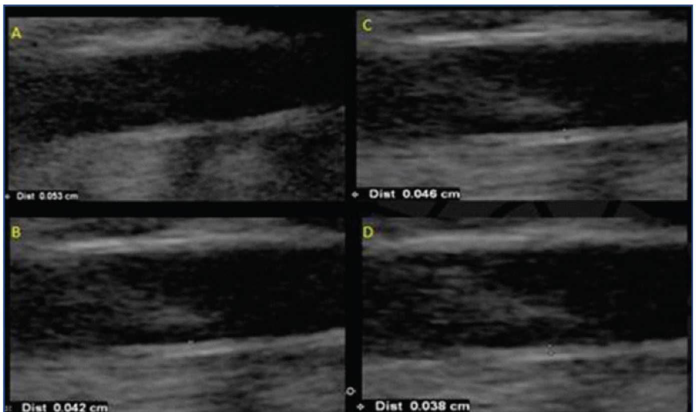
The mean and maximum IMT of abdominal aorta and carotid artery were calculated. The Mann Whitney test was applied to know the distribution of variables. The correlation between IMT of carotid and abdominal aorta and variables like maternal parity, maternal age, gestation in weeks, birth weight, sex, postnatal age, head circumference were performed. For univariate analysis, the Pearson correlation coefficients were used. Stepwise backward multivariate linear regression was used to establish the independent risk factors for cIMT and aIMT. Parameters which show p-value less than 0.1 on univariate analysis entered in multivariate linear regression model. The p-value of <0.05 was considered to designate a significant difference for all statistical analysis. Correlations were analysed by using Spearman test (Significant correlation considered at 0.01 levels). Software SPSS version 18.0 was used for above statistical analysis,

RESULTS

Neonatal and maternal demographic characteristics are shown in [Table/Fig-2]. Mean cIMT and aIMT were significantly increased in SGA term newborns (0.41±0.047 mm, 0.5±0.058 mm) than in AGA term newborns (0.35±0.032 mm, 0.45±0.041 mm) as shown in [Table/Fig-3,4]. Maximum cIMT and aIMT were also significantly increased in SGA term newborns (0.45±0.05 mm, 0.58±0.05 mm) as compared to AGA term newborns (0.40±0.05 mm 0.52±0.05 mm) as shown in [Table/Fig-4-6].

SL. NO	Parameters	AGA (n=100)	SGA (n=100)	p
1	Maternal parity	1.96±1.22	1.76±1.01	0.717
2	Maternal age (Years)	25.45±3.45	24.07±3.09	0.412
3	Gestational age (in completed weeks)	38 weeks	39 weeks	0.426
4	Birth weight (in KG)	2.90±0.32	2.0±0.27	<0.001
5	Sex of the neonate (% female)	26 (52%)	31 (62%)	0.415
6	Postnatal age (in days)	1.80±0.80	1.94±0.92	0.283
7	Length (in centimeters)	48.2±1.42	45.3±1.43	<0.001
8	Head circumference (in centimeters)	33.17±1.02	31.8±0.92	<0.001

[Table/Fig-2]: Characteristics of AGA and SGA.



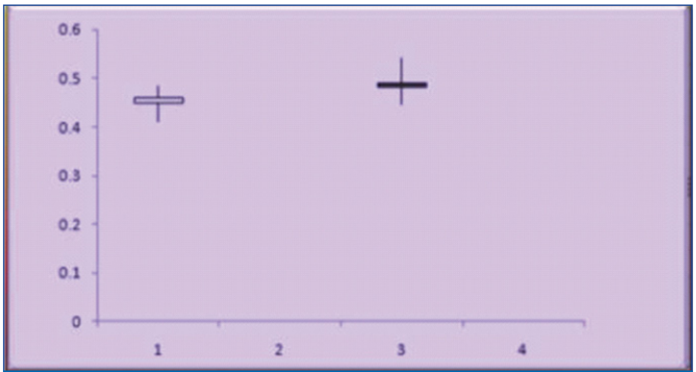
[Table/Fig-3]: High resolution ultrasound image of longitudinal section of abdominal aorta (A) and left common carotid artery (B) of term SGA and AGA (C,D) newborns showing intima media thickness respectively

AGA				SGA			
aIMT in mm		cIMT in mm		aIMT in mm		cIMT in mm	
MEAN	MAX	MEAN	MAX	MEAN	MAX	MEAN	MAX
0.45±0.041	0.52±0.05	0.35±0.032	0.4±0.05	0.5±0.058	0.58±0.05	0.41±0.047	0.45±0.05

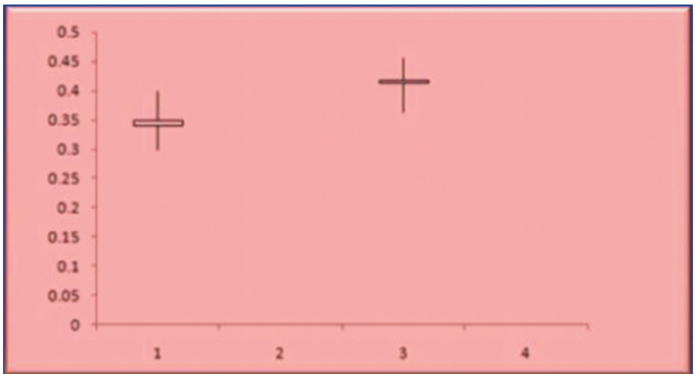
[Table/Fig-4]: Mean and Maximum aIMT and cIMT of AGA and SGA newborns.

On Univariate Analysis

Both maximum and mean aIMT and cIMT were negatively correlated with birth weight (<0.001), length (<0.001), and head circumference (<0.001). On multivariate regression analysis it was found that there is no significant association between above variables and mean and maximum aIMT and cIMT.



[Table/Fig-5]: Box plot graphs showing mean aIMT in AGA and SGA newborns.



[Table/Fig-6]: Box plot graphs showing mean cIMT in AGA and SGA newborns.

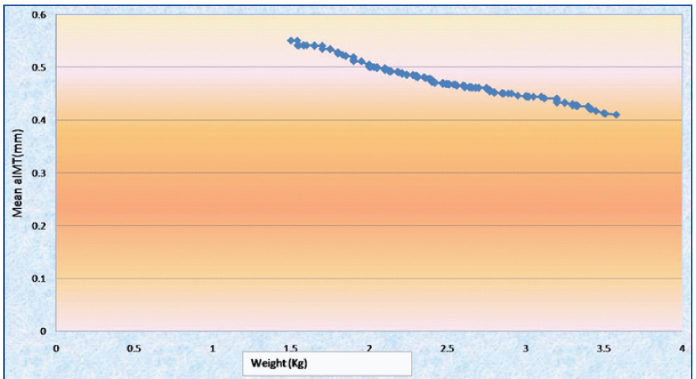
Correlations were analysed by using Spearman test (Significant correlation considered at 0.01 level.) as shown in [Table/Fig-7].

SL. NO	Parameters	Correlations	Mean aIMT	Mean cIMT
1	Birth weight (in KG)	Correlation coefficient	0.456	0.411
		Significance (2-tailed)	0.000	0.000
2	Length (in centimeters)	Correlation coefficient	0.436	0.382
		Significance (2-tailed)	0.000	0.000
3	Head circumference (in centimeteres)	Correlation coefficient	0.421	0.374
		Significance (2-tailed)	0.000	0.000

[Table/Fig-7]: Spearman's correlation.
Correlation is significant at 0.01 level (2tailed)

On Bivariate Analysis

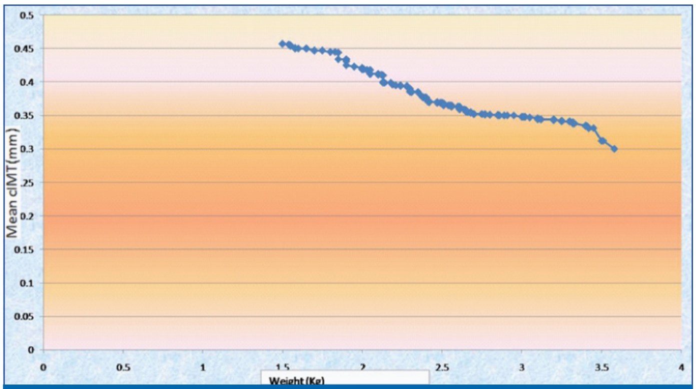
Both Mean and Maximum cIMT and aIMT were negatively associated with Birth weight (<0.001), length (<0.001) and head circumference (<0.001) as shown in [Table/Fig-8,9].



[Table/Fig-8]: Linear graphs showing negative correlation between birth weight and mean aIMT.

On Multivariate Regression Analysis

No significant association between maximum, mean aIMT, cIMT and above variables was found. A significant association between maximum aIMT and birth weight was found.



[Table/Fig-9]: Linear graphs showing negative correlation between birth weight and mean cIMT.

DISCUSSION

Atherosclerosis is the major cause of death and premature morbidity in both developed and developing countries and affects various regions of circulation preferentially and yields clinical manifestations depending on the circulatory bed affected [1,13]. Atherosclerosis of coronary arteries causes Myocardial infarction and angina pectoris, arteries supplying CNS usually provokes stroke and transient ischemic attack. In peripheral circulation atherosclerosis causes intermittent claudication and gangrene, involvement of splanchnic arteries causes mesenteric ischemia [1].

The first signs of atherosclerosis include lipid deposits, resulting in fatty streaks in the intima of systemic arteries. Advanced atherosclerotic lesions arise from these fatty streaks and their progression during childhood and adolescence is accelerated in the presence of risk factors for adult coronary artery disease, such as elevated LDL cholesterol, hypertension, diabetes and smoking [14]. These observations, therefore, emphasize that control of risk factors for the long-term prevention of atherosclerosis and its sequelae should begin in childhood.

Ability to diagnose preclinical atherosclerosis has been hampered due to the lack of accurate diagnostic tests. Hence, the advent of non-invasive tests could aid in the early diagnosis and management of high risk individuals. The early changes which can be found by diagnostic studies include thickening of vessel walls and impairment of arterial vasodilatory function [5]. Many studies have shown that low birth weight is associated with an increase in atherosclerotic disease [15-18].

Proposed mechanistic pathways that underlie the increased IMT in IUGR newborns may involve- Increased sympathetic tone, a dyslipidaemia (that is characterised by raised apolipoprotein B or reduced insulin like growthfactor–I), postnatal and maternal lipids, specifically LDL cholesterol and triglyceride, insulin-like growth factor I and insulin-like growth factor–binding protein 3, leptin levels are all associated with increased intima-media thickness [19].

The "fetal origin of adult disease" hypothesis by Barker DJ et al., postulated that cardiovascular disease has its origin in early life, when specific insults during critical periods of development may permanently alter a body's structure and metabolism [14, 20].

As per the study conducted by McGill HC et al., abdominal aorta is the first site of development of atherosclerosis. As abdominal aorta can be visualised early and clearly in high risk children, aIMT is a better index of preclinical atherosclerosis than cIMT [9].

Sodhi K et al., showed that maximum aIMT was significantly higher in intrauterine growth restricted newborns; significance was much greater after adjustment for birth weight [10]. Lipid profile and aIMT of intrauterine growth restricted newborns (measured by high resolution ultrasound) was compared with normal newborns by Koklu E et al., [21], they showed that maximum and mean aortic intima-media thicknesses were significantly higher in the babies with intrauterine growth restriction than in controls and it is more so after adjustment for birth-weight.

Pesonen E et al., showed that there is significant positive correlation between sum of the thickness of arterial intima and media (coronary artery) with birth weight - in low birth weight children [22]. The inverse association between birth weight and cIMT was shown by Oren A et al., in their study [23].

As regards vascular risk stratification, the gold-standard test is the radio contrast angiography [23], however the procedure carries anaesthetic risk, is more expensive and may be unsuitable in certain patient subsets (e.g., in renal failure). The alternatives to angiography, apart from cIMT, are use of computed tomography or magnetic resonance imaging angiography or intravascular ultrasound probe. Their applications are limited, as use of computed tomography involves heavy radiation exposure; MRI involves a high cost, while intravascular ultrasound is an invasive technique.

LIMITATION

Some limitations of the present study are: 1) Cases should be followed for long term to appreciate development of atherosclerosis to adulthood; 2) Further, work required in validate the findings in larger cohort.

CONCLUSION

The use of non invasive, inexpensive and easily available high resolution ultrasound measurement of aortic and carotid artery intima-media thickness is an attractive modality by which we can further explore and define the intrauterine factors which are associated with increased atherosclerosis and to assess the physical impact on the arterial wall. Screening of all SGA babies is necessary, as there has been an increasing emphasis on the early identification of those at an increased risk of developing disease so that we may provide them with early preventive and treatment options, thereby arresting or delaying the onset of morbidity and mortality.

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