RESEARCH PAPER

Correlation of Aortic Intima-Media Thickness With Birthweight in Healthy Term and Near Term Neonates

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Objectives: The primary objective was to correlate aortic intima-media thickness (aIMT) measured at L1-L2 with birth weight in neonates born at ≥35 week of gestation. The secondary objective was to compare aIMT in small for gestational age (SGA) and appropriate for gestational age (AGA) babies in this cohort. **Methods:** Prospective observational study enrolling 200 newborns. aIMT was measured on day 3 of life using 10-12 MHz ultrasound probe. Relevant maternal and baby details were collected and analyzed. **Results:** Mean (SD) aIMT was 0.43 (0.15) mm. There was a negative correlation between aIMT and birthweight (r= -0.64). Mean (SD) aIMT in AGA was significantly lesser than in SGA babies (0.36 (0.11) *vs*. 0.64 (0.08) mm; P<0.0001). **Conclusion:** aIMT progressively decreases with increase in birthweight.

Keywords: *Atherosclerosis, Barker hypothesis, Outcome, Small for gestational age*.

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Most of adult onset cardiovascular diseases and stroke are end result of atherosclerosis; which, contrary to prior belief, begins during fetal life itself [1,2]. The first atherosclerotic lesion begins in the abdominal aorta [3]. Ultrasound based measurement of aortic intima-media thickness (aIMT) is a feasible and accurate marker of atherosclerotic risk [4,5]. Studies in developed countries have demonstrated a difference in aIMT between small for gestational age (SGA) and appropriate for gestational age (AGA) babies but absolute aIMT values are conflicting [6-8]. There is a paucity of data on normative values of aIMT in various birthweight cohorts and data on aIMT values in SGA and AGA babies in Indian population. We conducted this study to correlate aIMT with birthweight in term and near-term babies and compared its value between AGA and SGA babies.

METHODS

This prospective study was conducted at Apollo BGS Hospital, Mysore from December, 2017 to November, 2018, after clearance from institutional ethics committee. After informed parental consent, babies of 35 to 41 weeks gestation were included in this study. Babies with congenital anomalies and babies who were discharged within two days of birth were excluded. Pre-pregnancy weight of mother was obtained from antenatal card. Mother's weight at the time of delivery was recorded using standard electronic weighing machine, and weight gain during pregnancy was calculated. Gestational age was calculated from last menstrual date, if not known, dating scan during first trimester or modified New Ballard scoring of neonates was used to ascertain gestational age. Birthweight was measured using a calibrated electronic weighing machine, and length was measured with an infantometer using standard methodology [9].

Intergrowth-21 charts were used to plot anthropometric details of the baby [10]. Ultrasound examination was done for all the enrolled babies on day 3 of life to measure aortic intima-media thickness. All the ultrasound scans were carried out by a single radiologist who was blinded to birthweight and weight group of the baby. High resolution B mode measurement was performed using linear high-resolution probe of 10-12 MHz at L1-L2 *i.e.* supra renal aorta using Philips HD 11xe ultrasound system (Koninklijke Philips NV). Intima-media thickness was defined as distance from the leading edge of first echogenic line to the second line. The first line represents lumen-intima interface, and second line represents collagen containing upper layer of the adventitia. The image was focused on the dorsal wall of the aorta, and a gain setting was used to optimize image quality.

Statistical analyses: All the data were entered in a Microsoft excel sheet and analyzed using SPSS 22.0. Pearson correlation coefficient was calculated for

continuous variables and ANOVA was used to compare aIMT across different birthweight categories. All the tests of significance were carried out at 5% level of significance.

RESULTS

A total of 200 (94 females) babies were enrolled in the study. Mean (SD) pre-pregnancy weight of the mothers was 55.32 (7.05) kg, mean (SD) height was 158 (4.67) cm and mean (SD) weight gain during pregnancy was 14.12 (2.62) kg. The mean (SD) birth weight of enrolled babies was 2.79 (0.60) kg, mean (SD) length was 48.75 (2.76) cm and mean (SD) head circumference was 33.03 (1.47) cm.

The mean (SD) aIMT observed in our study was 0.43 (0.15) mm. aIMT showed a negative correlation with birthweight and length of the baby with correlation coefficient (r) of –0.64 and –0.61 (***Fig.* 1**). However, there was a poor correlation of aIMT with gestational age (r= –0.31), maternal weight (r= –0.03), maternal height (r = –0.12) and weight gain during pregnancy (r= –0.29). There was no significant difference in mean (SD) aIMT in male and female babies [0.45 (0.16) and 0.43 (0.14)].

Value of aIMT was significantly more in SGA babies than their AGA counterparts (***Table* I**). For every given gestation, SGA babies had significantly higher aIMT than AGA babies (***Table* II**).

DISCUSSION

In this study, we enrolled 200 healthy neonates of 35-41 weeks of gestation and aIMT was measured on dorsal wall of aorta between L1-L2, and this was correlated with birth weight. aIMT was higher in babies with lower birth weight irrespective of gestational age. Similar correlation was found between length and aIMT. SGA babies in our study had significantly higher aIMT than their AGA counterparts. Mean aIMT value was fairly static across gestation age of 35-41 weeks within SGA and AGA categories.

Table I Aortic Intima-Media Thickness in Different Birthweight Groups (*N*=200)

	AGA (n=136)	*SGA (n=54)*	*LGA (n=10)*
Birthweight, kg	2.99 (0.35)	2.07 (0.36)	3.91 (0.37)
Gestational age, wk	38.2 (1.3)	37.3 (1.5)	38.9 (1.1)
aIMT,* mm	0.36 (0.08)	0.64 (0.11)	0.36 (0.08)

Values in mean (SD); *aIMT*: *aortic intima media thickness; *P<0.001; AGA: appropriate for gestational age; SGA: small for gestational age; LGA: large for gestational age.*

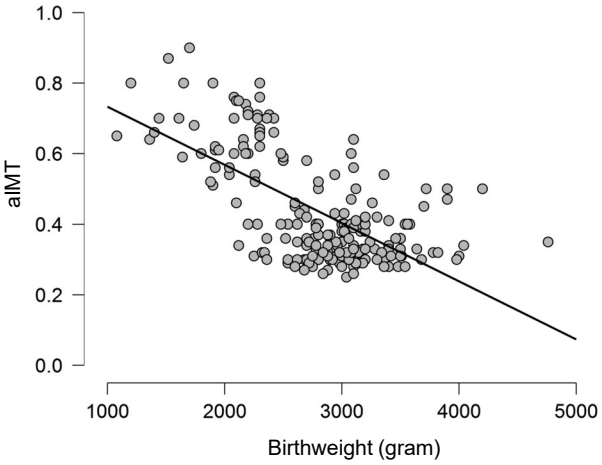

Fig. 1 *Scatter diagram of correlation of aortic intima-media thickness (aIMT)*

We had a relatively large sample size, and all the aIMT measurements were done by a single radiologist blinded to birthweight cohort, hence eliminating the possibility of any inter observer variation. However, we did not look into risk factors for SGA and possible differential effect of these risk factors on aIMT.

Our value of mean aIMT of 0.44 mm is comparable to the data reported from India [11,12]. AGA babies in our study had a mean aIMT of 0.36 mm which is lower compared to most of other reported values, and SGA babies had a mean aIMT of 0.64 mm which is higher than most other values reported from the Western population [1,6,7]. This difference could be either due to racial variation, or due to different nutritional and medical illness profile in Indian mothers.

Even though, aIMT has been investigated in newborn period, the natural history of these lesions and possible reversibility of these lesions has never been evaluated. Long term follow up of these babies for confirming evolution of these lesions into atherosclerotic plaques is needed.

Table II Aortic Intima-Media Thickness among Infants With Different Gestational Age (*N*=200)

Gestational age	*Aortic intima-media thickness, mm*			
	*AGA**		*SGA*	
	n	*mean (SD)*	*n*	*mean (SD)*
35-36 wk	16	0.41 (0.13)	17	0.66 (0.11)
37-38 wk	59	0.35 (0.07)	23	0.64 (0.12)
39-40 wk	61	0.36 (0.08)	14	0.62 (0.1)

AGA: *appropriate for gestational age; SGA: small for gestational age; P<0.001 for aortic intima-media thickness between SGA and AGA babies in different gestational age groups; *P=0.03 for comparison between different gestational age groups among AGA babies.*

WHAT THIS STUDY ADDS?

A negative correlation exists between birthweight and aortic intima-media thickness, with small for gestational age babies exhibiting higher values than appropriate for gestational age counterparts

Ethical clearance: Institutional ethics committee, Apollo BGS hospital; No. 11/2018. April 21, 2018.
Contributors: RD, VV, GG: formulated the study, drafted the protocol and involved in final writing of the article; RD, GG: collected and analyzed the data; VV: did the sonographic measurement of all cases.
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