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Comparative Study of Cord Lipid Profile in Small for Gestational Age and Appropriate for Gestational Age Newborn

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ABSTRACT

***Background*:** This study was conducted to compare the cord blood lipid profile in term small for gestation (SGA) and appropriate for gestational age (AGA) babies as determination of cord blood lipid profile is useful screening tool for early detection of babies at higher risk as atherosclerosis has its genesis in childhood.
***Methods*:** Study Design: Hospital based cross sectional study. Setting: neonatal unit of tertiary care hospital. Subjects: 200 full term babies born at SGRDIMSR during study period out of which 100 were AGA and 100 were SGA babies. Mean cord cholesterol, triglyceride, HDL, LDL, VLDL was measured in both the groups.
***Results*:** Mean cord blood cholesterol was 72.29± 21.13 mg/dL, triglycerides 67.18± 20.36 mg/dL, HDL 28.51± 5.68 mg/dL, LDL 34.94± 16.45 mg/dL, VLDL 13.43± 04.10 mg/dl in 100 AGA babies. In 100 SGA babies, mean total cholesterol was 100.85± 26.82 mg/dl, triglycerides 82±22.58 mg/dL, HDL 27.70± 7.79 mg/dL, LDL 44.93± 7.663 mg/dL, VLDL 16.40± 4.479 mg/dL.
Conclusion: Lipid profile values except HDL were significantly higher in SGA compared to AGA neonates (p <0.001 for all parameters).

Keywords: AGA, Cholesterol, HDL, LDL, SGA, Triglycerides

Introduction

Cardiovascular diseases, insulin resistance with its metabolic complications like hypertension, dyslipidemia, impaired glucose tolerance or type-2 diabetes have their origin in fetal life and are associated with fetal growth restriction and low birth weight (1, 2). Coronary artery disease is a major cause of global morbidity, mortality and will continue to dominate mortality trends in future (3). Atherosclerosis which is a major cause of coronary artery disease begins early in life and progresses silently for decades (4). David Barker proposed for the first time “fetal origin of coronary artery disease”. In 1995 British Medical Journal named this “Barker Hypothesis” which is now widely accepted (5,6). The developmental origins of health and disease (DOHaD) perspective explains how adverse events occurring during early phases of human development may affect the pattern of health and disease throughout life (7).

Glucose is the primary source of energy in intrauterine life and free fatty acids are alternative source of energy. AFD babies are in receipt of ready placental supply of nutrients, so there is very little need for lipolysis in utero. Growth restricted neonates activate lipid metabolism to generate energy and promote gluconeogenesis. As the supply of nutrients is limited, development of essential organs is favored as compared to non essential organ like kidney and pancreas (8). Free fatty acids are liberated. Those which escape oxidation for energy are synthesized in liver into triglycerides in LBW as compared to full term babies (9). This response is exaggerated by ante partum and intrapartum asphyxia (10). Vast difference between cord blood and maternal lipids reveal possible lack of maternal contribution of fetal lipids. However strong association between Adverse events in utero that predispose to cardiovascular disease in adulthood have been seen. (11).

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Fetus adapts to inadequate nutrient supply in a number of ways. FOAD hypothesis (fetal origin of adult diseases) states that although occurring in response to transient phenomenon these adaptations become permanent or programmed as they occur during critical period of early development. Programmed changes include reduced insulin sensitivity, low muscle mass, pancreatic beta cell mass, nephron numbers, altered arterial structure, up regulation of HPA axis and sympathetic nervous system.

Though lipid profiles have been extensively studied in adults, data is limited in pediatric population. There are studies showing direct relationship between abnormalities in lipid profile among SGA babies and occurrence of cardio-vascular diseases as adults (12). This study was undertaken to compare cord blood lipid profile in term AGA and SGA babies so as to pick up high risk babies for future monitoring.

Methods

Study design: This was a hospital based cross sectional study conducted at neonatal unit of tertiary care hospital from January 2013 to December 2014. After obtaining approval from ethical committee 200 full term babies born during study period were included out of which 100 were AGA and 100 were SGA babies. Exclusion criteria- Neonates with any congenital malformations; maternal illness like IDDM and gestational diabetes, tuberculosis, asthma, pregnancy induced hypertension; family history of Coronary artery disease and hypercholeste-rolaemia, any maternal medication except iron and vitamin supplements, instrumental delivery, Apgar score <7 at 1 minute

Newborns delivered at tertiary hospital by normal vaginal delivery were enrolled after obtaining written informed consent from parents/ guardians. 5 ml of cord blood was collected from umbilical cord immediately after delivery from placental end of cord and was allowed to clot. Serum was separated and stored at -20°C until analysis. Lipid profile was done using auto analyzer (SPECTRA). Total cholesterol was estimated by CHOD-PAP method, triglyceride was measured by GPO-PAP method and HDL was estimated by clearance method. Values of LDL and VLDL were derived by Fried-wield formula.

Weight of the baby, length, head circumference, chest circumference was recorded. Babies were classified as AGA, SGA with the help of intrauterine growth charts and ponderal index. Any baby whose weight was less than 10th centile was classified as small for gestational age (SGA) and between 10th and 90th centile were classified as appropriate for gestational age (AGA). Ponderal index was computed as weight (grams)/ length (cm^3) × 100. PI< 2 was taken as cutoff value to classify as SGA.

Statistical Analysis

Results were expressed as mean ± SD for continuous variables and as number and proportion (%) for categorical data. Since all data are known to be normally distributed, the parametric tests were used for statistical analysis. Differences between SGA and AGA neonates as well as male and female neonates were determined by student's t test. Chi square test was applied to test the association between two categorical factors. All the tests of significance were applied at 5% level of significance.

Results

200 neonates born during study period fulfilling inclusion criteria were enrolled in the study. Neonates were classified as AGA and SGA based on anthropometric measurements. Cord blood lipid profile was analyzed. Gender distribution was equal in both groups. 49 were males and 51 females in SGA group. 46 were males and 54 females in AGA group. Difference in all anthropometric parameters was statistically significant in both groups (Table 1). 52 SGA neonates had ponderal index <2 and 48 neonates had ponderal index between 2-2.5, whereas majority of neonates among AGA had ponderal index >2.5(95%).All lipid profile values except HDL were significantly higher in SGA babies as compared to AGA babies (Table 2). More SGA babies 65 (65%) had HDL values below 50th centile as compared to 57 (57%) in AGA babies.

Table 1. Gender distribution and anthropometric parameters

	SGA n=100	AGA n=100	P-value
Male/Female	49/51	46/54	<0.05 Significant
Weight (kgs) (mean±SD)	1.98±0.15	2.88±0.369	<0.01
Length (cms) (mean±SD)	47.08±0.990	47.66±1.368	0.002
Head circumference(cms) (mean±SD)	32.98±0.900	33.46±1.101	0.003
Ponderal Index	1.97±0.145	2.62±0.172	0.001

Table 2. Comparison of cord lipid profile values among AGA and SGA neonates

Lipid profile (mg/dl) (mean±SD)	AGA n=100	SGA n=100	P-value
Total Cholesterol	72.299 ±21.132	100.85± 26.826	<0.001
Triglycerides	67.18 ±20.362	82 ±22.58	<0.001
High density lipoproteins	28.512± 5.686	27.7 ±7.790	<0.452
Low density lipoproteins	34.94 ±16.452	44.93± 7.663	<0.001
Very low density lipoproteins	13.43± 4.102	16.40± 4.479	<0.001

More AGA babies 28(28%) had HDL values between 50th to 75th centile. Majority of AGA babies 64 (64%) had cholesterol value below 50th centile whereas 60 (60%) SGA babies had cholesterol values between 75th to 95th centile. 15(15%) SGA babies had cholesterol values above 95th centile as compared to 4 (4%) in AGA babies. Majority of AGA babies 60 (60%) and triglyceride values below 50th centile whereas majority of SGA babies 54 (54%) had values between 75th to 95th centile. Majority of AGA babies 64 (64%) had LDL values below 50th centile whereas majority of SGA babies 83(83%) had LDL values between 50th to 75th centile. Difference in all lipid profile parameters between two groups was statistically significant (Table 3). Difference between cord lipid profile values of male and female AGA neonates was not statistically significant (Table 4). No statistically significant difference was observed in male and female SGA babies in serum triglyceride, HDL and VLDL levels. However serum cholesterol and LDL were higher in females as compared to males and the difference was statistically significant (Table 5). Values of cholesterol, triglycerides and VLDL were higher in SGA males as compared to AGA male babies. However difference in the HDL and LDL values was not statistically significant (Table 6). Among female neonates; cholesterol, triglycerides, LDL, VLDL were higher in SGA babies as compared to AGA babies. The difference was statistically significant. HDL values however did not show statistically significant difference among two groups (Table 7).

Table 3. Percentile distribution of lipid profile values in AGA and SGA babies

mg/dL	Centile*	AGA=100 n (%)	SGA=100 n (%)	P-value
HDL	<50th (<28.5)	57 (57)	65 (65)	0.033
	50th-75th (28.5-32.5)	28 (28)	16 (16)	0.042
	75th-95th (35.2-47.4)	15 (15)	19 (19)	0.26
Cholesterol	<50th(<72.5)	64 (64)	6 (6)	<0.001
	50th-75th (72.5-85)	15 (15)	19 (19)	0.26
	75th-95th (85-120)	17 (17)	60 (60)	<0.001
	>95th	4 (4)	15 (15)	0.007
Triglyceride	<50th (<68.1)	60 (60)	21 (21)	<0.001
	50th-75th (68.1-76.2)	21 (21)	9 (9)	<0.01
	75th-95th (76.2-105)	10 (10)	54 (54)	<0.001
	>95th (>105)	9 (9)	16 (16)	<0.075
LDL	<50th(<39.5)	64 (64)	15 (15)	<0.001
	50th-75th (39.5-58.4)	24 (24)	83 (83)	<0.001
	75th-95th (58.4-65.1)	11 (11)	1 (1)	0.004
	>95th (>65.1)	1 (1)	1 (1)	

Table 4. Comparison of cord blood lipid profile in AGA neonates as per gender

Lipid profile (mg/dL)	Male (46)		Female (54)		T value	P-value
	Mean ± SD	Std error mean	Mean ± SD	Std error mean		
TC	77.05± 24.104	3.963	68.19± 17.456	2.662	1.902	0.061
Triglycerides	68.43± 24.092	3.961	66.09± 16.727	2.551	0.510	0.612
High density lipoproteins	28.43± 5.645	0.928	28.58± 5.787	0.882	-0.116	0.908
Low density lipoproteins	38.30± 18.484	3.031	32.05± 14.118	2.153	1.715	0.09
Very low density lipoproteins	13.65± 4.923	0.809	13.23± 3.287	0.501	0.45	0.654

Table 5. Cord lipid profile in SGA neonates as per gender

(mg/dL)	Male (49)		Female (51)		T value	P value
	Mean±SD	Std error mean	Mean± SD	Std error mean		
TC	92.62± 19.168	3.069	108.68± 30.713	4.797	-2.79	0.007
Triglycerides	82.77± 19.129	3.063	81.27± 25.661	4.008	0.295	0.768
HDL	28.82± 9.058	1.450	26.63± 6.288	0.982	1.259	0.212
LDL	42.92± 8.196	1.312	46.83± 6.674	1.042	-2.34	0.022
VLDL	16.74± 3.775	0.604	16.07± 5.086	0.794	0.667	0.507

Table 6. Cord blood lipid profile in male AGA and SGA babies

(mg/dL)	AGA (46)		SGA (49)		T value	P value
	Mean± SD	Std error mean	Mean± SD	Std error mean		
TC	77.05± 14.104	3.963	92.62± 19.168	3.069	-3.123	0.003
Triglycerides	68.43± 24.092	3.961	82.77± 19.129	3.063	-2.881	0.005
HDL	28.43± 5.645	0.928	28.82± 9.058	1.450	-0.223	0.824
LDL	38.30± 18.434	3.031	42.92± 8.196	1.312	-1.426	0.158
VLDL	13.65± 4.923	0.809	16.74± 3.775	0.604	-3.085	0.003

Table 7. Cord blood lipid profile in female AGA and SGA babies

(mg/dL)	AGA (54)		SGA(51)		T value	P value
	Mean± SD	Mean std error	Mean± SD	Mean std error		
TC	68.19± 17.456	2.662	108.68± 30.713	4.797	-7.474	<0.001
Triglycerides	66.09± 16.727	2.551	81.27± 25.661	4.008	-3.228	0.002
HDL	28.58± 5.787	0.882	26.63± 6.288	0.982	1.478	0.143
LDL	32.05± 14.118	2.153	46.83± 6.672	1.042	-6.086	<0.001
VLDL	13.23± 3.287	0.501	16.07± 5.086	0.794	-3.054	0.003

Discussion

Cord lipid profile is a reflection of lipid metabolism during fetal life and at birth because most fetal lipids are synthesized de novo through conversion of glucose to various fatty acid containing compounds. Only part of it is derived from placental circulation. Present study was conducted to evaluate lipid profile abnormalities in SGA babies in comparison to AGA babies so that these high risk babies can be kept under vigilant monitoring in future. Out of total 200 subjects, males were 95 and females were 105. In the present study, mean birth weight in SGA babies was 1.98± 0.15 kg as compared to 2.88± 0.369 kg in AGA babies which was statistically significant. Pardo et al (13) and Jones et al (14) reported mean birth weight as 2.04± 0.76 kg and 2.07± 0.53 kg respectively in SGA babies which was statistically significant when compared to AGA babies. However Kelishadi et al (15) and Wang et al (16) did not find any significant difference in mean birth weight of SGA and AGA babies. Average length of SGA babies in present study was 47.08± 0.990 cm as compared to 47.66± 1.368 cm in AGA babies which was statistically significant. Similar results were observed by Pardo et al. (13). Significant difference in ponderal index was observed in present study between SGA and AGA babies. Only one study by Kelishadi et al (15) compared ponderal index between AGA and SGA babies and they did not find statistically significant difference between two groups.

More number of SGA babies 65 (65%) had HDL values below 50th centile as compared to AGA babies 57(57%). Difference was statistically significant. 28(28%) AGA babies had HDL levels between 50th-75th centile as compared to 16(16%) in SGA babies which was again statistically significant. Cholesterol levels were below 50th centile in 64(64%) AFD babies whereas only 6(6%) SGA babies had cholesterol level below 50th centile. Majority of SGA babies 60(60%) had cholesterol level between 75th to 95th centile as compared to 17(17%) in AGA group. 15(15%) SGA babies had cholesterol level above 95th centile as compared to 4(4%) in AGA group. Difference was statistically significant. Triglyceride levels were below 50th centile in majority of AGA babies whereas majority of SGA babies 54(54%) had their triglyceride level between 75th to 95th centile. 16(16%) SGA babies had triglyceride levels above 95th centile. Difference between two groups was statistically significant. When LDL levels compared between two groups,higher number of SGA babies 83(83%) had LDL levels between 50th to 75th centile. Majority of AGA babies 64(64%) had values below 50th centile as compared to 15(15%) SGA babies. Difference was statistically significant. Kelishadi et al (15) have made percentile distribution of values without comparative study between different categories.

Mean Total Cholesterol(100.85± 26.82 mg/dL), triglycerides(82± 22.58 mg/dL), LDL (44.93± 7.663 mg/dL) and VLDL levels (16.40± 4.479 mg/dL) were significantly elevated with SGA babies as compared to AGA babies (p-value <0.001) who had mean cord blood values of total cholesterol 72.29± 21.13 mg/dL, triglycerides 67.18± 20.36 mg/dL, LDL 34.94± 16.45 mg/dL, VLDL 13.43± 04.10 mg/dl . Difference in HDL was not significant between two groups. Similar observations were made by Pardo et al (13), Jones et al (14), Kelishadi et al (15) and Wang et al (16). Due to lack of glucose as a fuel, SGA babies use alternate source like amino acids and lipids and generate glucose by gluconeogenesis. There is increased hepatic generation of lipids particularly

LDL, VLDL and chylomicrons coupled with decreased peripheral utilization of lipids due to decreased activity of lipoprotein lipase (17-20).

In the AGA group there was no significant difference in lipid profile among male and female babies in the present study. Similar results were reported by Chander et al (21). However Badiee et al. (22) reported higher levels of total cholesterol and LDL in females as compared to male babies. In SGA babies total cholesterol and LDL values were higher in female as compared to male babies, difference being statistically significant.

Among male babies TC, triglycerides and VLDL levels were higher in SGA babies as compared to AGA babies. There was no statistically significant difference in HDL and LDL values. Among female babies all values were significantly higher in SGA as compared to AGA except HDL value. Search of literature did not show any gender comparison hence further studies with larger sample size may throw more light on this aspect.

Coronary heart disease has its roots traceable to intrauterine life (23). In addition to genetic and lifestyle factors, fetal origin of adult disease emphasizes the role of primordial and primary prevention.

Conclusion

In 200 neonates enrolled in this study, mean cord blood cholesterol was 72.29± 21.13 mg/dL, triglycerides 67.18± 20.36 mg/dL, HDL 28.51± 5.68 mg/dL, LDL 34.94± 16.45 mg/dL, VLDL 13.43± 04.10 mg/dl in 100 AGA babies. In 100 SGA babies, mean total cholesterol was 100.85± 26.82 mg/dl, triglycerides 82±22.58 mg/dL, HDL 27.70± 7.79 mg/dL, LDL 44.93± 7.663 mg/dL, VLDL 16.40± 4.479 mg/dL. Lipid profile values except HDL were significantly higher in SGA compared to AGA neonates.

More number of AGA babies had HDL values between 50^{th} to 75^{th} percentile as compared to SGA babies whereas significant majority of SGA babies had triglyceride levels and cholesterol levels between 75^{th}-95^{th} centile and LDL levels between 50^{th}-75^{th} centile. In the AGA group there was no significant difference in lipid profile among male and female neonates. In SGA babies TC and LDL values were higher in female as compared to male neonates. Among male babies total cholesterol, triglycerides and VLDL levels were higher in SGA babies as compared to AGA babies whereas there was no statistically significant difference in HDL and LDL values. Among female babies all values except HDL were significantly higher in SGA as compared to AGA babies.

Thus strategy to prevent coronary heart disease must include primordial and primary prevention by adopting the measures to improve fetal growth , early detection of hyperlipidemia and dietary intervention during infancy and later childhood.

Conflicts of interests

None declared.

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