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A correlative study between maternal cord blood lipid profile and birth anthropometry in full-term newborns

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Abstract: David Barker proposed a hypothesis on the "Fetal origin of cardiovascular disease" in 1995, suggesting the origin of the disease lies in-utero and requisite adaptations occur in the under-nourished fetus during middle-to-late gestation. Objective of the study to compare the cord blood lipid profiles between the Small for Gestational Age (SGA) and Appropriate for Gestational Age (AGA) full-term newborns.This hospital-based cross-sectional comparative study was conducted from February 2021 to August 2022, enrolling 59 SGA babies as the study group and 59 healthy AGA babies as the control group. After taking written informed consent and collecting relevant maternal data, cord blood was collected immediately after the delivery and sent for a lipid profile. All the babies were examined, and relevant anthropometric variables were recorded and then classified into SGA or AGA using AIIMS Intrauterine growth charts and Ponderal index.Comparisons of cord blood lipid profile parameters were made among groups of neonates classified as per gestational age. Total Cholesterol (TC) and Triglycerides (TG) levels of SGA babies were significantly higher than those of AGA babies. The variations in High-Density Lipoprotein (HDL) values were marginal while Low-Density Lipoprotein (LDL) values showed an appreciable increase among SGA neonates. SGA neonates exhibited elevated lipid profiles as compared to AGA neonates. Thus, inferring that maternal changes in-utero during gestation may bear a profound impact on lipid metabolism in neonates. Therefore, SGA newborns need close monitoring for cardiovascular morbidities early in life.

Keywords: Anthropometric variables; SGA; AGA; Cord blood; Lipid profile.

1. Introduction

The physiology and metabolism of human foetuses are reported to change permanently while adapting to the supply of nutrients in-utero [1]. These programmed changes could later lead to the origin of cardiovascular diseases, a widely established cause of morbidity and mortality worldwide. The incidence depends on genetic and environmental risk factors [2]. David Barker [3] proposed a hypothesis on the "Foetal origin of cardiovascular disease" in 1995, suggesting the origin of the disease lies in-utero and requisite adaptations occur in the under-nourished foetus during middle-to-late gestation.

This postulate emphasised the importance of monitoring lipid profiles in the paediatric age group [4]. The pathogenesis in these diseases starts early during fetal life and is associated with fetal growth restriction and low birth weight. Thus, these growth-restricted neonates often need to use their endogenous reserves by activating lipid metabolism that generates energy and promotes gluconeogenesis. The lipid profile is a marker of an underlying cardiovascular status. It includes the measurement of cholesterol and its derivatives and various atherogenic indices. The studies on the relationship between cord-blood lipid profile in neonates, their anthropometric data and their predictive role as markers for adulthood diseases are rather limited in India [5].

Hence, the present study is designed with a defined approach for drawing broader conclusions on the school of thought on cord-blood lipid profile and their relationship with anthropometry at birth among the Indian subjects.

2. Material and methods

The study population consisted 118 consecutive, singleton, live-born term babies (59 as the study group and 59 as the control group) born between February 2021 and August 2022 at Vydehi Institute of Medical Sciences and Research Centre, Bangalore with written informed consent duly signed. Inclusion criteria includes full-term neonates (37 - 42 weeks) and APGAR score of >6 at one minute and 8 - 10 at five minutes of birth. Exclusion Criteria includes neonates born with perinatal asphyxia, pre-term babies, neonates born with congenital anomalies, newborns with birth weight >4 kg, newborns admitted to NICU and the mothers who were multi-gravida or had complications such as cardiac disease, obesity, hypercholesterolemia or dyslipidemia during pregnancy.

The mother's age, parity, weight and height before pregnancy, antenatal events or complications, maternal health problems, and socio-economic history were recorded. Recorded characteristics of newborns included sex, gestational age at birth, APGAR score at the 1st and 5thminute after birth, and anthropometric data, including birth weight, birth length, and HC. After the delivery, the birth weight was measured with an electronic scale to the nearest 10 grams. Newborn length was recorded using an infantometer to the nearest centimetre.

In all the 118 enrolled newborns, under aseptic conditions, a cord blood sample (5 mL) was collected immediately by clamping the umbilical cord post-delivery and before the placenta delivery in sterile serum tubes. The samples were allowed to clot for 10 minutes and were transported to the central laboratory for biochemical analysis of serum lipid profile for Triglycerides (TG), Total Cholesterol (TC), High-Density Lipoprotein (HDL) and Low-Density Lipoprotein (LDL) (Figure 1).

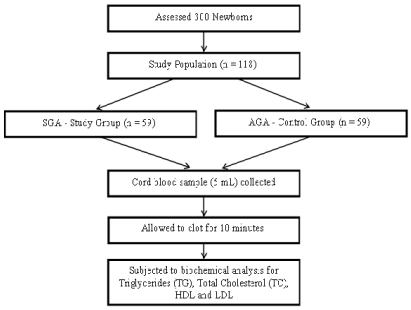

Figure 1. Flow chart of scheme of study

3. Results

The present study is a cross-sectional comparative study in which the lipid profile of the cord blood of SGA babies was compared with the lipid profile of the cord blood of AGA babies. The data obtained from the study and control groups using different parameters, like neonatal anthropometry and lipid profile, were analysed.

The gender distribution was nearly equal in the study and control groups. Study group had males - 28 and females - 31; control group had males - 29 and females - 30. The mean birth weight of SGA neonates was 2.26 ± 0.24 kg, and that of AGA neonates was 2.84 ± 0.46 kg. In the present study, weights and lengths were statistically significant (p =0.001 and $p \leq 0.001$, respectively) among study and control group neonates (Table 1).

Table 1. Anthropometric parameters of SGA and AGA neonatesa

Variable	Study group (n=59)	Control group (n=59)	P-value
Weight (kg)	2.26 ± 0.24	2.84 ± 0.46	0.001
Length (cm)	50.14 ± 1.52	47.84 ± 2.39	<0.001

Birth weight and length values significantly different among the groups ($P \leq 0.001$)

In the present study, the SGA neonates were equally distributed among Ponderal Index (PI)$\leq$2.0 (50.8%) and $\leq$2.2 (49.2%). However, incidentally, there were no AGA neonates with PI between 2.0-2.2 (Table 2).

Table 2. Ponderal Index values of SGA and AGA neonates

Gestational age	Study group (n=59)			Control group (n=59)		
Weeks	PI	Number	%	PI	Number	%
29-37	=2.0	30	50.8	>2.0	0	0
>37	=2.2	29	49.2	>2.2	59	100

The lipid profile parameters, TC, TG, HDL and LDL were analysed in cord blood samples of study and control group neonates. TC and TG values of lower birth weight (2.0 - 2.5 kg) group neonates were significantly greater (Figure 2) than the other two higher birth weight range groups of neonates ($p = 0.009$ and $p < 0.001$, respectively).

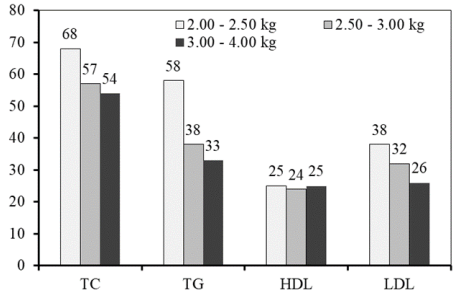

Figure 2. Comparison of cord lipid profile according to birth weight

The study group neonates exhibited higher TC, TG and LDL values compared to their counterparts in the control group (Table 3).

Table 3. Cord blood lipid profile of SGA and AGA neonates

Lipid Profile	**Study group (n=59)**	**Control group (n=59)**	**P-value**
TC (mg/dL)	69.85 ± 28.25	56.83 ± 16.36	0.008*
TG (mg/dL)	60.38 ± 22.72	36.59 ± 18.87	<0.001*
HDL (mg/dL)	24.96 ± 12.13	25.16 ± 7.02	0.983
LDL (mg/dL)	40.03 ± 23.86	29.81 ± 14.86	0.070

*Significance: *p<0.05*

Whereas, the HDL values of study group neonates were marginally lower. However, only TC and TG values of the study group were significantly higher compared to the control groups, with a p-value of 0.008 and <0.001, respectively. A comparison was also made among the study group and control group neonates based on their lipid profile parameters and PI (Table 4). TG and LDL values were higher in asymmetrical IUGR (PI $x \leq y$ 2.2), but it was statistically significant for TG values (p value 0.028).

Table 4. Cord blood lipid profile and Ponderal Index among SGA and AGA neonates

Lipid Profile	**Ponderal Index (PI)**		**P-value**
	$x \leq y$2.2	>2.2	
TC (mg/dL)	61.82 ± 32.05	63.62 ± 23.20	0.778
TG (mg/dL)	63.27 ± 20.09	47.19 ± 23.96	0.028*
HDL (mg/dL)	24.60 ± 11.77	25.11 ± 9.76	0.993
LDL (mg/dL)	38.72 ± 23.97	34.62 ± 20.22	0.694

4. Discussion

Lipid profile is a marker of an underlying cardiovascular status, and there is a direct correlation between the abnormalities in lipid profile and the occurrence of cardiovascular morbidities and mortality. Many studies show the direct relationship between the abnormalities in lipid profile among SGA babies and the occurrence of cardiovascular diseases[1,3]. The present study was undertaken to detect abnormalities in the lipid profile at

the earliest (at birth) amongst the SGA babies, so that these high-risk babies can be under vigilant monitoring in the future.

Both the study and control groups were age-matched and nearly sex/gender matched. Economic Survey of 2022[6] revealed that the number of females per 1,000 males in India has increased from 991 in 2015-16 to 1,020 in 2019-21. In a few of the earlier studies, this approach of gender match had been missing[7].

In the present study, the average birth weight of SGA neonates was 2.26 ± 0.24 kg, which was statistically different (P <0.001) from control group AGA neonates (2.84 ± 0.46 kg) (Table 5). Similarly, Wang et al.[2], Jones et al.[8] and Kelishadi et al.[9] also observed that the average birth weight of SGA neonates was significantly lower than their counterpart of control group. Wang et al.[2] and Jones et al.[8] reported similar mean birth weight values of SGA neonates as in the present study, while Kelishadi et al.[9] reported lower birth weight values of SGA neonates.

Table 5. Comparison of anthropometry parameters of SGA and AGA neonates

Neonatal Parameters	Present study		Wang et al.[2]		Kelishadi et al.[9]	
	SGA	AGA	SGA	AGA	SGA	AGA
Birth Weight (kg)	2.26 ± 0.24**	2.84 ± 0.46	2.35 ± 0.05	3.34 ± 0.02	1.95	3.10
Length (cm)	50.14 ± 1.52**	47.84 ± 2.39	46.7 ± 0.4	50.3 ± 0.2	44.1	49.1

The average birth length of SGA neonates in the present study was 50.14 ± 1.52 cm, which was significantly higher (P <0.001) than the counterpart of the control group (47.84 $x \pm y$ 2.39 cm). Wang et al.[2] and Kelishadi et al.[9] reported higher mean birth length for AGA neonates (Table 5). Besides, it is noted that the birth lengths for the SGA neonates in the above studies conducted in China[2] and Iran[9] were comparatively lower than the corresponding values reported in the present study for the SGA neonates from the author's Institute in India.

Relevant antenatal and neonatal data were collected from the study and control groups, and their effect on cord blood lipid profile was analysed (Table 6). In the present study, TG levels showed a significant elevation in the study group (60.38 $x \pm y$ 22.72 mg/dL) compared to the control group (36.59 $x \pm y$ 18.87 mg/dL). Similarly, Wang et al.[2] and Hossain et al.[10] reported significant elevation in the TG levels (Table 6). Likewise, TC levels also generally showed an increase in SGA neonates compared to AGA neonates.

Table 6. Comparison of cord lipid profile of SGA and AGA neonates

Lipid profile	Present study		Wang et al. [2]		Kelishadi et al. [9]		Hossain et al.[10]	
	SGA	AGA	SGA	AGA	SGA	AGA	SGA	AGA
TC (mg/dL)	69.85 ± 28.25**	56.83 ± 16.36	42.30 ± 2.16**	32.76 ± 3.96	79.5 ± 19.4*	79.9 ± 19.6	-	
TG (mg/dL)	60.38 ± 22.72***	36.59 ± 18.87	41.22 ± 4.14**	28.26 ± 2.34	64.7 ± 8.5*	67.6 ± 11.0	54.4 ± 11.2**	38.7 ± 5.8
HDL (mg/dL)	24.96 ± 12.13	25.16 ± 7.02	-	-	31.5 ± 5.2*	30.1 ± 9.3	-	
LDL (mg/dL)	40.03 ± 23.86	29.81 ± 14.86	37.98 ± 10.44*	22.32 ± 10.98	35.9 ± 7.1*	32.1 ± 7.3	-	

*Significance: *p<0.05, **p<0.01, ***p<0.001*

In the present study, HDL levels of neonates in the study group showed a marginal decrease compared to the control group while Kelishadi et al.[9] reported a marginal increase (Table 6). However, LDL levels showed a significant increase among neonates in the study group (40.03 $x \pm y$ 23.86 mg/dL) compared to the control group (29.81 $x \pm y$ 14.86 mg/dL). Interestingly, similar observation of increase in LDL in SGA neonates has been reported in all other studies (Table 6).

The analysis of cord blood profiles of SGA and AGA neonates suggest that generally there is an elevation in TG and TC levels among SGA neonates compared to AGA neonates (Table 6). It also revealed there is no significant change in HDL levels while there was an appreciable increase in the LDL levels among the SGA neonates in various studies including the present study. This analysis suggest that LDL level could be the most responsive change among the various lipid profile parameters.

The researchers explained and concurred with the hypothesis for the elevation in cord blood lipid profile values among SGA neonates compared to AGA neonates. Two facts explain the higher concentration of

plasma lipids in SGA babies[2,7,8]. There is a lack of glucose as fuel in SGA babies. So, these babies use alternative sources (amino acid and lipids) as fuel and generate glucose (gluconeogenesis). Thereby activating lipid and other metabolisms, so there will be an increased hepatic generation of lipids (particularly VLDL and chylomicrons). Secondly, there is also decreased peripheral utilisation of lipids because of decreased activity of LPL enzyme in growth-restricted babies.

4.1. Limitations of the study

1. A bigger sample size would have been better
2. Only term babies were part of the study
3. Maternal lipid profile, which is known to influence the cord blood lipid profile values, was not measured, which would have provided more insight into the study
4. Long-term follow-up of these babies with an abnormal lipid profile is required to support the conclusions

5. Conclusion

The analysis of cord blood profiles of SGA and AGA neonates revealed that there is an elevated lipid profile among SGA neonates. Generally, significant increase in TG and TC levels among SGA neonates has been reported in many studies. Researchers have also observed that there is no significant difference in the HDL levels between the SGA and AGA neonates. Nevertheless, there is an appreciable increase observed in LDL among SGA neonates in various studies including the present study suggesting that LDL probably could be employed as an indicative parameter. The variations in lipid profiles and anthropometry at birth may be explained by the abnormal intrauterine environment that was caused by maternal alterations throughout pregnancy. Therefore, lipid-related diseases and co-morbidities should be routinely examined in low birth weight, small for gestational age infants.

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Conflicts of Interest: The authors declare that they do not have any conflict of interests.

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