CORRELATION OF CORD BLOOD LIPID PROFILE AND NEONATAL ANTHROPOMETRIC MEASUREMENTS AT BIRTH

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Abstract:

Background: When a foetus experiences intrauterine stress, it may undergo programmed changes that alter its metabolism and put it at risk for disorders later in life.

Objective: The current study sought to determine the relationship between the lipid profile of cord blood and anthropometric data in new-borns.

Material and methods: This was prospective observational study of 150 neonates over 24 months from June 2020 to May 2022 in rural tertiary care hospital Karad. The inclusion criteria was neonates with informed consent of their parents and 1 minute Apgar score >7. Whereas we excluded perinatal hypoxia, perinatal sepsis and neonates with congenital anomalies. The neonate's birth weights were measured and their neonatal ponderal indices (NPI) were calculated. The lipid profile of the neonates' umbilical cord serum was examined, including total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), very low density lipoprotein (VLDL), and low density lipoprotein (LDL).

Results: In our study average values of Total cholesterol, LDL, VLDL and TG were significantly higher in SGA compared to AGA and LGA with $p<0.05$. There was a statistically significant negative correlation between the neonate's birth weight and TG ($P = 0.00$, $r = -0.374$), TC ($P = 0.05$, $r = -0.1630$), LDL ($P = 0.01$, $r = -0.210$), and VLDL ($P < 0.001$, $r = -0.392$,) cholesterol level. HDL showed non-significant positive correlation ($P = 0.73$, $r = 0.03$). Birth weight increases with decreasing TG, TC, LDL & VLDL with $p<0.05$, whereas HDL increase with Birth weight increment.

Conclusion: The current study has made us conclude that there is correlation between some of the lipid profile parameters and anthropometry at birth of neonates. The babies born with a LBW or with a PI less than 10th percentile or were SGA have exhibited a significantly higher higher LDL, HDL and TC levels as compared to AGA babies.

Keywords: Cord blood, Lipid profile, Neonates, Anthropometry

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Introduction:
Human foetuses are known to permanently change their physiology and metabolism to adapt to limited supply of nutrients in utero. These programmed changes can later be the cause for the origin of diseases like coronary artery disease, diabetes mellitus and hypertension. The cord blood lipid profile may be associated with lifelong changes in the metabolic functions of the individual.

The relationship between low birth weight and adult cardiovascular disease has been attributed to intrauterine effects on fetal tissue development.

The correlation of cord blood lipid profile in neonates with their anthropometric data and their predictive role as markers for adulthood diseases is still not completely explored.
Many studies have confirmed the importance of proper intrauterine development and all the factors that affect it will affect the future life. Past studies have reported that the concentration of total cholesterol, LDL, HDL, apolipoproteins were higher in preterm than in term babies. Whereas triglycerides level will be higher in preterm babies than in term babies. [1]

Hence the present study was designed to study any such novel patterns of cord blood lipid profile among neonates and their correlation with anthropometry at birth in a Tertiary care hospital.

Aim:
To evaluate the relationship between cord blood lipid profile and neonatal anthropometric measurements at birth.

Objectives:
- To assess the relationship between different parameters of cord blood lipid profile with neonatal abdominal circumference, head circumference and birth weight.
- To assess different parameters of cord blood lipid profile in small for gestational age, appropriate for gestational age and large for gestational age neonates.
- To assess the relationship between different parameters of cord blood lipid profile in neonates and Ponderal Index.

Materials and Methods
This was observational, cross sectional study where study Duration was 24 Months at Tertiary care hospital (Krishna Hospital, Karad) among Neonates born in Krishna Institute of Medical Sciences within the study period.

Inclusion criteria:
1. Neonates with informed consent of their parents.
2. 1 minute APGAR score >7.

Exclusion criteria:
1. Perinatal hypoxia.
2. Perinatal sepsis.
3. Neonates with congenital anomalies.

Sample Size:
Using an assumed prevalence of 11%, a total sample size of 150 was calculated using the Cochrane formula:
$N=Z^2xP(1-P)/E^2$=150 neonates as per inclusion and exclusion criteria.

Anthropometric Data:
Using an electronic weighing scale, birth weight (BW) was calculated with an accuracy of up to 5 gm. using an infantometer, length was measured. The head circumference (HC) was measured using non-stretchable tape that crossed the occipital protuberance and supraorbital ridge. With a non-stretchable tape through the umbilicus, the abdominal circumference (AC) was measured. Using the equation Weight (g)/Length (cm3) X 100, the Ponderal Index (PI) was derived. Based on PI less than or larger than the 10th percentile, neonates were divided into two groups. Ballard score or the most recent menstrual cycle were used to determine gestational age. The newborns were divided into three categories: small for gestational age (estimated foetal weight below 10th percentile), appropriate for gestational age (estimated foetal weight between 10-90th percentile), and large for gestational age (estimated foetal weight greater than 90th percentile) (estimated foetal weight greater than 90th percentile).

Biochemical Estimations:
1. Total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), and triglycerides were analysed in the cord blood lipid profile (TG).
2. The umbilical cord blood sample was collected by clipping the cord after the delivery but before the placenta was delivered, and it was then discharged into a sterile plain bulb.
3. Modified polyvinyl sulfonic acid (PVS) and polyethylene glycol methyl ether (PGME)

paired with the traditional precipitation method were used to determine the parameters.

Statistical analysis and results:
Primary data was collected in paper based CRF. All the Data entry was in MS-Excel 2016 and analysed using IBM SPSS Version 20. The relationship between anthropometric data and cord blood lipid profile was analysed using the Pearson correlation coefficient. Distribution was represented by pie charts or bar graphs. Continuous variables were expressed in the descriptive statistics tables as means, standard deviation, maximum and minimum value.

Averages were compared using ANOVA (Analysis of Variance) for 3 variables and independent sample T test for two variables. P value < 0.05 was considered significant and p value < 0.01 was considered highly significant.

Results:
In the study population, the mean total cholesterol was 83.4 SD 25.0, with values ranging from 20 mg/dl to 107 mg/dl. In the study population, the mean triglyceride was 55.4 SD 13.8 and ranged from 32 mg/dl to 97 mg/dl. In the study population, the mean HDL cholesterol was 25.2 SD 4.2 and ranged from 19 mg/dl to 43 mg/dl. In the study population, the mean LDL cholesterol was 59.5 SD 14.3, with values ranging from 18 mg/dl to 76 mg/dl. In the study population, the mean VLDL cholesterol was 9.4 SD 2.9, with a range of 4 to 16 mg/dl. **(Table 1)**

The average total Birth weight (g) was 2688.9 SD 441.32 gm., it ranged between 201860 g to 3650 g. The mean of head circumference (HC) was 33.4 SD 2.32 cm, HC range was between 30- 37cm. The mean of abdominal circumference was 30.0 SD 2.7 cm, AC ranged between 26 cm and 35 cm. The mean length of new born babies were 48.6 SD 2.4 Cm. It reveals that the highest percentage of infants 68.67% were born between ponderal index ranges of 2.1 and 3. Babies born between ponderal index range 1.1 to 2 and above 3 comprised the remaining 24.00% and 7.33% of births. The comparison of cord blood lipid profile in neonates with PI ≤ 2.25 (Group A) and PI >2.25 (Group B) are shown. The mean TG, VLDL and LDL levels in Group A was significantly higher than those in Group B (P = 0.02, 0.00, 0.03) which implies that neonates who are thin at birth with low PI have had higher TG, VLDL and LDL levels. Other than these the mean TC levels in Group A was none significantly higher than those in Group B (P >0.05) and the mean HDL levels in Group A was no significantly lower than those in Group B (P >0.05).

It shows the all three-birth weight category SGA, AGA and LGA had same 33.33 % of study population. Among 52% infant boys and 48% infant girls in this study. In which 54% of females were in the LGA, 52% in the SGA, and 38% in the AGA birth group, whereas 62% of boys were in the AGA, 48% in the SGA, and 46% in the LGA. The mean LDL Cholesterol of Boys group was 57.2 SD 16.4 (mg/dl) and Girls group was 61.9 SD 11.3 (mg/dl), and the mean difference between two groups was statistically significant (P value 0.04). The mean triglycerides of Boys group were 56.2 SD 12.6 (mg/dl) and Girls group was 54.5 SD 15.1(mg/dl), (P =0.454). The mean total Cholesterol of Boys group was 80.8 SD 26.8 (mg/dl) and Girls group was 86.16 SD 22.9 (mg/dl), and the mean difference between two groups was statistically non-significant (P value 0.19). The mean HDL Cholesterol of Boys group was 25.35 ± 4.45 (mg/dl) and Girls group was 25.08 ± 3.85 (mg/dl), and the mean difference between two groups was statistically non-significant (P value 0.6927). The mean VLDL Cholesterol of Boys group was 9.24 SD 3.8 (mg/dl) and Girls group was 9.61 SD 2.73 (mg/dl). (p = 0.44).
The mean triglycerides of SGA group was 58.40 ± 9.74 (mg/dl), AGA group was 56.64 ± 15.79 (mg/dl) and LGA group was 51.12 ± 14.46 and the mean difference between three groups was statistically significant (P value =0.02). The mean total cholesterol of SGA group was 95.26 ± 10.03 (mg/dl), AGA group was 76.08 ± 28.73 (mg/dl) and LGA group was 78.86 ± 27.59 (mg/dl), and the mean difference between three groups were statistically significant (P value= 0.000). The mean HDL Cholesterol of SGA group was 23.80 ± 2.34 (mg/dl), AGA group was 26.12 ± 5.11 (mg/dl) and LGA group was 25.74 ± 4.27 (mg/dl), and the mean difference between three groups were statistically significant (P value= 0.011). Here the HDL cholesterol level was low in SGA babies. The mean LDL Cholesterol of SGA group was 66.50 ± 7.04 (mg/dl), AGA group was 54.28 ± 16.35 (mg/dl) and LGA group was 57.68 ± 14.96 (mg/dl), and the mean difference between three groups was statistically significant (P value= 0.000). The mean VLDL Cholesterol of SGA group was 11.32 ± 2.56 (mg/dl), AGA group was 8.74 ± 3.04 (mg/dl) and LGA group was 8.20 ± 2.31 (mg/dl), and the mean difference between three groups was statistically not significant (P value= 0.000). **(Table 2)**

72 % neonates were multi gravida and 28% neonates were Primi gravida. In which 80 % multi gravida were in the LGA, 70 % in the AGA, and 66 % in the SGA group, whereas 34 % Primi gravida were in the SGA, 30 % in the AGA, and 20 % in the LGA. Babies are categorized in groups by use of AIIMS intrauterine growth charts.

The mean triglycerides of Primi gravida group was 54.2 SD 13.2 (mg/dl) and multi gravida group was 56.1 SD 14.2 (mg/dl), and the mean difference between two groups was statistically non-significant (P value 0.410).
The mean total cholesterol of primi gravida group was 81.27 ± 26.21 (mg/dl) and multi gravida group was 84.59 ± 24.37 (mg/dl), and the mean difference between two groups was statistically non-significant (P value 0.437).

The mean HDL cholesterol for primi gravida was 25.9 SD 3.9 (mg/dl) and the mean for multi gravida was 24.8 SD 4.3 (mg/dl), and the mean difference between the two groups was statistically insignificant (P value 0.131).
Primi gravida group had a mean LDL cholesterol of 58.6 SD15.9 mg/dl, whereas multi gravida group had a mean of 59.9 SD 13.3 mg/dl, and the mean difference between the two groups was statistically insignificant (P value 0.5832). The mean VLDL Cholesterol of primi gravida group was 9.1 SD 3.02 (mg/dl) and multi gravida group was 9.6 SD 2.94 (mg/dl), and the mean difference between two groups was statistically non-significant (P =0.36).

Neonates were divided into three groups based on their abdominal circumference for comparison of their LDL and HDL levels. Group 1 had AC between 26.1 and 29 cm, Group II with AC between 29.1 and 32 cm and Group III with AC > 32 cm. Group III neonates had significantly higher LDL levels than group II (P = 0.019). However, there was no statistically significant difference between HDL and LDL levels among these groups. 48 % neonates abdominal circumference were between 27 to 30 cm. 48.67 % neonates head circumference were above 33 cm. 67.33 % neonates' length were between 46 to 50 cm

There was a statistically significant negative correlation between the neonate's birth weight and TG (P = 0.00, r = -0.374), TC (P = 0.05, r = -0.1630), LDL (P = 0.01, r = -0.210), and VLDL (P = 0.00,) cholesterol level. HDL showed non-significant positive correlation (P = 0.73, r = 0.03). **(Table 3)** There were no significant correlation between lipid profile of neonates and their anthropometric data Head circumference. (P>0.05) **(Table 4)** There were no significant correlation between lipid profile of neonates and their anthropometric data abdominal circumference. (P>0.05) **(Table 5)**

Table 1: Cord blood lipid profile in neonates (n = 150).

Serum Lipid Parameter	Minimum	Maximum	mean	SD
TG	32	97	55.39	13.84
TC	20	107	83.40	25.04
VLDL	4	16	9.42	2.97
LDL	18	76	59.49	14.30
HDL	19	43	25.22	4.17

Table 2: Comparison of lipid profile of neonates grouped based on gestational age.

Serum Lipid		Mean	SD	p
TG	SGA (N=50)	58.40	9.74	0.022
	AGA (N=50)	56.64	15.79	
	LGA (N=50)	51.12	14.46	
TC	SGA (N=50)	95.26	10.03	0.000
	AGA (N=50)	76.08	28.73	
	LGA (N=50)	78.86	27.59	
VLDL	SGA (N=50)	11.32	2.56	0.000
	AGA (N=50)	8.74	3.04	
	LGA (N=50)	8.20	2.31	
LDL	SGA (N=50)	66.50	7.04	0.000
	AGA (N=50)	54.28	16.35	
	LGA (N=50)	57.68	14.96	
HDL	SGA (N=50)	23.80	2.34	0.011
	AGA (N=50)	26.12	5.11	
	LGA (N=50)	25.74	4.27	

*significant when p<0.05

Table 3: Relationship between lipid profile of neonates and their anthropometric data Birth Weight.

	TG	**TC**	**LDL**	**HDL**	**VLDL**
Birth Weight (r(Correlation coefficient)	-.374*	-.163*	-.210*	0.03	-0.392*
p	0.00	0.05	0.01	0.73	0.00
N	150.00	150.00	150.00	150.00	150.00

*significant when p<0.05

Table 4: Relationship between lipid profile of neonates and their anthropometric data Head circumference

	TG	TC	LDL	HDL	VLDL
HC (r(Correlation coefficient)	0.13	0.01	0.04	0.05	0.09
P	0.13	0.86	0.60	0.57	0.21
N	150.00	150.00	150.00	150.00	150.00

*significant when p<0.05

Table 5: Relationship between lipid profile of neonates and their anthropometric data abdominal circumference.

	TG	TC	LDL	HDL	VLDL
ABD CIRCUMFEREANCE (r(Correlation coefficient)	0.01	-0.01	-0.05	0.00	0.06
P	0.89	0.90	0.57	0.96	0.50
N	150.00	150.00	150.00	150.00	150.00

*significant when p<0.05

Discussion:

Since early childhood is considered to be the beginning of atherogenic abnormalities and serum lipid disorders, there has recently been a rise in interest in cord lipids. There is a clear link between abnormalities in lipid profile and the onset of cardiovascular morbidities and death, making lipid profile a sign of an underlying cardiovascular state.

The levels of lipids and lipoproteins in the cord serum should represent the newborn's plasma lipid metabolism at birth because the majority of foetal lipids are created de novo through the conversion of glucose to different fatty acid-containing molecules. Analyzing the lipid profile of cord blood at delivery is equivalent to investigating the lipid metabolism during foetal life because only a small portion of it is derived from placental circulation. Elevated plasma levels of cholesterol as well as triglycerides are considered to be the most crucial of the numerous variables connected to the onset of atherosclerosis. Furthermore, high LDL and low HDL are now widely recognised as the two primary risk factors for the beginning and progression of atherosclerotic vascular diseases.

An important tool in the early identification of infants at risk is the assessment of the cord lipid profile because many studies believe that the genesis of atherosclerotic lesions may originate in infancy.

Past studies have demonstrated a link between the fatal weight and other anthropometry parameters in preterm and SGA infants' abnormal lipid profiles. The goal of the current study was to assess the relationship between different parameters of cord blood lipid profile with neonatal abdominal circumference, head circumference and birth weight in not just SGA but also AGA and LGA babies.

Characteristics of the Study Subjects

Total 150 neonates were enrolled falling in all 3 gestational assessment categories SGA, AGA and LGA and were enrolled equally thus all 3 categories had same i.e. 33.33 % of study population.

The study included up to 52% infant boys and 48% infant girls. In which 54% of girls were in the LGA, 52% in the SGA, and 38% in the AGA birth group. Whereas, 62% of boys were in the AGA, 48% in the SGA, and 46% in the LGA.

Table D1: Comparison of gestation-based weight groups of current study with recent studies.

Study	**SGA**	**AGA**	**LGA**
Present Study	Included	Included	Included
Gupta et al (2020) [2]	Included	Included	Not included
Yashoda HT et al (2018) [3]	Included	Included	Not included
Ramy N et al (2017) [4]	Included	Included	Included

While majority of the studies included SGA and AGA babies, Ramy et al also had LGA babies similar to the present study. In a study to examine the lipid profiles and atherogenic indices in late preterm and term infants, Yashoda HT et al. (2018), compared the gender distribution between the two groups of neonates. Out of 170 neonates, 77 (45.3%) were female and 93 (54.7%) were male [67]3 this was comparable to the present study.

Table D2: Comparison of Influence of Gender on Neonate Cord Blood Lipid Profile

Study	Mean Total cholesterol	Mean Triglycerides	Mean LDL	Mean VLDL	Mean HDL
Present Study	Comparable	Comparable	Higher in Females	Comparable	Comparable
Kermani et al (2020) [5]	High in males	High in females	High in male	High in male	High in males
Sehra RN.et al (2020)[6]	Included	Included	-	-	Not included
Yashoda HT et al (2018) [3]	Comparable	Comparable	Comparable	Comparable	Comparable

There is no consensus on correlation of average lipid profile values with new-borns gender among contemporary researchers. In the present study the mean LDL Cholesterol of Boys group was significantly lower (57.2 SD 16.4 (mg/dl) to that of Girls group which was 61.9 SD 11.3 (mg/dl), (P = 0.04). Other lipid parameters were found comparable between male and female new-borns. Kermani et al (2020) reported that except for triglycerides in the female neonates, lipid profiles were significantly higher among the male neonates [5]. Yashoda HT et al (2018) reported that the new-born's gender had no impact on the lipid levels in the cord blood [3].

Sehra RN.et al (2020) reported that Low Density Lipoprotein (LDL) and High-Density Lipoprotein (HDL) were higher in male babies in both the groups as compared to female babies (p>0.05).[6]

Table D3: Correlation of Ponderal Index (PI) with Cord Blood Lipid Profile

Study	Mean Total cholesterol	Mean Triglycerides	Mean LDL	Mean VLDL	Mean HDL
Present Study	Negative correlation	Negative correlation	Negative correlation	Strong Negative correlation	Positive correlation
Ramy N et al (2017) [4]	NA	Strong Negative correlation	Strong Negative correlation	NA	NA
Nayak CD et al (2013) [7]	NA	Positive correlation		NA	NA

The comparison of cord blood lipid profile in neonates with PI ≤ 2.25 (Group A) and PI >2.25 (Group B) are shown. The mean TG, VLDL and LDL levels in Group A were significantly higher than those in Group B (P = 0.02, 0.00, 0.03) which implies that neonates who had low PI having higher TG, VLDL and LDL levels. Other than these the mean TC levels in Group A was no significantly higher than those in Group B (P >0.05) and the mean HDL levels in Group A was non significantly lower than those in Group B (P >0.05). Ramy N et al (2017) reported a strong negative correlation between TGL and each of birth weight, abdominal circumference, and ponderal index. The same was reported for LDL [69]. However Nayak CD et al (2013) [7] reported the opposite findings. Triglycerides were observed to be considerably greater in infants with a higher ponderal index (PI) compared to infants with a lower PI (P = 0.011).

Table D 4: Comparison of average values of Cord Blood Lipid Parameters between AGA, SGA and LGA

Study	Mean Total cholesterol	Mean Triglycerides	Mean LDL	Mean VLDL	Mean HDL
Present Study	High in SGA	High in SGA	High in SGA	High in SGA	High in AGA
Gupta et al (2020) [2]	High in SGA	High in SGA	High in SGA	High in SGA	Comparable
Yashoda HT et al (2018) [3]	High in SGA	High in SGA	High in SGA	High in SGA	Comparable
Ramy N et al (2017) [4]	Comparable	High in SGA	High in SGA	High in SGA	High in SGA
Nayak CD et al (2013) [7]	NA	High in SGA	NA	NA	NA

In the present study average values of TG, TC, VLDL, LDL levels of SGA babies were significantly higher than those of AGA & LGA babies. HDL levels of AGA babies were

significantly higher than SGA & LGA With $p<0.05$.

Majority of the studies compared [2, 3, 4] showed the congruence with our findings. Wherein the negative correlation was found between gestational age and cord blood lipid profiles. While a negative correlation between gestational age and fatal cholesterol levels is found and preterm infants have higher plasma cholesterol levels than term infants in a number of studies, not all studies show this same relationship. Indeed, some studies have shown no effect of gestational age on fatal cholesterol levels or even an increase in plasma cholesterol level with gestational age [8] The differences in results found in plasma collected from new-borns born prematurely versus at term could relate to the design of the studies because some studies collect blood from the new-born infant while others collect cord blood from the placenta to analyse, which should be similar but may not be depending on the timing of sample collection. Also, gestational age may be defined differently depending on the method used to define gestational age (ultrasound or the last menstrual cycle of the female). Finally, differences could be related to the preterm population studied as some preterm infants are thought to have other metabolic issues that affect their sterol metabolism, leading to unexpected differences in plasma cholesterol levels.

Table D 5: Correlation of Cord Blood Lipid Parameters between with Abdominal Circumference and Head Circumference

Study	Abdominal Circumference with Lipid Parameters	Head Circumference with Lipid Parameters
Present Study	No correlation	Negative correlation
Ramy N et al (2017) [4]	Strong Negative correlation	Strong Negative correlation
Nayak CD et al (2013) [7]	Positive correlation	NA
Li J, Wang ZN et al (2012) [9]	Strong Negative correlation	NA
Narayanaswamy A.G. et al (2022) [10]	No correlation	No correlation

We found no significant correlation of abdominal circumference and negative correlation of head circumference with the lipid parameters in the cord blood. Narayanaswamy A.G. et al (2022) [10] did not find any correlation of lipid parameters with either AC or HC.

While Ramy N et al [4] and Li J, Wang ZN et al [9] reported very strong negative correlation between lipids and AC, Nayak CD et al [7] reported positive correlation.

Negative correlation of HC with lipid parameters similar to our study was reported by Ramy N et al [4]

Strengths of This Study:

Comparison of various anthropometric parameters of the neonate with different lipid parameters was done in equal numbers of SGA, AGA and LGA. Our study has taken into consideration not only the weight based on the gestational age but also the anthropometric parameters like head circumference, abdominal circumference and Ponderal Index.

Conclusion:

The current study has made us conclude that there is correlation between some of the lipid profile parameters and anthropometry at birth of neonates. The babies born with a LBW or with a PI less than 10^{th} percentile or were SGA have exhibited a significantly higher LDL, HDL and TC levels as compared to AGA babies.

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