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Correlation of cord blood lipid profile with neonatal and maternal factors

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Abstract:
Cord blood lipid profiles may reflect early fetal metabolic programming and may be influenced by maternal and neonatal factors. Therefore, it is of interest to assess the cord blood lipid parameters in 174 mother–newborn pairs and their associations with neonatal and maternal characteristics. Late-preterm neonates had higher total cholesterol, LDL-C, triglycerides and atherogenic index of plasma (AIP) than term neonates, while HDL-C and VLDL-C did not differ significantly. Lipid parameters were not significantly associated with neonatal gender; AIP showed a marginal inverse correlation with birth weight, while maternal calorie intake correlated positively with VLDL-C and physical activity inversely with total cholesterol. These findings link cord blood lipid variation with gestational maturity, birth weight and selected maternal lifestyle factors, providing evidence for early-life differences in cardiovascular risk-related metabolic profiles.

Keywords: Cord blood, lipid profile, gestational age, birth weight, maternal BMI, physical activity, atherogenic index.

Background:
Cord lipid profile is a manifestation of fetal lipid metabolism and can offer early clues as to metabolic and cardiometabolic risk that starts in fetal life. At birth, levels of the lipids are related to gestation period, fetal growth and maturation, metabolism of the placenta and/or maternal metabolism **[1]**. Katragadda *et al.* found the lipid parameters in chemically defined cord bloods from the small-for-gestational-age and appropriate-for-gestational-age groups are significantly different, implying that cord blood lipid metabolism is related to the gestation and the growth of the fetus **[1].** Other important contributors are differences in cord blood lipid profiles among term and preterm infants indicating a relationship between gestational maturity and cord blood lipid status **[2, 3].** Kumar *et al.* also found variations in cord blood lipid profile and atherogenic index between term and preterm newborns, indicating an association between gestational maturity and neonatal lipid status **[3].** Birth weight is another prime indicator and studies have shown significant correlations between cord blood lipid fractions and birth weight **[4].** The levels of lipids in the cord blood are also different among children based on their gestational stage and anthropometric parameters of the newborn. Similarly, cord blood lipid parameters were reported to be associated with both gestational age and birth weight by Obaji *et al.* **[5]** and the cord blood lipidome, apolipoproteins and atherogenic indices were shown to be different according to the gestational years by Samar *et al.* **[6]**, all more recent findings. Birth weight, early neonatal outcomes and the cord blood lipidome have all been linked, according to more current lipidomic data **[7].** Therefore, it is of interest to find out the correlation of cord blood lipid profile with the neonatal and maternal factors, in the term and late term preterm babies.

Materials and Methods:
Study design and setting:
A single center analytical, cross-sectional study was undertaken in Department of Pediatrics and Labour Room/Operation theatre, Department of Obstetrics and Gynaecology, Kamla Raja hospital, Gajra Raja Medical college, Gwalior, Madhya Pradesh in 2 years period from 2022-2024. Simple random sampling was used to enroll a total of 174 mother–newborn pairs that met the eligibility criteria.

Sample size:
For Quantitative Variable Sample Size was calculated at:

$$n = \frac{Z^2\sigma^2}{L^2}$$

So, Z=1.96, σ=33, allowable absolute error (L)=5. The calculated sample size was around 167; after allowance for possible incomplete data were added for the total of 174.

Eligibility criteria:
Term newborns (37-<42 weeks) and late preterm newborns (34-<37 weeks) were included in this study after their parent written consent form. Neonates that needed resuscitation, those admitted to SNCU and those that were obviously congenital anomaly were excluded. Additionally, mothers who have hypertension, gestational diabetes, cardiac diseases, obesity, complicated labour, or do not have a record of their weight in the first trimester were not included.

Maternal assessment:
A semi-structured proforma was used to record: maternal age, education, socioeconomic status, calorie intake and level of physical activity in the first and second pregnancy trimesters. The information on first-trimester weight was collected from the antenatal records and the height was measured with a stadiometer.
BMI was calculated as:

$$BMI = \frac{\text{Weight (kg)}}{\text{Height (m)}^2}$$

Mothers were classified as underweight (<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), or overweight (25.0–29.9 kg/m²). The physical activity of the mothers was measured on self-reported

mean level of their occupied and leisure activity duration and intensity and based on cycling and occupation and categorized as inactive, moderately active and active.

Neonatal assessment:
After birth neonatal sex and weight, head circumference and gestation age were recorded. When necessary, gestational age was determined using the New Ballard Score. Newborns were classified by birth weight as 1500–2499 g, 2500–3499 g, or ≥3500 g. They were classified based on weight for gestational age as SGA (<10th percentile), AGA (10th-90th percentile) or LGA (<90th percentile). Gestational age was defined as being late preterm or term.

Cord blood lipid profile:
Umbilical cord blood (about 2 mL) was collected aseptically and analyzed for total cholesterol, triglycerides, HDL-C, LDL-C and other available lipid fractions immediately after a newborn's birth and umbilical cord cutting.
The atherogenic index of plasma (AIP) was calculated as:

$$AIP = \log_{10}\left(\frac{TG}{HDL - C}\right)$$

Using triglyceride and HDL-C concentrations in molar units.

Study variables:
Factors included in the neonatal variables were birth weight, gestational age and sex and weight-for-gestational-age category. Maternal variables were age, level of education, calorie intake, BMI and physical activity. Cord blood lipid parameters and AIP constituted the principal outcome variables.

Statistical analysis:
Data were analyzed with SPSS software version 16.0 and also with Epi Info software version 7.0. Continuous variables were presented as mean ± SD or median (IQR) and categorical presented as frequency and percentage. An independent sample t-test or Mann–Whitney U-test was used for two-group comparisons and one-way ANOVA or Kruskal-Wallis test was used to compare three or more groups. Pearson's or Spearman's correlation was used to assess associations between continuous variables. Multivariable linear regression analyses were used to determine independent predictor variables for cord blood lipid parameters, in each case where appropriate. A p-value of < 0.05 was interpreted as being statistically pertinent.

Results:
A total of 174 mother–newborn dyads participated in the study. Among the mothers (121, 69.5%) were under 31 years of age and the majority of them had primary education. Normal BMI was observed in 103 (59.2%) mothers, while 55 (31.6%) were underweight and 16 (9.2%) were overweight. As far as physical activity was concerned, 94 (54.0%) mothers were somewhat active, 44 (25.3%) mother were active and 36 (20.7%) mother were inactive. Among the newborns, 90 (51.7%) were male and 84 (48.3%) were female. There were 68 (39.1%) late-preterm and 106 (60.9%) term neonates. Most neonates weighed 2500–3499 g (58.6%), while 28.2% weighed 1500–2499 g and 13.2% weighed >3500 g. According to weight for gestational age, 108 (62.1%) were AGA, 49 (28.2%) SGA and 17 (9.8%) LGA **(Table 1)**. The overall mean cord blood total cholesterol was 69.41 ± 10.50 mg/dL, LDL-C was 36.57 ± 8.25 mg/dL, HDL-C was 24.98 ± 4.44 mg/dL, VLDL-C was 19.90 ± 1.58 mg/dL, triglyceride level was 61.86 ± 6.74 mg/dL and mean atherogenic index of plasma (AIP) was 2.695 ± 0.291. One of the strongest associations was with gestational age for cord blood lipid profile. The total cholesterol, LDL-C, triglycerides and AIP were significantly higher in late-preterm neonates compared to term neonates. Total cholesterol was 72.44 ± 9.84 versus 67.46 ± 10.50 mg/dL (p=0.002), while LDL-C was 45.29 ± 5.37 versus 30.98 ± 3.61 mg/dL (p<0.001). Late-preterm neonates also had significantly high triglycerides and AIP. HDL-C and VLDL-C resulted in no significant difference **(Table 2).** There were no significant differences in cord blood lipid profile at neonatal gender. There was no statistical significance for the minor differences between the male and female groups in terms of total cholesterol (70.24mg/dl vs. 68.51), LDL-C (37.02mg/dl vs. 36.10) or AIP (2.723 vs. 2.665). There was variation in the lipid pattern for the weight-for-gestational-age category and there was significant difference between AIP's of AGA, LGA and SGA groups (p=0.004) **(Table 3).** There was an also significant association between maternal physical activity with neonatal cord blood and total cholesterol. Mean total cholesterol dropped among the mother who were inactive compared to the mother who were somewhat active and active (p<0.001) respectively from 75.67mg/dL to 67.96mg/dL and 67.39mg/dL. Maternal physical activity category did not appear to significantly differ for LDL-C, HDL-C or VLDL-C or for triglycerides. The calorie-intake categories had no significant difference between groups in terms of mean levels of total cholesterol, LDL-C, HDL-C, VLDL-C, triglycerides or AIP. There were however a significant positive correlation between maternal calorie consumption and cord blood VLDL-C (r=0.152, p=0.045) found on correlation analysis. There was a negative significant correlation between maternal physical activity and TC level in the cord blood (r=−0.271, p<0.001) **(Table 4).** Therefore the main outcomes of the study reliably revealed that gestational age was very closely correlated with the lipid profile of these newborns, since late-preterm newborns had significantly higher total cholesterol, LDL-C, triglyceride and AIP. Total cholesterol was inversely associated with maternal physical activity and cord blood VLDL-C was positively associated with maternal calorie intake, regardless of whether they were carried out in infancy, childhood, or in both age groups. Neonatal total cholesterol had an inverse significant but rather weak association with maternal physical activity and increasing calorie intake in both infant and childhood was positively associated with cord blood VLDL-C.

Table 1: Maternal and neonatal characteristics of the study population

Characteristic	Category	n (%)
Maternal age	<30 years	121 (69.5)
	>30 years	53 (30.4)
Maternal BMI	<18.5 kg/m²	55 (31.6)
	18.5–24.9 kg/m²	103 (59.2)
	25.0–29.9 kg/m²	16 (9.2)
Maternal physical activity	Inactive	36 (20.7)
	Somewhat active	94 (54.0)
	Active	44 (25.3)
Neonatal gender	Male	90 (51.7)
	Female	84 (48.3)
Gestational age	Late preterm	68 (39.1)
	Term	106 (60.9)
Birth weight	1500–2499 g	49 (28.2)
	2500–3499 g	102 (58.6)
	>3500 g	23 (13.2)
Weight for gestational age	SGA	49 (28.2)
	AGA	108 (62.1)
	LGA	17 (9.8)

Table 2: Association of cord blood lipid profile with gestational age

Cord blood parameter	Late preterm (n=68), Mean ± SD	Term (n=106), Mean ± SD	p-value
Total cholesterol (mg/dL)	72.44 ± 9.84	67.46 ± 10.50	**0.002**
LDL-C (mg/dL)	45.29 ± 5.37	30.98 ± 3.61	**<0.001**
HDL-C (mg/dL)	24.85 ± 3.86	25.06 ± 4.79	0.769
VLDL-C (mg/dL)	19.91 ± 1.23	19.90 ± 1.78	0.950
Triglycerides (mg/dL)	66.63 ± 5.02	58.80 ± 5.88	**<0.001**
Atherogenic index of plasma	2.974 ± 0.211	2.517 ± 0.170	**<0.001**

Bold p-values indicate statistical significance (p<0.05)

Table 3: Major neonatal factors associated with cord blood lipid parameters

Neonatal factor	Cord blood parameter/finding	Statistical result
Gestational age	Total cholesterol higher in late preterm	**p=0.002**
	LDL-C higher in late preterm	**p<0.001**
	Triglycerides higher in late preterm	**p<0.001**
	AIP higher in late preterm	**p<0.001**
	HDL-C	p=0.769
	VLDL-C	p=0.950
Gender	Total cholesterol	p=0.278
	LDL-C	p=0.461
	HDL-C	p=0.588
	Triglycerides	p=0.747
	AIP	p=0.191
Weight for gestational age	AIP	**p=0.004**
Birth weight	AIP, negative correlation	**r = −0.0184; p=0.015**

Table 4: Correlation of selected maternal and neonatal factors with cord blood lipid profile

Factor	Cord blood parameter	Correlation coefficient (r)	p-value	Interpretation
Birth weight	AIP	−0.0184	**0.015**	Significant negative correlation
Maternal calorie intake	VLDL-C	+0.152	**0.045**	Significant positive correlation
Maternal physical activity	Total cholesterol	−0.271	**<0.001**	Significant negative correlation
Maternal BMI	Total cholesterol	−0.078	0.309	No significant correlation
Maternal calorie intake	Total cholesterol	−0.075	0.323	No significant correlation
Birth weight	Total cholesterol	−0.019	0.808	No significant correlation

Discussion:

In this study, lipid profile in the cord blood was analyzed in relation to neonatal and maternal factors in 174 mother–newborn pairs. The main results were that the gestational age was significantly associated with cord blood lipids, with significantly higher total cholesterol, LDL-C, triglycerides and atherogenic index of plasma (AIP) in the late preterm neonates when compared with term neonates. There was also a statistically significant, inverse relationship between maternal physical activity and cord blood total cholesterol and a positive relationship between maternal calorie intake and cord blood VLDL-C, with the relationships being weak. Birth weight also showed a statistically significant, but weak negative correlation with AIP. Characteristics of the maternal diet have the potential to impact the environment in which the fetus develops in utero and consequently neonatal lipid metabolism. Harris *et al.* showed that maternal diet during pregnancy was associated with the cord blood metabolite profile, supporting the concept that maternal nutritional exposures can influence fetal metabolic programming **[8].** Similarly, a study of preterm neonates with

respiratory distress syndrome reported positive correlations between maternal and cord blood lipid concentrations and between maternal gestational weight gain and neonatal lipid levels, highlighting the potential influence of maternal metabolic status on neonatal lipid profiles **[9].** This present study has shown that maternal calorie consumption did not significantly affect majority of cord blood lipid fractions between Maternal and Cord Blood (CB) in categorical analysis, but a significant positive correlation was observed with VLDL-C. This suggests that the dietary energy exposure may have preferential effects on only selective fractions of neonatal lipids. The recent Indian data have also highlighted the need to assess the maternal and neonatal factors that affect cord blood lipid levels **[10].** A large cross-sectional study involving 3,157 neonates in India evaluated cord blood lipid profiles across preterm, term, and post-term groups, providing additional population-specific data on neonatal lipid concentrations and their relationship with gestational age and birth weight **[11].** Maternal lipid metabolism is also closely linked to the lipid status of the fetus. A lipidome of umbilical cord blood was used to assess how maternal lipid concentrations throughout gestation affected the lipidome of birth-weight to evaluate the influence of maternal metabolism on fetal lipid handling and Lipid concentration concentrations across pregnancy were reported to have a measurable impact on infant birth weight **[10].** One of the major results of the present study was that the physical activity of the mother was associated with cord blood total cholesterol in a significant inverse way. There was no difference between the inactive and active mothers in terms of cholestrol levels ($p<0.001$): inactive mother: 75.67 mg/dL, active mother: 67.39 mg/dL. The results of Collings *et al.* also explored this relationship between maternal PA and neonatal cord blood lipid parameters and confirmed that PA during pregnancy can have an effect on fetal metabolic environment **[11].** All of this indicates that exercise during pregnancy can have an effect on increasing the baby's weight and this may be beneficial in terms of the lipid characteristics of the babies. Maternal vascular and metabolic conditions can also modify placental lipid transfer. LaBarre *et al.* demonstrated associations between maternal and umbilical cord lipid parameters and uterine and fetoplacental blood flow, indicating that placental perfusion may be an important determinant of fetal lipid exposure **[12].** In the present study, mothers with major metabolic and hypertensive risk factors were excluded, which may partly explain why several maternal variables showed relatively weak associations with cord blood lipid fractions. Another aspect of the present analysis was neonatal anthropometry. Collings *et al.* reported correlations between cord blood lipid profile, neonatal birth weight and maternal anthropometry **[13].** Similarly, Hessami *et al.* noticed that cord blood lipid concentrations were heterogeneous according to the neonatal anthropometric parameters in the week before birth **[14]** and birth weight in our study was weakly but statistically inversely correlated with AIP, which points to the fact that lower birth weights may be associated with more atherogenic neonatal lipid pattern. The newborn's and mother's lipid profiles could also be correlated. Gestational maturity seemed to be one of the strongest factors in the present study, however, as found by Mandraha *et al.* in their research of the different association with maternal and cord blood lipid profile **[15]**. The total cholesterol, LDL-C, triglycerides and AIP levels were significantly associated with the late-preterm neonates when compared to the term neonates and the HDL-C and VLDL-C levels were similar. This is similar to the results of Nayak *et al.,* Zohra *et al.* and Kenchappa and Behera who showed that cord blood lipid levels were related to sex and birth weight of neonates and gestational age **[16-18].** The study also revealed that there were no significant differences between the cord blood lipids fractions based on gender of the newborns. Thus, it appears that cord blood lipid concentrations may be shaped more by weight gain in pregnancy, sex-specific fetal growth and mother's lifestyle processes than by sex, in the immediate neonatal period. As a whole, the results support the idea that lipid metabolism in the fetus is dependent upon a range of factors, including gestational maturity, growth characteristics and maternal behaviour. This study had limitations of a single center cross sectional type of study and was dependent on self-reported measurements of maternal calorie intake and physical activity and this may led to recall bias. In all subjects, maternal serum lipid levels were not analyzed at the same time and long-term analysis of neonatal serum lipid were not carried out. However, this study offers valuable data on factors that may be amenable to change during pregnancy and the newborn period that predispose to cord blood lipid metabolism.

Conclusion:

Late-preterm neonates had significantly higher total cholesterol, LDL-C, triglycerides and AIP than term neonates, highlighting the influence of gestational maturity on lipid metabolism at birth. Maternal physical activity and calorie intake were significantly associated with neonatal lipid parameters, while AIP showed a weak inverse association with birth weight. Thus, data shows that both intrauterine maturity and maternal lifestyle may contribute to early neonatal lipid programming with potential implications for later cardiometabolic risk.

Advancement to knowledge:

The study identifies associations between cord blood lipid profiles, gestational maturity, birth weight and maternal lifestyle factors, highlighting potential early-life influences on metabolic and cardiovascular risk profiles.

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