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Original Article

Paediatrics Section

# Comparison of Cord Blood Lipid Profile among Appropriate for Gestational Age and Small for Gestational Age Term Neonates: A Cross-sectional Study

JASIM QURESHI[1], SAMAN BEG[2], JAIGHAM ABBAS[3], ASHISH VERMA[4], AKANKSHA SRIVASTAVA[5], KHATIBUR RAHMAN[6]

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## ABSTRACT

**Introduction:** Antenatal factors such as prematurity and Intrauterine Growth Restriction (IUGR) may influence the levels of various cord blood lipoproteins and subsequently predispose infants to early-onset ischaemic heart diseases. In order to provide insight on abnormalities in the lipid profile as soon as feasible (at birth) among newborns, especially in term and Small for Gestational Age (SGA) infants, the need for present study arose so that these high-risk babies could be continuously monitored.

**Aim:** To estimate the cord lipid profile in term neonates and compare lipid levels between Appropriate for Gestational Age (AGA) and Small for Gestational Gge (SGA) infants.

**Materials and Methods:** This cross-sectional study was conducted on 130 neonates with gestational ages of 37-42 weeks in the Department of Paediatrics at the Career Institute of Medical Sciences and Hospital (CIMSH), Lucknow, Uttar Pradesh, India from December 2022 to May 2024. The neonates were divided into two groups: Group A consisted of 65 term neonates who were AGA, and Group B consisted of 65 term neonates who were SGA. Parameters assessed included Total Cholesterol (TC), Triglycerides (TG), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), and Very Low-Density Lipoprotein (VLDL). Pearson correlation was used to assess relationships between lipid profiles, gestational age and birth weight. Significance was set at p-value<0.05.

**Results:** Baseline characteristics, including gender distribution and birth weight, were comparable across groups (p-value>0.05). Group B (SGA) neonates exhibited significantly higher levels of TG, TC, LDL, and VLDL than Group A (AGA) (p-value<0.05). HDL levels, although higher in Group B, were not statistically significant (p-value>0.05). TC, HDL and LDL levels showed a significant negative correlation with gestational age and birth weight (p-value<0.05). TG and VLDL levels exhibited a weak and statistically insignificant correlation.

**Conclusion:** The SGA babies showed noticeably greater cord blood levels of LDL cholesterol, TG and TC than the AGA group of newborns. Therefore, it is important to routinely monitor SGA and low birth weight neonates throughout their adolescence and adulthood to implement prompt therapies and prevent the rapid development of cardiovascular disease.


**Keywords:** Cardiovascular risk, Cholesterol levels, Foetal growth restriction, Neonatal lipid profile

## INTRODUCTION

The IUGR is a common antenatal diagnosis frequently associated with maternal, placental, or foetal factors. IUGR not only increases the risk of perinatal mortality and morbidity but also predisposes individuals to a higher likelihood of developing various diseases later in life, including early-onset cardiovascular conditions. Investigating the early determinants of these illnesses is crucial, especially given the rising incidence of factors such as obesity and hyperlipidaemia in the paediatric population [1]. Cardiovascular illnesses, primarily ischaemic heart disease and stroke, are the leading causes of mortality worldwide [2]. Hereditary and lifestyle risk factors, such as smoking, obesity, hypercholesterolaemia, high blood pressure and insufficient physical activity, are known to be associated with these illnesses. Study suggest that cardiovascular disorders may originate in infancy, with atherosclerosis potentially beginning as early as the prenatal period [3].

Cholesterol is a primary causal risk factor for the development of atherosclerosis and Cardiovascular Disease (CVD). LDL is the component of TC that is most closely associated with CVD risk [4]. Prematurity and foetal malnutrition affect the levels of various types of cord blood lipoproteins [5,6]. Elevated levels of apo C-1, a type of HDL, TG-rich lipoproteins, and apolipoprotein B are factors that place babies born early or underweight at a higher risk of cardiovascular disease [7,8].

An unfavourable prenatal and early postnatal environment is increasingly linked to the development of disrupted physiological and metabolic conditions in both the foetus and the infant [9,10]. These newborns are at an increased risk of heart disease in the future due to the physiological adjustments that follow. The burden of Coronary Artery Disease (CAD) is more prevalent in developing nations [11]. It has been proposed that the foetal origin of adult disorders, such as metabolic syndrome and CAD, is due to a permanently altered program that enables the foetus to adapt to intrauterine stress or malnutrition [12]. Fatty streaks were found in 2.9% of aortas in infants under one-year-old and in 3.1% of coronary arteries in children aged one to nine years, according to a nationwide autopsy-based study on atherosclerosis in young Japanese individuals (aged 1 month to 39 years) [13].

While lipid profiles and blood cholesterol levels in adults and older children have been extensively studied, neonates, especially in India, have not received as much attention [14-16]. There is limited

information available on the blood lipid levels of term neonates (AGA and SGA). Hence, present study was conducted to estimate the cord lipid profile in term neonates, comparing those with normal birth weight to those classified as SGA.

## MATERIALS AND METHODS

A cross-sectional study was conducted at the Neonatology Division, Department of Paediatrics, Career Institute of Medical Sciences and Hospital, Lucknow, Uttar Pradesh, India, over 18-month period (December 2022 - May 2024). This study was duly approved by the Institutional Ethics Committee (IEC) of Career Institute of Medical Sciences and Hospital, Lucknow (Ref No. CIMSH/IEC/NOV/2022/1011, dated 16/11/2022). Written informed consent was obtained from parents or guardians of all participants.

**Inclusion criteria:** Healthy term neonates (37-42 weeks) with an APGAR score of ≥7 at one minute with parental consent were included in the study.

**Exclusion criteria:** Neonates with congenital malformations, maternal history of medications affecting lipid metabolism, an APGAR score of <7, multiple gestations, large for gestational age (LGA) neonates, sepsis, or maternal conditions such as diabetes or thyroid disorders were excluded from the study.

**Sample size:** The sample size was calculated based on the study by Yashodha HT and Anjum SK [17]. The mean difference in the TC/HDL ratio between term neonates (3.10) and preterm neonates (3.5) was found to be 0.4, with a variance ($\sigma^2$) of 0.8. The following formula was used to calculate the sample size:

$$\text{Sample size (n)} = \frac{2\times(Z_{\alpha/2}+Z_{1-\beta})\sigma^2}{(\mu_1-\mu_2)^2}$$

Where:

- $Z_{\alpha/2}$=1.96 (for a significance level of 0.05)
- $Z_{1-\beta}$=0.84 (for a power of 80%)
- $\sigma^2$=0.8 (variance)
- $\mu_1-\mu_2$=0.4 (mean difference between groups)

Using these values, the sample size was calculated as:

$$\frac{2\times(1.96+0.84)^2\times0.8}{0.4^2}$$

n=78.4

Thus, the total sample size required was 79 neonates. However, considering feasibility and rounding off, 65 neonates were included in each group, resulting in a total of 130 neonates for the study.

The sampling method used in the study was convenience sampling. The study group consisted of 130 neonates, divided into two groups:

- Group-A: 65 AGA neonates.
- Group-B: 65 SGA neonates.

### Study Procedure

Gestational age was determined based on the first day of the most recent menstrual cycle and validated through clinical and radiological evaluation. Written informed consent was obtained from parents or guardians of all participants. The attending paediatrician extracted five millilitres of cord blood from the umbilical cord using a syringe immediately after delivery and placed the sample in a plain vacutainer. Postdelivery, the initial APGAR score was used to assess eligibility for inclusion in the study. Neonates with an APGAR score of 7 or above were considered suitable.

The neonates were examined for weight (measured using a digital baby scale), length, head circumference and chest circumference (measured with a non stretchable tape), along with other relevant anthropometric data. Based on this anthropometric data, neonates were classified as AGA or SGA using an intrauterine growth chart (Intergrowth 21st-WHO) and assigned to their respective groups [18].

The cord blood was allowed to clot and was then immediately sent to the hospital laboratory, where the samples were centrifuged at 1500 rotations per minute for five minutes. A 2-3 mL aliquot of serum was separated and analysed for TC, TG, HDL, LDL, VLDL using a fully automated analyser (Merilyser Autoquant 200 Excelus, 2023 model, with control checks conducted twice weekly). Normal range for cord blood were as follows: TC - 50-120 mg/dL, TG - 38-105 mg/dL, HDL - 18-47 mg/dL, LDL - 25-65 mg/dL [19]. The results were reported by the attending pathologist within 3-4 hours.

## STATISTICAL ANALYSIS

The data analysis for this study was conducted using Statistical Package for the Social Sciences (SPSS) version 25.0. The statistical tests applied to calculate the p-value included: Chi-square test and Pearson correlation test. The level of significance considered was 0.05.

## RESULTS

In this study, a total of 130 neonates were enrolled, comprising 65 AGA neonates (Group A) and 65 SGA neonates (Group B). The distribution of neonates based on gender was statistically insignificant in both groups (p-value>0.05, p-value=0.861). Gender distribution. gestational age and mode of delivery is shown in [Table/Fig-1].

| Parameters | Group A (Mean±SD) | Group B (Mean±SD) |
|---|---|---|
| **Gender n (%)** | | |
| Male | 30 (46.2) | 32 (49.2) |
| Female | 35 (53.8) | 33 (50.8) |
| Gestational age (weeks) | 38±3 | 39±1 |
| **Mode of delivery n (%)** | | |
| NVD | 45 (69.3) | 48 (73.9) |
| LSCS | 20 (30.7) | 17 (26.1) |

**[Table/Fig-1]:** Baseline data of the study participants.
NVD: Normal vaginal delivery; LSCS: Lower segment caesarean section

In the present study, a comparison of lipid profiles revealed that TGs, TC, LDL, and VLDL levels were significantly higher in Group B compared to Group A (0.040, <0.001, <0.001, 0.042). However, HDL levels were higher in Group B than in Group though this difference was not statistically significant (p-value=0.057) [Table/Fig-2].

Bivariate analysis using Pearson correlation revealed that TC, HDL, and LDL levels were significantly negatively correlated with gestational age and weight. TGs and VLDL levels also showed

| Lipid profile | Group A (Mean±SD) | Group B (Mean±SD) | p-value |
|---|---|---|---|
| TG (mg/dL) | 69.7±32 | 82.5±38.3 | 0.040 |
| TC (mg/dL) | 79.6±26 | 100.3±28 | <0.001 |
| HDL (mg/dL) | 32.3±10.3 | 36.4±13.6 | 0.057 |
| LDL (mg/dL) | 33.4±18.8 | 47.8±16.4 | <0.001 |
| VLDL (mg/dL) | 13.9±6.4 | 16.3±7.8 | 0.042 |

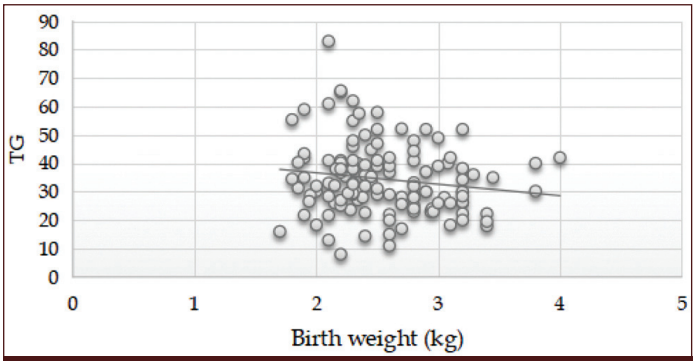
**[Table/Fig-2]:** Comparison of lipid profile between both groups.
TG: Triglyceride; TC: Total cholesterol; HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: Very low density lipoprotein

a negative correlation, but the association was not statistically significant. The negative correlation indicates an inverse proportional relationship [Table/Fig-3].

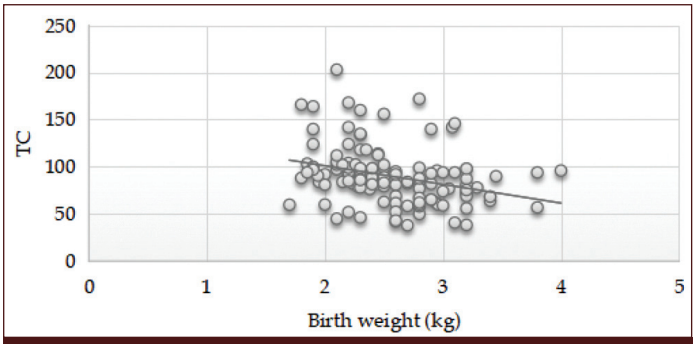
| Lipid profile | | Gestational age (SGA/AGA) | Weight |
|---|---|---|---|
| TG | Pearson correlation | -0.133 | -0.152 |
| | Sig. (2-tailed) | 0.132 | 0.084 |
| TC | Pearson correlation | -0.351** | -0.315** |
| | Sig. (2-tailed) | **<0.001** | **<0.001** |
| HDL | Pearson correlation | -0.179* | -0.192* |
| | Sig. (2-tailed) | **0.042** | **0.028** |
| LDL | Pearson correlation | -0.377** | -0.325** |
| | Sig. (2-tailed) | **<0.001** | **<0.001** |
| VLDL | Pearson correlation | -.0167 | -0.154 |
| | Sig. (2-tailed) | 0.057 | 0.081 |

**[Table/Fig-3]:** Correlation between lipid profile values, gestational age, and birth weight.

The study showed that birth weight was inversely proportional to TGs [Table/Fig-4], TC [Table/Fig-5], LDL [Table/Fig-6], VLDL [Table/Fig-7], and HDL [Table/Fig-8].



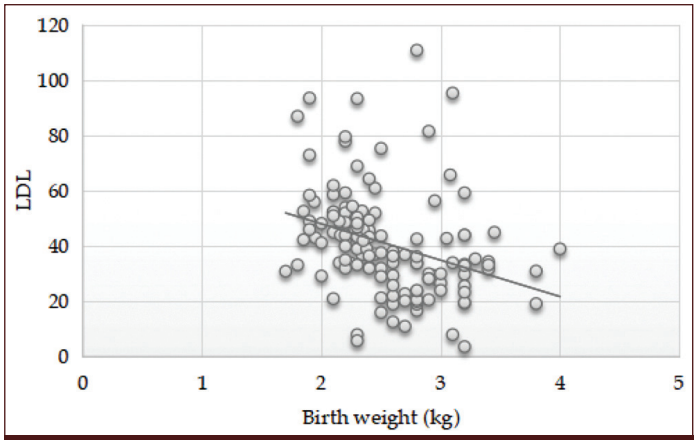

**[Table/Fig-4]:** Correlation of TG (mg/dL) values with birth weight (kg).



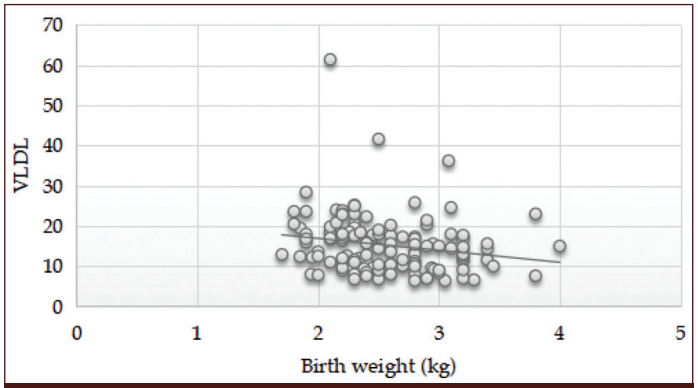

**[Table/Fig-5]:** Correlation of TC values with birth weight (kg).

## DISCUSSION

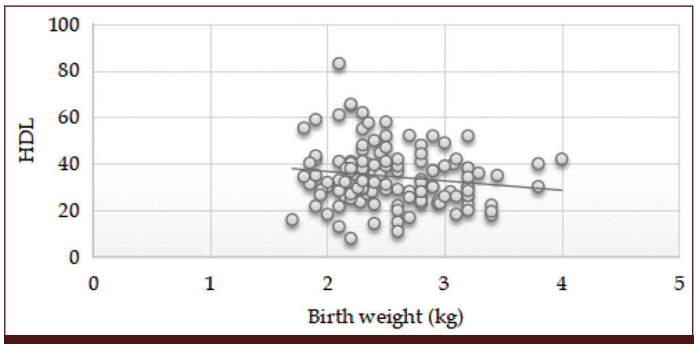
The findings of the present study revealed that TGs, TC, LDL, and VLDL levels were significantly higher in Group B (term SGA) than in Group A (healthy term newborns) (p-value <0.05). However, HDL levels were insignificantly higher in Group B compared to Group A (p-value>0.05).




**[Table/Fig-6]:** Correlation of LDL values with birth weight (kg).




**[Table/Fig-7]:** Correlation of VLDL values with birth weight (kg).




**[Table/Fig-8]:** Correlation of HDL values with birth weight (kg).

Studies have shown that low birth weight increases the risk of Coronary Heart Disease (CHD) in both men and women [3,9]. The foetal origins hypothesis explains that adverse conditions during foetal development, such as malnutrition, can impair intrauterine growth, leading to permanent changes in the foetus's physiology and metabolism. These changes may contribute to the development of CAD in adulthood [20]. It is proposed that the origins of adult disorders, such as metabolic syndrome and CAD, are linked to foetal programming that adapts to intrauterine stress or starvation. In response to these adverse conditions, growth-restricted newborns often rely on their stored resources, which triggers lipid metabolism, generates energy and promotes gluconeogenesis [12].

Evidence from the literature indicates that atherosclerosis begins in early life and progresses into adulthood, making it beneficial to assess cord blood lipid profiles at birth. Abnormal lipid levels in newborns may persist into adulthood, and early intervention could help prevent future cardiovascular complications [14]. This

study aimed to explore the relationship between birth weight, gestational age, and the lipid profile of umbilical cord blood in term newborns.

In a study by Jadhao AN et al., the lipid profile of umbilical cord blood in near-term and term neonates was analysed, showing no significant difference between male and female infants. However, female newborns had higher mean levels of all lipid indicators, except for TGs and VLDL. No significant differences were found in lipid profiles between term SGA and AGA neonates or between near-term SGA and AGA neonates [15]. Conversely, Gupta R et al., found that TC, TG, and LDL were significantly higher in SGA newborns compared to AGA neonates (p-value<0.05) [16]. Similarly, Joshi SH et al., in a cross-sectional observational study, observed that lipid levels were notably elevated in low-birth-weight, preterm and SGA newborns. They recommended regular monitoring of lipid-related disorders and co-morbidities in these groups [21]. Studies by Mandraha S et al., and Lobo LL et al., also found that SGA neonates had higher lipid profiles than AGA newborns, underscoring the importance of monitoring cardiovascular risk factors during infancy, adolescence and early adulthood [22,23].

The results of present study are consistent with previous studies conducted in India and other countries [15,19]. A comparison between groups showed that SGA babies had significantly higher levels of TC, TGs and LDL cholesterol than AGA newborns. Additionally, bivariate analysis (Pearson correlation) revealed that TC, HDL, and LDL were significantly negatively correlated with gestational age and birth weight, while TGs and VLDL were negatively but insignificantly associated.

### Limitation(s)

Present study had several limitations. Firstly, the findings did not allow for a clear distinction between SGA and IUGR, which may have impacted the interpretation of results. Secondly, the limited sample size might have affected the statistical power and generalisability of present study findings, while potential selection bias in choosing cases and controls could have skewed the results. Additionally, differences in maternal factors, including diet, health conditions and lifestyle, may have influenced the relationship between lipid profiles and birth weight, introducing potential confounding factors. Lastly, the study may not have accounted for all possible confounding variables, such as genetic influences or intrauterine growth conditions, which could have affected the observed associations.

## CONCLUSION(S)

The study found that term SGA neonates had significantly higher levels of cord blood TGs, TC, LDL cholesterol and VLDL compared to term AGA neonates. Although HDL levels were higher in SGA neonates, the difference was not statistically significant. Additionally, TC, HDL, and LDL levels showed a significant negative correlation with gestational age and birth weight, indicating that as gestational age and weight increase, these lipid levels tend to decrease. In contrast, TGs and VLDL levels had weak and insignificant correlations with these variables.

These findings suggest that SGA neonates have an altered lipid profile compared to AGA neonates, which could be indicative of a higher risk for future cardiovascular issues. Given the significant differences observed, it is important to monitor SGA neonates for lipid abnormalities and cardiovascular risks throughout their development. Further research may be needed to explore the implications of elevated HDL levels and to validate these findings in diverse populations.

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**PARTICULARS OF CONTRIBUTORS:**
1. Junior Resident, Department of Paediatrics, Career Institute of Medical Sciences and Hospital, Lucknow, Uttar Pradesh, India.
2. Assistant Professor, Department of Paediatrics, Career Institute of Medical Sciences and Hospital, Lucknow, Uttar Pradesh, India.
3. Professor, Department of Paediatrics, Career Institute of Medical Sciences and Hospital, Lucknow, Uttar Pradesh, India.
4. Professor, Department of Paediatrics, Career Institute of Medical Sciences and Hospital, Lucknow, Uttar Pradesh, India.
5. Assistant Professor, Department of Paediatrics, Career Institute of Medical Sciences and Hospital, Lucknow, Uttar Pradesh, India.
6. Senior Resident, Department of Paediatrics, Career Institute of Medical Sciences and Hospital, Lucknow, Uttar Pradesh, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Saman Beg,
Flat No. 302, Tower No. 8, Bloomberg Tower, Omaxe Heights, Vibhuti Khand,
Gomti Nagar, Lucknow, Uttar Pradesh, India.
E-mail: samanbeg.alig@gmail.com

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