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**Original Research Article**

# Study of cord blood lipid profile of term (appropriate and small for gestational age) and preterm (appropriate and small for gestational age) newborns with special reference to atherogenic index: a cross-sectional study

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## ABSTRACT

**Background:** Atherosclerotic cardiovascular diseases is a major cause for morbidity and mortality in adult population. Increasing awareness about the origin of the atherosclerosis in early life has renewed interest in determination of various lipid fractions in paediatric age group. Therefore, the present study was planned to estimate the lipid levels in Term (Appropriate and small for Date) and Preterm (Appropriate and Small for Date) newborn as well to plan meticulous follow-up of babies with a deranged profile. Aim was to study cord blood lipid profile of term and preterm (appropriate and small for date) newborns with special reference to atherogenic index.
**Methods:** This cross-sectional study was conducted at neonatal section of department of paediatrics in collaboration with department of obstetrics and gynaecology and Rajiv Gandhi centre for diabetes and endocrinology Jawaharlal Nehru medical college, Aligarh Muslim University. A total of 200 newborns were enrolled in the study. Cord blood samples were collected from placental side at birth and analysed for lipid profile which includes total cholesterol, triglycerides, low density and high-density lipoprotein and atherogenic index.
**Results:** All the lipid parameters were higher among the low-birth weight babies when compared with the normal birth-weight babies, the difference was statistically significant for total cholesterol, triglyceride, HDL and VLDL cholesterol.
**Conclusion**s: Prematurity is a factor associated with a more Atherogenic lipid profile is reaffirmed and SGA as an additional risk factor has been proven giving scope for future research and primordial prevention.

**Keywords**: Apolipoprotein B, Atherogenic Index, HDL, LDL, VLDL

## INTRODUCTION

Coronary artery disease is a leading cause of significant morbidity and mortality around the globe. There is mounting evidence regarding the role of adverse prenatal and early postnatal environment as a determinant of deranged physiological and metabolic milieu in the fetus as well as the newborn. The resulting adaptations predispose such babies to later cardiac disease. The prevalence of coronary artery disease related burden is especially prominent in the developing countries.[1]

The lipid profile of an individual provides vital information about their cardiovascular health. Hyperlipidemia detected at any age is a well-known cardiovascular disease risk factor. There is a considerable independent relationship between blood lipid levels in childhood and later adulthood. Beginning early in

childhood, the derangements if present, continue to advance with the growing years if corrective steps are not taken.[2]

Young age can be viewed as a period for initiating preventative actions to lower the future risk for cardiovascular disorders. The other long-term consequences of these metabolic alterations increase the risk of other metabolic diseases like hypertension and type 2 diabetes. The estimation of lipid levels includes measuring cholesterol, its by-products as well as numerous other atherogenic indicators. The unhealthy lipid levels in the cord blood are an indicator of deranged lipid metabolism and altered placental function during pregnancy. The functions of foetal-placental unit are negatively impacted by a variety of maternal and foetal high-risk factors. Pregnancy-induced hypertension, chronic maternal diseases like diabetes mellitus and hypertension, ante-partum haemorrhage, prolonged labour, premature rupture of membranes, foetal distress, low Apgar score, low birth weight and prematurity are some of the well-known and documented maternal and foetal risk factors.[3]

### *Gaps in knowledge and need for this study*

Despite the fact that blood cholesterol levels and lipid profiles have been widely researched in adults, there hasn't been much research done on children, particularly in our country. Data on the blood lipid levels of term (AGA and SGA) and preterm (AGA and SGA) infants are limited. The current study, a hospital-based cross-sectional study conducted from November 2020 to October 2022 done in the Neonatal Section of the Department of Paediatrics in collaboration with Department of Obstetrics and Gynaecology and Rajiv Gandhi Centre for Endocrinology at JN Medical College, AMU, Aligarh. The goal of the study in newborns was to identify any abnormalities in the lipid profile as soon as possible (at delivery), particularly in Preterm and SGA infants, so that these at-risk infants may be closely watched in the future.

## METHODS

This hospital based cross-sectional study was carried out at JNMCH, AMU, Aligarh from November 2020 to October 2022 in the Neonatal Section of Department of Paediatrics in collaboration with Department of Obstetrics and Gynaecology and Rajiv Gandhi Centre for Diabetes and Endocrinology, JNMC, AMU, Aligarh. New born babies delivered at JNMC during this period who fulfilled the inclusion criteria were enrolled in this study. All the subjects were included after obtaining written informed consent from parents.

### *Inclusion criteria*

All Term and Preterm neonates delivered in JNMC, AMU, Aligarh, one minute APGAR score more than 7 were included.

### *Exclusion criteria*

Newborns with any significant and apparent congenital defect, neonates born to mothers with a history of thyroid disease, pregnancy-induced hypertension, diabetes mellitus, IDDM, tuberculosis, and asthma, newborns with a family history of hypercholesterolemia or coronary heart disease and drug abuse in mother except regular supplements

Informed parental consent was obtained from the parents of the babies enrolled in the study. Relevant personal, clinical and socio-demographic data of the mothers were collected and entered in the predesigned proforma. The baseline neonatal details were entered in the proforma. 5 ml of cord blood was collected from the umbilical cord at the time of delivery from the placental site and placed in a plain vial. After allowing the cord blood to coagulate, the samples were centrifuged at 400 times for 10 minutes in the Rajiv Gandhi centre for endocrinology's lab in order to extract the serum, which was then kept at -20 degrees Celsius until analysis. Following delivery, the infants underwent a physical examination, and conventional techniques were used to measure their length, head circumference, chest circumference, and other pertinent anthropometric measurements. The first day of the most recent period was used to determine gestational age, which was then verified through clinical evaluation using a modified version of New Ballard's Scoring.

### *Sample size*

Sample size was sample of convenience. A total of consecutive 200 babies were included in the study, of which 116 were term and 80 were preterm. Of them, 108 were AGA and 87 were SGA. The study group consisted of preterm and SGA infants, while the control group included term and AGA infants.

### *Statistical analysis*

For continuous variables, results were presented as Mean±SD, and for categorical data, they were presented as a number and a percentage. Since it is known that the data are normally distributed, statistical analysis was done using parametric tests. The Student's t test was used to examine the differences between newborns that were SGA, AGA and preterm or term. To investigate the relationship between two categorical parameters, the chi-square test was used. The 5% threshold of significance was considered for all significance tests.

## RESULTS

During the study period of 2 years from November 2020 to October 2022. A total of 200 new-borns were included in the study out of which (69%) were born to primi gravida mothers. In our study the mean gestational age of the mother was 36.7 weeks±2.5 and ranged between 30 and 42

weeks with normal distribution of gestational age. The included babies were 116 term and 80 preterm.

**Table 1: Gestation-wise distribution of study population.**

| GA | N | % |
|---|---|---|
| **Term** | 116 | 58 |
| **Preterm** | 80 | 40 |
| **Post Term** | 04 | 2 |
| **Total** | 200 | 100 |

**Table 2: Distribution of babies according to birth weight.**

| Birth weight | N | % |
|---|---|---|
| **Low** | 122 | 61 |
| **Normal** | 78 | 39 |

The mean birth weight of the pre-term children was 1.74 kg ±0.4 and the mean birth weight of the term babies was 2.54 Kg±0.48. Normal birth weight group had a mean total cholesterol of 91.8±29.8 whereas low birth weight group had a mean total cholesterol of 100.4±27.0.

**Table 3: Comparison of lipid profile based on birth weight (n=200).**

| Parameter | Birth weight category | | Mean difference | P value |
|---|---|---|---|---|
| | Normal BW Mean±SD | Low BW Mean±SD | | |
| **Total cholesterol (mg/dl)** | 91.8±29.8 | 100.4±27.0 | 8.6 | <0.03 |
| **Triglycerides (mg/dl)** | 67.7±23.7 | 79.8±22.7 | 12.1 | <0.001 |
| **HDL cholesterol (mg/dl)** | 36.4±11.0 | 31.8±9.2 | 4.6 | 0.002 |
| **LDL cholesterol (mg/dl)** | 48.5±23.7 | 50.4±16.5 | 1.9 | <0.5 |
| **VLDL cholesterol (mg/dl)** | 13.7±5.0 | 16.1±4.6 | 2.4 | <0.001 |
| **Atherogenic Index** | 2.6±1.0 | 3.4±1.5 | 0.8 | <0.001 |

**Table 4: Comparison of cord lipid profile based on gestational age (n=196).**

| Parameter | Gestational age | | Mean difference | P value |
|---|---|---|---|---|
| | Pre-term Mean±SD | Term Mean±SD | | |
| **Total cholesterol (mg/dl)** | 101.3±28.2 | 94.2±28.2 | 7.1 | 0.09 |
| **Triglycerides (mg/dl)** | 76.5±24.1 | 74.1±23.7 | 2.4 | 0.48 |
| **HDL cholesterol (mg/dl)** | 33.9±11.2 | 33.4±9.4 | 0.5 | 0.73 |
| **LDL cholesterol (mg/dl)** | 52.1±19.7 | 48.0±19.5 | 4.1 | 0.15 |
| **VLDL cholesterol (mg/dl)** | 15.5±5.0 | 15.0±4.9 | 0.5 | 0.44 |
| **Atherogenic Index** | 3.0±1.5 | 3.3±1.3 | 0.3 | 0.12 |

The mean difference between the two groups was statistically significant (p value 0.03). With a statistically significant p value of 0.001, the mean triglycerides of the group with normal birth weight was 67.7±23.7 and those of the group with low birth weight was 79.8±22.7. With a statistically significant p value, the mean HDL cholesterol of the normal birth weight group was 36.4±11.0 and that of the low birth weight group was 31.8±9.2. The mean Total Cholesterol was 101.3±28.2 which was higher among preterm babies however there was no statistically significant difference between them. The mean Triglycerides, HDL cholesterol, LDL Cholesterol and VLDL Cholesterol was also higher among preterm babies, however there was no statistically significant difference. Among the term babies we analysed the difference in lipid parameters between AGA and SGA babies. All the lipids were high among the AGA babies, except for the VLDL cholesterol which was significantly high among the SGA babies.

## DISCUSSION

The present study was done to study cord blood lipid profile in Healthy newborns with an objective to estimate and compare cord lipid profile (Total Cholesterol, Triglyceride, High density lipoprotein, Low density lipoprotein, Very low density lipoprotein) and Atherogenic index in Term and Preterm AGA and SGA neonates. The mean values of various lipids include Total cholesterol (mg/dl 90.0±29.0, Triglycerides (mg/dl) 72. 9±22.6, HDL cholesterol (mg/dl)-30.9±9.0, LDL cholesterol (mg/dl) 43.8±18.3, and VLDL cholesterol (mg/dl) 14.7±4.6. These are similar with various studies done earlier in which a study Pardo et al in 2005 on Brazilian neonates obtained a TC of 70.42±1.63 mg/dl. A

study done by Molina et al in 2000 from Spain found TG of 36±19 mg/dl in normal neonates and in Iran Kelishadi et al 2007 found TG of 69.4±11.9 mg/dl.[4-6] The mean of all the lipids were higher among the low-birth weight babies when compared with the normal birth-weight babies. The mean difference was statistically significant for total cholesterol, triglyceride, HDL cholesterol, and VLDL cholesterol which was similar to a study by Agrawal et al in 2017, where the mean values of serum triglyceride (141.56±69.67 mg/dl vs. 113.67±33.38 mg/dl; p <0.006; 95% CI = 8.31 to 47.46) and serum apo-B/apo-A-1 ratio (0.67±0.28 vs. 0.55±0.20; p < 0.007; 95% CI = 0.033 to 0.206) were significantly high and that of serum high density cholesterol (35.84±10.42 mg/dl vs. 40.73±11.70 mg/dl; p < 0.014; 95% 9 CI = -8.79 to -0.98) and Apo-A1 [87.59±12.44 mg/dl vs. 101.87±35.07 mg/dl; p=0.002; 95% CI=-23.39 to -5.16) were significantly low in SGA newborns.[7] Though all the lipid parameters including total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride and VLDL cholesterol was higher among the pre-term babies, the difference was not statistically significant but in a study by Ghaemi et al in 2014, significant differences existed between cord blood concentrations of triglycerides, total cholesterol, and LDL-C in the term, late preterm and preterm infants (p<0.05).[8] The highest (61.69 mg/dl) and lowest (47.03 mg/dl) concentrations of triglycerides were documented in term and preterm newborns, respectively. Late preterm infants had the highest concentration of cord blood cholesterol. The lowest amount of cholesterol was found in term newborns (72.51 mg/dl). When the distribution is considered according to the size of the newborns, there was a significant difference in all the lipids (p<0.05), except for total cholesterol. While total cholesterol, triglycerides, and VLDL cholesterol was high among the SGA babies, HDL cholesterol was high among the AGA babies and LDL cholesterol was high among the LGA babies. Similar results were obtained in studies by Agrawal et al and Molina et al where total cholesterol, triglycerides, and VLDL cholesterol was high among the SGA babies, HDL cholesterol was high among the AGA babies.[9] Among the term babies we analysed the difference in lipid parameters between AGA and SGA babies. All the lipids were high among the AGA babies, except for the VLDL cholesterol which was significantly high among the SGA babies. Among AGA babies, total cholesterol, triglycerides, HDL cholesterol, and AI was significantly higher which was similar to a study by Ramaraj et al where in AGA neonates, mean TC (total cholesterol), LDL (low density lipoprotein cholesterol), HDL (high density lipoprotein cholesterol) and triglycerides were $103.92 \pm 47.79$, $51.70 \pm 23.03$, 23.35±11.41 and 187.62±144.44 mg/dl respectively.[10] AGA neonates had more TC and LDL than SGA neonates (p<0.05). The mean atherogenic index of the subjects was 2.1 (SD: 1.3) and the median was 2.8. The range of AI was 1.21 to 8.89. The atherogenic index is distributed normally in the subjects. The atherogenic index was high among the low-birth weight babies (p<0.05) compared to normal birth weight babies. Though male babies and term babies had higher AI, the difference was not statistically significant. Similar results were obtained in a study by Katragadda et al in 2017, where preterm Small for Gestational Age (SGA) neonates had statistically significant higher values of triglycerides, Apo B and atherogenic index compared to preterm Appropriate for Gestational Age (AGA) neonates.[11] Lipid profile is a marker of an underlying cardiovascular status, and direct correlation exists between the abnormalities in lipid profile and incidence of many chronic diseases. Among various factors theorized in the development of atherosclerosis, increased plasma levels of cholesterol and or triglycerides are considered to be of most important factors. Atherosclerosis begins early in life, and the studies conducted on cord blood lipid profile had inconsistent findings.[12] Primarily, the incidence of the cardiovascular disease depends on the prevalence of the un-modifiable and modifiable risk factors. Obesity, metabolic syndrome, insulin resistance, diabetes mellitus are its well-known secondary factors. However, the much-discussed recent concept of Barker's fetal programming hypothesis has totally revived the understanding of triggering events of these diseases which states that adverse nutrition in early life has increased susceptibility to the metabolic syndrome.[13]

### *Limitations*

The study focused on a limited number of subjects for a limited period of time and the main limitation of our study is its cross-sectional nature. Future longitudinal studies with long-term follow-up are necessary to verify the clinical implications of the current findings.

## CONCLUSION

Lipid profile was analysed based on total cholesterol, serum triglyceride, HDL cholesterol, LDL cholesterol, VLDL cholesterol and atherogenic index which is ratio of Apo lipoprotein A and B. The mean of all the lipids (total cholesterol, triglyceride, HDL cholesterol, and VLDL cholesterol) were significantly higher among the low-birth weight babies when compared with the normal birth-weight babies which implies LBW babies are more prone to atherogenesis related complications and hence the need for follow-up. The lipid profile of both males and females were similar. For total cholesterol, HDL cholesterol, and LDL cholesterol, males had higher values and triglyceride and VLDL cholesterol was higher among females but both were statistically not significant which implies no significant change is observed between the two genders. Though all the lipid parameters including total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride and VLDL cholesterol was higher among the pre-term babies, which implies preterm babies are more prone to atherogenesis related complications and hence the need for follow-up.

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