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Original Research Article

A comparative study of cord blood lipid profile in term, pre term and small for gestational age, appropriate for gestational age neonates

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ABSTRACT

Background: Cord blood lipid profile in neonates helps to screen for neonatal dyslipidaemia which is associated with long term morbidity mainly cardiovascular disease.
Methods: The present study is a observational study done in government medical college, Chidambaram for a period of 2 years from October-2020 till September-2022 with 222 term and pre-term small or appropriate for gestational age (AGA) neonates using cord blood lipid profile.
Results: In the present study of above mentioned 222 neonates, preterm accounts for 30.1% and term neonates accounts for 69.9%. AGA was 63.1% and SGA was 36.9%. Term AGA was 38.2%, term SGA 31.5%, preterm AGA was 24%, preterm SGA was 5.4%.
Conclusions: Preterm AGA had higher cord lipid profile values compared to the term AGA neonates. Preterm SGA neonates had lower cord lipid profile of HDL, and LDL as compared to preterm AGA neonates. SGA neonates had higher total cholesterol, triglycerides and VLDL compared to AGA neonates. SGA neonates had lower LDL and HDL as compared to AGA neonates.

Keywords: Cord blood lipid profile, Preterm, Term, AGA, Small for gestational age

INTRODUCTION

The increasing morbidity and mortality due to coronary heart diseases among male and female in early middle age is a major cause for concern in most industrialized countries. Coronary heart diseases appear as a significant cause of death after 40 years of age. The incidence of coronary artery disease depends on the prevalence of genetic and environmental risk factors.

There is a concept known as "fetal origin of cardiovascular disease hypothesis" which suggests that an adverse intrauterine environment during a critical period of development could program or imprint the development of fetal tissues and organs, and permanently determine responses that produce later dysfunction and disease. Thus, the arterial hypertension of adults, dyslipidaemia, type 2 diabetes, for all these, diseases process start during fetal life and are associated with fetal growth restriction and low birth weight.[1]

Lipid profile is a marker of an underlying cardiovascular status. Lipid profile includes measurement of cholesterol and its derivatives and various atherogenic indices. Studies have shown that SGA babies had abnormal lipid profile compared to AGA babies.

There are many studies showing the direct relationship between the abnormalities in lipid profile among the SGA babies and occurrence of cardiovascular diseases. The present study was undertaken for early detection of abnormalities in the lipid profile at the earliest (at birth), especially in preterm and SGA babies, so that these high-risk babies can be under vigilant monitoring in future.

Early diagnosis followed by prudent dietary supplementation and drug therapy in these high risk neonates may provide an opportunity for long range primary melioration of risk factors that contribute to development of cardio vascular diseases in adult life.

METHODS

Study type

Hospital based prospective observational study type was used.

Study place

Study carried out at Cuddalore government medical college, Chidambaram.

Study period

Study conducted for two years from October 2020 to September 2022

Study population

All neonates who are delivered in Cuddalore government medical college, except post term and large for gestational age neonates

Inclusion criteria

Term and preterm who are small or AGA neonates who are delivered in government medical college, Chidambaram were included

Exclusion criteria

Neonates with any Congenital malformations, large gestational age and post term neonates were excluded from the study.

The subjects are included after obtaining written informed consent from parents/ guardian.

Babies are classified as AGA and SGA with the help of fenton growth chart.

Any baby whose weight less than the 10^{th} percentile for the respective age is classified as SGA and neonates who between 10^{th} and 90^{th} percentiles are classified as AGA.

five ml of cord blood should be collected from the umbilical cord immediately after the delivery in a plain dry test tube. Cord blood is allowed to clot and then immediately send to lab where the samples are centrifuged at 400×for 10 minutes, and then serum is separated and stored at -20°C until analysis.

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After the delivery, the babies were examined, weight was recorded on electronic weighing scale, length was recorded with the help of infantometer, head circumference, chest circumference and other relevant anthropometric data were recorded using non stretchable measuring tape. Gestational age was calculated from the first day of the last menstrual period and confirmed by clinical assessment using modified New Ballard's score.

A thorough clinical examination of the newborn was done and weight of the baby was calculated by electronic weighing scale. Classification of infants was done based on gestational age as term and preterm newborn based on New Ballard's scoring.

Babies were classified as AGA and SGA with the help of intrauterine growth charts and Ponderal index. Intrauterine growth charts developed at AIIMS were used to assess the weight for gestational age. Any baby whose weight was less than the 10^{th} percentile for the respective age was classified as SGA and neonates who were between 10th and 90th percentiles were classified as AGA Ponderal index was computed as, PI=Weight (GM)/Length (CM)3 × 100. Ponderal index of <2.0 between 29 and 37 weeks of gestation and <2.2 beyond 37 weeks of gestation was taken as a cut off value to classify SGA babies.

Lipid profile was done by using Auto analyser (Erba Mannheim, Transasia bio-medical LTD). TC estimated by using Modified Roeschlau method, TG estimated by using Wako and the modification by McGowan et al and Fossati et al HDL and LDL estimated based on a modified polyvinyl sulfonic acid (PSV) and polyethylene- glycol methyl ether (PEGME) coupled classic precipitation method with the improvements in using optimized quantities of PSV/PEGME and selected detergents. VLDL estimated by TC/5 and Atherogenic index (AI) by TC/HDL.

Statistical analysis

Results were expressed as mean ± standard deviation for continuous variables and as number and proportion (%) for categorical data. Since all data are known to be normally distributed, the parametric tests were used for statistical analyses.

Differences between SGA, AGA neonates and preterm, term neonates as well as between male and female neonates were determined by student's t test. Chi-square

test was applied to test the association between two categorical factors. All the tests of significance were applied at 5% level of significance.

Statistical software: The package EPI-INFO version 3.5.3 was used for the analysis of the data and Microsoft excel was used for data entry as well as to generate graphs, tables etc.

RESULTS

The study was conducted over a period of 3 years from 2020 to 2023, involving 222 neonates, comprising 155 term, 67 preterm, and 6 post-term neonates in NICU of department of paediatrics, Government medical college, Chidambaram.

Gestational age distribution

In the total 222 neonates included in the study, 67 were preterm neonates and 165 were term neonates.

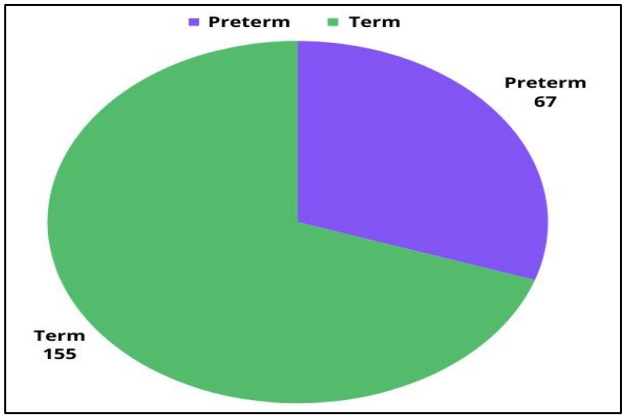

Figure 1: Gestational age distribution.

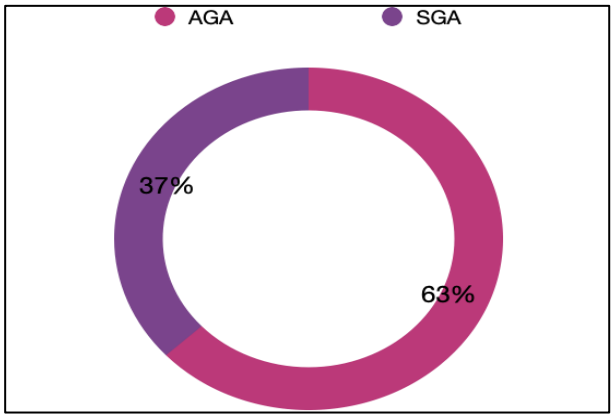

Figure 2: Birth weight distribution

Birth weight distribution

In the study population, 37 percent were AGA neonatal babies and 63 percent were small for gestational age (SGA) neonatal babies.

Gender distribution

There are 43 percent males and 57 percent females were included in the study.

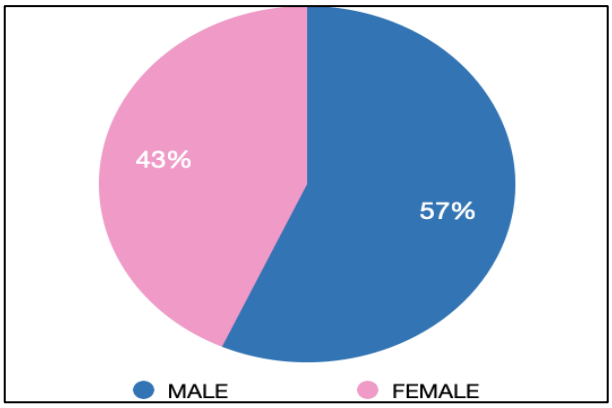

Figure 3: Gender distribution.

Gestational age and birth weight distribution

In the study, 38.2 percent were Term AGA, 31.5 percent were term SGA, 24% percent were pre term AGA and 5.4 percent Pre term SGA

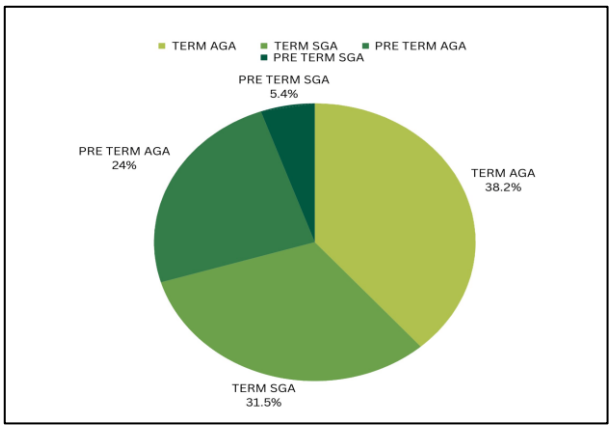

Figure 4: Gestational age and birth weight distribution.

Table 1: Gestational age distribution according to weeks.

GA (in weeks)	Term	Percent (%)	Pre-term	Percent (%)
<34	0	0	34	15.3
34-37	0	0	33	14.8
37-42	155	69.8	0	0

Term neonates with gestational age more than 37 weeks were around 69.8 percent and pre term neonates with 34-37 weeks gestational age were around 14.8 percent and Pre term neonates with gestational age less than 34 weeks were around 15.3 percent.

Table 2: Comparison of mean values and standard deviation of cord lipid profile among term AGA and preterm AGA neonates.

Lipid profile	TC	TG	HDL	LDL	VLDL
Term AGA	71.70±21.25	66.28±19.95	27.95±5.34	34.26±16.05	13.24±03.98
PT AGA	105.82±27.21	77.50±24.69	41.32±9.49	60.10±24.01	15.50±04.53
P value	<0.001	<0.05	<0.001	<0.001	<0.01

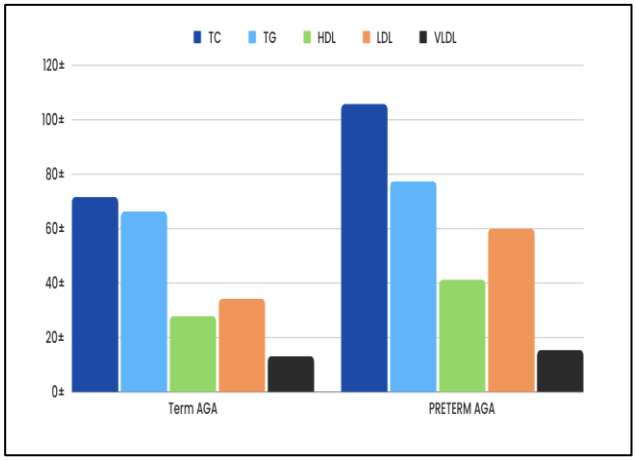

Figure 5: Cord lipid profile among term AGA and preterm AGA neonates.

P values were less than 0.001 for the TC, HDL and LDL group and p values were less than 0.01 for the VLDL group and p values were less than 0.05 for the TG group (Table 2).

P values were more than 0.05 in all groups including TC, HDL and LDL group TG and VLDL group (Table 3).

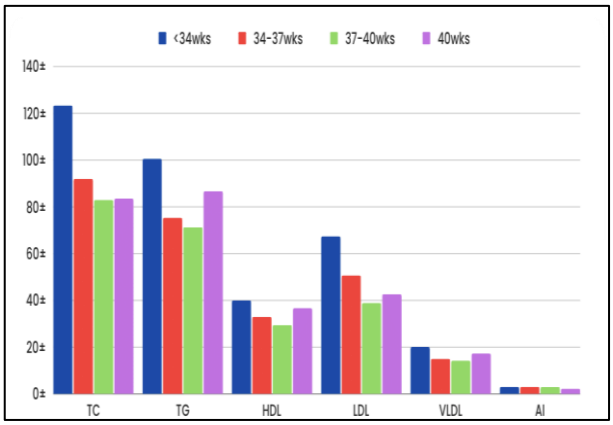

Figure 6: Cord lipid profile according to gain in weeks.

P values were less than 0.001 and statistically significant in all groups (Table 4).

Table 3: Comparison of mean values and standard deviation of cord lipid profile among term SGA and preterm SGA neonates.

Lipid profile	TC	TG	HDL	LDL	VLDL
Term SGA	101.11±27.03	81.95±22.70	29.02±07.90	45.64±08.48	16.39±04.54
PT SGA	92.00±24.40	84.00±17.81	27.80±07.39	48.45±21.26	16.80±03.56
P Value	0.1176	0.6545	0.4763	0.4456	0.6545

Table 4: Comparison of mean values and standard deviation of cord lipid profile according to gain in weeks.

Lipid profile	Gestational age (in weeks)				P value
	<34	**34-37**	**37-40**	**40**	
TC	123.41±25.15	92.03±23.03	82.97±27.18	83.50±09.57	<0.001
TG	100.58±14.86	75.39±20.07	71.27±22.17	86.75±14.03	<0.001
HDL	40.11±05.66	33.06±11.44	29.50±06.35	36.75±05.85	<0.001
LDL	67.52±25.99	50.69±29.33	38.91±50.02	42.75±05.82	<0.001
VLDL	20.11±02.97	15.07±04.01	14.27±04.43	17.35±02.80	<0.001
AI	3.11±0.71	3.07±1.15	3.04±1.29	2.29±0.18	0.643

DISCUSSION

The aim of this study was to investigate variations in cord blood lipid profiles between preterm and term neonates, as well as SGA and AGA neonates. Following written informed consent, relevant maternal data was collected. Cord blood was obtained immediately after delivery, allowed to clot for serum separation, and sent to lab for analysis. Neonates were categorized as term or preterm using the new Ballard score, and as SGA/AGA using AIIMS intrauterine growth charts, with further classification into symmetrical/asymmetrical intrauterine growth restriction (IUGR) based on the Ponderal index.

This hospital-based case-control study spanned from 2020 to 2023, involving 222 neonates, comprising 155

term, 67 preterm, and 6 post-term neonates. Out of these, 140 were AGA, and 82 were SGA. Males constituted the majority of neonates (51.5%), with a higher proportion of female term neonates (60.8%) and male preterm neonates (44.7%). AGA neonates had more males (60.2%), while SGA neonates had more females (48.5%), with no statistically significant gender differences among groups.

Birth weight was significantly lower in SGA babies (1.81±0.34) compared to AGA babies (2.82±0.25) ($p<0.05$). Other neonatal variables like length and head circumference were similar between the two groups.

Cord lipid profile values were higher in preterm neonates compared to term neonates. SGA neonates also exhibited higher cord lipid profile values compared to AGA neonates, except for HDL (32.77±09.57), which was lower in SGA neonates. Ponderal index showed a significant correlation with cord blood lipid profile ($p<0.05$), with asymmetrical IUGR neonates having higher levels of TG (86.70±17.72) and VLDL (17.34±3.54).

Cord lipid profiles in preterm neonates were as follows: TG (80.75±12.84), TC (98.91±26.60), HDL (34.56±05.35), LDL (53.77±25.25), VLDL (16.15±04.30). Term neonates exhibited the following values: TC (82.63±27.16), TG (71.21±22.35), HDL (28.36±06.29), LDL (39.85±14.10), VLDL (14.43±04.47). The differences were statistically significant ($P<0.01$). Cord lipid profiles in AGA neonates were: TC (86.08±25.49), TG (82.96±19.82), HDL (28.98±07.76), LDL (40.75±15.66), VLDL (16.15±04.30). SGA neonates exhibited the following values: TC (83.99±28.64), TG (70.32±22.33), HDL (32.77±09.57), LDL (48.57±22.88), VLDL (14.43±04.47). The differences were statistically significant ($p<0.05$), except for HDL ($p<0.05$), which was lower in SGA neonates.

Asymmetrical IUGR cord lipid profile values were: TC (93.55±22.45), TG (86.70±17.72), LDL (47.23±17.49), HDL (28.89±7.51), VLDL (17.34±3.54). Symmetrical IUGR cord lipid profile values were: TC (103.92±32.65), TG (71.38±21.86), LDL (45.28±7.72), HDL (29.28±8.68), VLDL (14.39±4.39).

Asymmetrical IUGR neonates showed a significant correlation with higher TG and VLDL values ($p<0.05$) than symmetrical IUGR neonates.

Kelishadi et al and Pardo et al in their study concluded similar result in terms of decrease of cord blood HDL levels which was also found in the present study.[4,5] Daniel et al, Wang et al and Hossain et al in their studies had similar results.[7-9]

In the present study cord blood lipid profile values in SGA were elevated when compared to AGA, the reason is that, there is lack of glucose as fuel in SGA babies, so these babies use alternative source as a fuel (amino acid and lipids) and generate glucose (gluconeogenesis), where by activating lipid and other metabolism, so there will be increased hepatic generation of lipids (particularly VLDL and chylomicrons) also, there is decreased peripheral utilization of lipids because of decreased activity of lipoprotein lipase enzyme in growth restricted babies, these two facts explain higher concentration of plasma lipids in SGA babies.[5,8]

Barker hypothesis demonstrated that low birth weight correlated with an increased prevalence of cardiovascular disease, hypertension and type 2 diabetes mellitus and suggested that this association reflects the phenomenon known as programming, whereby a stimulation or insult during a critical period of intrauterine life could also result in alterations of physiology and metabolism during adult life.[11,12]

In the present study term SGA had higher cord blood lipid profile values compared to the term AGA. Oba et al in their study they concluded that preterm SGA had higher values of TC, TG, LDL, HDL compared to preterm AGA which was statistically significant with $p<0.0001$, <0.01, <0.0001, <0.0001 respectively and term SGA had higher values of TC, TG, LDL, HDL compared to term AGA which was statistically significant with $p<0.0001$, <0.01, <0.0001, <0.0001 respectively.[10]

In the present study the average birth weight of SGA was1.77±0.35, and it was statistically significant with $p<0.001$. Similarly Study conducted by Pardo et al and Jones et al found the birth weight to be 2.04±0.76 and 2.07±0.53 respectively, which was also statistically significant with a p value of $p<0.01$.[5,6] But in studies done by Kelishadi et al and Wang et al mean birth weight was 2.34 and 2.22±0.55 respectively which was higher when compared to present study because they have used only term SGA babies as cases where as in present study and Pardo et al study both term and preterm SGA were included in the study group.[4,5,8]

In the present study average Ponderal index was 1.83±0.23 which was statistically significant with a $p<0.001$ and in study by Kelishadi et al.[4] It was 2.18, and it was not significant statistically.

In the present study gestational age was found out to be 36.78±2.09 weeks, which was similar to the study by Pardo et al with a gestational age of 35.57±0.11 weeks, as both studies have included both term and preterm SGA neonates in the study group.[5] Other studies like Kelishadi et al and Wang et al had higher gestational age as they had included only term SGA neonates in study group.[4,8]

In the present study preterm had significantly higher values of TC, TG, HDL, LDL, VLDL ($p<0.001$, <0.01, <0.001, <0.001, <0.01 respectively) compared to term neonates. AI values were more in preterm compared to term which was not statistically significant.

Haridas et al in their study concluded that preterm neonates have higher TG and TC levels but statistically significant difference was found only in TC ($p<0.001$) levels.[15]

Mathur et al in their study concluded that in preterm TC value was significantly high ($p<0.001$).[16]

Oba et al in their study concluded that TC, LDL, HDL values were significantly higher in preterm neonates ($p<0.0001$), TG value was significantly lower in preterm neonates ($p<0.01$).[10]

Pardo et al in their study concluded that TC, LDL, HDL were higher in Preterm neonates compared to term neonates with statistically significant difference in TC and LDL ($p<0.001$) levels, but HDL had no statistically significant difference.[5] AI values were more in preterm compared to term which was not statistically significant.

Kalra et al in their study concluded that all cord lipid profile values were lower in preterm neonates compared to term neonates but statistically significant difference was found with TC levels ($p<0.001$) and no statistically significant difference was found with HDL and LDL levels.[13]

Singh et al in their study concluded that term neonates had higher TC compared to preterm neonates with statistically significant difference ($p<0.05$).[6]

Mishra et al in their study concluded that TG levels were more in term compared to term with no statistically significant difference.[14]

In our study higher cord lipid levels in preterm babies could be explained by the fact that preterm babies lack both hepatic carbohydrate and subcutaneous adipose stores, with a result that circulating fuel are low and may run out. Rise in cord blood cholesterol levels may reflect the metabolic adaptation to provide adequate energy, especially to organs like brain

Limitations

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. The various factors affecting neonatal birth weight like maternal nutrition, pre pregnancy weight, and weight gain during pregnancy were not considered in this study. Another major limitation of our study was its inability to determine the cut-off lipid levels for cardiovascular risk stratification. The study area may not be the complete representation of the entire population. Hence, further prospective, analytical studies must be conducted in the present and other settings, to study and confirm the predictors and outcomes found to be associated in our study. The study does not follow babies to assess the outcome of the risk factors in future. It is interesting to follow up and see whether these SGA babies with high lipids do develop cardiovascular diseases in adult life in future, also it is needed to study the relation of high maternal lipids and its implications in babies. Non-inclusion of the extremely preterm neonates due to natural factors during the period of study may have skewed the findings to more mature babies. Their inclusion would have given a broader representation of the study population. Exclusion of newborns with family history of hypercholesterolemia was largely dependent on access to past documented evidence which was lacking in most cases. Study could have helped to elucidate the outcome of the findings over time. The study of important lipid like Apoprotein A and B was hampered by facilities.

CONCLUSION

The study found that there was no significant difference in cord lipid profile between males and females in both term and preterm neonates. Preterm neonates had higher values of TC, TG, HDL, LDL, VLDL compared to term neonates, and values were statistically significant.

Cord blood lipid profile values for TG, TC, LDL and VLDL were significantly higher, and HDL were significantly lower in the SGA neonates compared to AGA neonates.

Term SGA had significantly higher cord blood lipid profile values compared to the Term AGA, except HDL levels. Preterm AGA had higher cord lipid profile values compared to the Term AGA neonates, and values were statistically significant. Preterm SGA neonates had lower cord lipid profile of TC, HDL, and LDL as compared to Preterm AGA, which were statistically significant. TG and VLDL were significantly higher in asymmetrical IUGR compared to symmetrical IUGR. AI was significantly higher in <1.5 kg, indicating an increased risk for atherosclerosis.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Kent L, Thomburg. Fetal Origins of Cardiovascular Disease. Am Academy Pediatr. 2004;5(12):527-34.
2. Verkauskiene R, Czernichow P, Claire LM. Long-term metabolic consequences of being born small for gestational age. Expert Rev Endocrinol Metabol. 2006;1(1):439-47.
3. Jones J N, Taylor Gercel, Taylor Doughlas D. Altered cord serum lipid levels associated with small for gestational age infants. J Am College Obstetr Gynaecol. 1999;93:527-31.
4. Kelishadi R, Badiee Z, Adeli K. Cord blood lipid profile and associated factors: bascline data of a birth

cohort study. Paediatric Perinatal Epidemiol. 2007;21:518-24.
5. Pardo IMCG, Geloneze B, Tambascia MA, Barros Filho AA. Atherogenic lipid profile of Brazilian near term newborns. Braz J Med Biolog Res. 2005;38(5):755-60.
6. Singh J, Purohit M, Singh P, Thappa DM. Cord Blood Cholesterol in Term and Preteterm Newborns. Indian Pediatr. 1994(31):1278-80.
7. Daniel ML, Walter JM. Factors affecting the lipid and Apolipoprotein levels of cord sera. Pediatr Res. 1983;17:83-91.
8. Averna MR, Barbagallo CM, Dipaola G, Labisi M, Pinna G, Marino G, et al. Total cholesterol IDL-Cholesterol and lipoprotein B in umbilical cord blood: cross sectional study. Minerva-Pediatr. 1992;44:395-9.
9. Hossain MA, Islam MN, Shahidullah M, Akhter H. Serum triglyceride level in IUGR babies and its comparison with preterm AGA and term normal babies. Mymensingh Med J. 2006;15(2):180-82.
10. Oba J, Sirlei Donega, Raul C, Maranhao Concentration of serum lipids and Apolipoprotein B in Newborn. Arquivos Brasileiros Cardiol. 2006;31(86):6.
11. Leon DA, Lithell HO, Vagero D, Koupilova I, Mohsen R, Berglund L, et al. Reduced fetal growth rate and increased risk of death from ischaemic heart disease: cohort study of 15000 Swedish men and women born 1915-29. Br Med J. 1998;317(7153):241-5.
12. Rich-Edwards JW, Stampfer MJ, Manson JE, Rosner B, Hankinson SE, Colditz GA, et al. Birth weight and risk of cardiovascular disease in a cohort of women followed up since 1976. Br Med J. 1997;315(3):96-400.
13. Kalra A, Kalra K, Agarwal MC, Prasad R, Pant MC Bhatia R, et al. Serum lipid profile in term and preterm infants in early neonatal period Indian Pediatr. 1988;2:977-81.
14. Mishra PK, Tiwari DK, Sharma B, Kaul R. Free fatty acids and Triglycerides in normoglycemic low birth weight newborns in Carly neonatal period. Indian J Pediatr. 1984;51(1):637-41.
15. Haridas N, Acharya PT. Serum Lipid Status in neonates. Indian Pediatr. 1984;21(4):327-34.
16. Mathur PP, Prasad R, Jain SK, Pandey DH, Singh SP. Cord blood Cholesterol in term and preterm newborns. Indian Pediatr 1986;23(2):103-6.

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