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Research Article

NEONATAL LIPID LEVELS – CAN THEY BE A BENCHMARK FOR LIPID LOWERING IN ADULTS?

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ABSTRACT

Background: Cord blood lipid estimation in healthy newborns is an opportunity to assess lipid profile parameters at the beginning of life and this might serve as a guide for determining the minimum levels of cholesterol and other lipoprotein required for maintaining normal bodily physiological functions. Various lipid parameters are targeted by interventions in adults in the management of atherosclerotic coronary artery diseases be it for primary prevention or secondary prevention. The guidelines recommend reduction of low-density lipoprotein cholesterol (LDL-C) to less than 70% mg in high risk group individuals. The impact of these low levels of lipids on physiological functions of tissues is a concern to be answered. Hence, it's hypothesized that probably the lipids at birth in healthy newborns are the bare minimum required to maintain the normal physiological bodily metabolism. Hence, this study was conceived.

Objectives: The present study is to determine the baseline lipid profile at birth in healthy newborns and indirectly to ascertain the minimum level to which lipids can be lowered in adults by therapeutic interventions. Further, we also explored the influence of maternal factors on cord blood lipid parameters.

Methods: The study group consisted of 100 term newborns and their mothers. Cord blood and fasting maternal serum samples were analyzed for lipid profile, blood sugar and the HbA1c estimation. Mean and standard deviations were calculated. Paired t test and ANOVA test of variance were applied to compare lipid profile parameters of mother with the cord blood.

Results: Lipid profile parameters were significantly low in cord blood. Mean LDL-C in cord blood was 36.63 mg/dl, mean triglycerides was 49.38 mg/dl, mean total cholesterol (TC) was 73.83 mg/dl, mean high-density lipoprotein cholesterol (HDL-C) was 21.13 mg/dl, mean LDL/HDL was 1.84 and mean TC/HDL-C was 3.74. Cord blood lipid parameters were significantly altered in mothers with dyslipidemia, diabetes and hypertension.

Conclusion: This study has revealed a LDL-C level of 36.63 mg% in healthy term newborns. Reducing LDL-C to <70 mg% may not interfere with physiological bodily metabolism in adults as hypothesized, but reducing it to a level <35 mg% may interfere with normal bodily metabolism.

Keywords: Neonatal lipids, Maternal lipids, Cord blood lipids, Lipid lowering therapy, Lipid and normal metabolism.

INTRODUCTION

Cholesterol is the essential structural component of mammalian cell membrane. It is required for maintaining cell membrane stability, intracellular signaling, nerve conduction and intracellular transport. It serves as a precursor for steroid hormones and vitamin D. However in excess, cholesterol is strongly associated with atherosclerosis and coronary heart disease.

Atherosclerotic cardiovascular disease (CVD) is a major cause for morbidity and mortality in the adult population. Altered lipid levels are the recognized factors [1]. This process is considered to begin in early life and progress silently over decades [2]. An increase in low-density lipoprotein cholesterol (LDL-C) and decrease in high-density lipoprotein cholesterol (HDL-C) levels are associated with the atherosclerotic process, with its prodromal stages starting in early life [3-5]. Hyperlipidemia is uncommon in pediatric age group, however there is evidence that children with cholesterol levels in upper quartiles are at increased risk for subsequent atherosclerosis [6-8]. Genetic and environmental influences might affect cord blood lipids, but the mechanism remains uncertain [9].

Cord blood would be a feasible and simple method for detecting cholesterol level at birth. This can be viewed as an opportunity to assess lipid profile parameters at beginning of life where there is no atherosclerosis and no risk for CVD. Neonatal lipids level could serve as a guide to know the physiological levels of lipids required for maintaining various normal bodily metabolisms. Various lipid parameters are targeted by interventions in adults in the management of atherosclerotic coronary artery diseases be it for primary prevention or secondary prevention. The guidelines recommend reduction of LDL-C to less than 130 mg% and further to 70 mg% in high risk group individuals. The impact of these low levels of lipids on physiological functions of tissues is a concern to be answered. Hence, it is hypothesized that probably the lipids at birth in healthy newborns are the bare minimum required to maintain the normal physiological bodily metabolism. Reduction of lipid parameters by therapeutic interventions to less than these levels may interfere with normal physiological metabolism. Hence, this study was conceived to know the lipid levels in healthy term newborns. Though there are many studies on cord blood lipids, they have looked from angles of atherogenic lipids and maternal factors influencing neonatal lipids. Indian literature on this subject is very limited.

In view of increasing evidence that cardiovascular risk may have prenatal antecedents, this would seem an important area for further investigation.

Objectives of the study

The present study is to determine the baseline lipid profile at birth in healthy newborns and indirectly to ascertain the minimum level to which lipids can be lowered in adults by therapeutic interventions. Further, we also explored the influence of maternal factors on cord blood lipid parameters.

MATERIALS AND METHODS

The study group included 100 full term newborns delivered at JSS Hospital, Mysore. The study was initiated after obtaining permission from the Institutional Ethics Committee, JSS Medical College, JSS University, Mysore.

Preterm babies born before 37 weeks of pregnancy and babies with congenital anomalies-detected by clinical examination and ultrasonography were excluded from the study.

A volume of 5 ml of fasting blood sample was drawn from cubital vein of the mother and 5 ml of cord blood was drawn from the umbilical cord immediately after a normal delivery and were allowed to clot for 45 minutes at room temperature. Serum was separated after centrifugation and was analyzed on the same day for estimation of lipid profile, blood sugar and HbA1c.

Statistical analysis

Obtained data were computed as mean and standard deviation. Paired t-test was used to compare lipid profile parameters in mother with cord blood. Mothers were grouped into two groups: Normal and abnormal based on their lipid characteristics. ANOVA test of variance was applied to compare lipid profile of mother with the cord blood $p<0.05$ were considered to be significant.

RESULTS

Of the 100 newborns, all were term babies. Males were 53, and females were 47. All mothers were in the age group of 18-26 years. No significant difference in lipid profile parameters was noted between male and female babies. The mean cord blood sugar level was 40.01±13.31 mg/dl (range 20-72 mg/dl). The mean cord blood total cholesterol (TC) level was 73.83±15.83 mg/dl (range 30-112 mg/dl). The mean cord blood HDL-C was 21.13±6.00 mg/dl (range 7-41 mg/dl). The mean cord blood LDL-C was 36.63±12.82 mg/dl (range 15-83 mg/dl). The mean cord blood triglycerides (TG) were 49.38±23.81 mg/dl (range 4-102 mg/dl).

ANOVA test of variance was used to compare mother's lipid profile with cord blood lipid (Fig. 1):

a) Comparison of LDL-C of mother and the cord blood (Fig. 1a): Cord blood LDL-C was significantly high in newborns of mothers with LDL≥100mg/dl (p=0.017).
b) Comparison of HDL-C of mother and cord blood (Fig. 1b): Cord blood HDL-C was significantly low in newborns of mothers with HDL-C<50 mg/dl (p=0.00).
c) Comparison of TG of mother and cord blood (Fig. 1c): Cord blood TG were significantly high in newborns of mothers with TG level 150 mg/dl (p=0.032).
d) Comparison of TC of mothers and cord blood (Fig. 1d): Cord blood TC was significantly high in newborns of mothers with high TC level.
e) Maternal diabetes: On comparing cord blood lipid profile among mothers with diabetes and non-diabetes, Cord blood LDL-C, TG and TC were significantly high among newborns of diabetics, while HDL-C was not significantly associated (Table 1).
f) Maternal hypertension: On comparing cord blood lipid profile among newborns of mothers with hypertension and non-hypertensives, cord blood LDL-C was significantly high among newborns of hypertensives, while TG, TC, and HDL-C were not significantly associated (Table 2).

DISCUSSION

Human body needs a considerable amount of cholesterol for maintenance of tissue and various bodily metabolisms.

Earlier evidence suggests that cord blood lipoprotein might be influenced by factors like placental insufficiency, mode of delivery and conditions affecting fetal growth [10,11]. In the present study, all cord blood samples were taken from normal healthy, uncomplicated, term vaginal delivery so that foregoing factors did not interfere with our results. Cord sera contain all well characterized adult lipoproteins and apolipoproteins [12]. Earlier data suggests that cord blood lipid profile parameters were significantly low when compared to maternal lipid profile or adult reference values [13-17] **(**Table 3).

Plasma depletion of cholesterol occurring at birth might be related to increased uptake of LDL-C by fetal adrenal gland for steroid hormone production [11]. After birth, human lipid transport system is transformed from the one containing a low LDL levels to adults system with a relative by high LDL level and this process continues to increase with age.

Our findings were in agreement with those reported earlier in the literature. The mean TC in our study was 73.83±15.83, mean LDL-C was 36.63±12.82, mean HDL-C was 21.13±6.00, and mean TG were 49.38±23.81 respectively. These values were significantly low when compared to adult reference ranges and when compared to maternal lipid profile **(**Fig. 2).

There is increasing evidence that levels of apolipoprotein B and apolipoprotein A-1 are better predictors of CVD. However, detection of these apolipoproteins are not a standard part of blood lipid estimation and adds to additional cost. Existing guidelines for CVD (ATP III) focus on plasma LDL as the primary target. Hence, we adhered to familiar and proven measurements of LDL/HDL ratio. LDL/HDL ratio reflects the two way traffic of cholesterol entering and leaving the arterial intima. The mean LDL/HDL ratio in cord blood was 1.84; this was significantly low when compared with mother and adult reference ranges.

Evidence from animal experiments and human studies shows that the intrauterine environment might influence the development of risk factors for CVD [18].

Table 1: ANOVA test of variance, comparison of cord blood lipid parameters among diabetic and non-diabetic mothers

Cord lipid parameters	Non-diabetic mothers (n=90)	Diabetic mothers (n=4)	p value
Blood sugar (mg/dl)	38.78	48.75	0.181
Total cholesterol (mg/dl)	73.83	98.5	0.003
HDL cholesterol (mg/dl)	21.13	5.94	0.210
LDL cholesterol (mg/dl)	36.63	65.5	0.000
Triglycerides (mg/dl)	49.39	110.25	0.000
VLDL cholesterol (mg/dl)	13.57	8	0.512
TC/HDL	3.74	4.15	0.523
LDL/HDL	1.84	2.78	0.029

TC: Total cholesterol, HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, VLDL: Very low-density lipoprotein cholesterol, ANOVA: Analysis of variance

Table 2: ANOVA test of variance, comparison of cord blood lipid parameters among hypertensive and non-hypertensive mothers

Cord lipid parameters	Non-hypertensive mothers (n=90)	Hypertensive mothers (n=6)	p value
Total cholesterol (mg/dl)	73.83	82.5	0.187
HDL cholesterol (mg/dl)	21.13	19.5	0.512
LDL cholesterol (mg/dl)	36.63	61.17	0.000
Triglycerides (mg/dl)	49.39	70.67	0.003
VLDL cholesterol (mg/dl)	13.57	13.5	0.991
TC/HDL	3.74	4.33	0.26
LDL/HDL	1.84	3.19	0.000

TC: Total cholesterol, HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, VLDL: Very low-density lipoprotein cholesterol, ANOVA: Analysis of variance

Table 3: Cord blood lipid parameters in present study and earlier evidence

Mean(mg/dl)	Pardo *et al*[16]	SV Esfarjani *et al*[17]	Schaefer Graf U M *et al*[18]	Rakhi Jain *et al*[19]	KARB s *et al*[20]	Present study
Total Cholesterol	70.42 ± 1.63	81.02 ± 19.75	63.5 ± 17.7	98.2 ± 34.9	73.64 ± 21.64	73.83 ± 15.83
HDL Cholesterol	26.75 ± 0.65	25.09 ± 7.34	-	29 ± 10.7	23.25 ± 7.66	21.13 ± 6.00
LDL Cholesterol	34.38 ± 1.29	48.92 ± 16.34	-	36.4 ± 20	41.81 ± 17.88	36.63 ± 12.82
Triglycerides	-	42 ± 29.10	41.6 ±21.8	118.5 ± 9	33.75 ± 16.39	49.38 ±23.81
VLDL Cholesterol	-	-	-	28.6 ± 17.5	12.8 ± 11.08	13.58 ± 16.83
TC/HDL	2.71± 0.06	2.33	-	3.52 ± 1.4	-	3.74 ± 1.25
LDL/HDL	-	-	-	1.41 ± 0.8	-	1.84 ± 0.82
RBS	-	-	85 ± 21.4	-	-	38.78 ± 14.31
HbA1c	-	-	-	-	-	2%

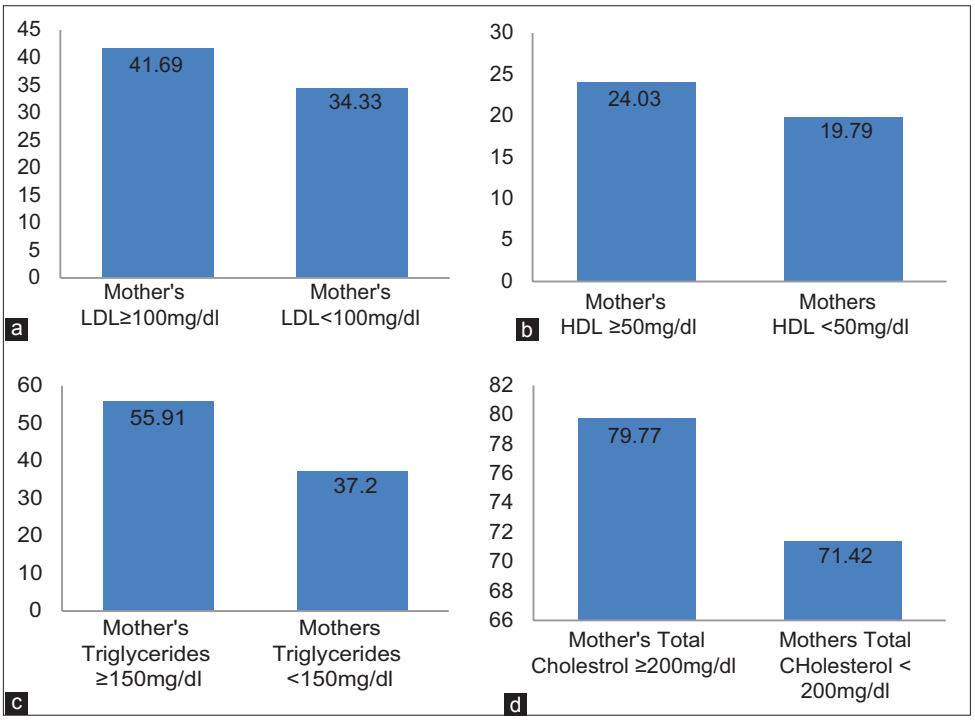

Fig. 1: (a) Comparison of cord blood low-density lipoprotein cholesterol (LDL-C) with maternal LDL-C revealed higher values among newborns of mothers' with higher LDL-C (p=0.017), (b) Comparison of cord blood high-density lipoprotein cholesterol (HDL-C) with maternal HDL-C revealed higher values among newborns of mothers' with higher HDL-C (p=0.001), (c) Comparison of cord blood triglycerides (TG) with maternal TG revealed higher values among newborns of mothers' with higher low-density lipoprotein cholesterol (p=0.032), (d) Comparison of cord blood total cholesterol (TC) with maternal TC revealed higher values among newborns of mothers' with higher TC (p=0.0008)

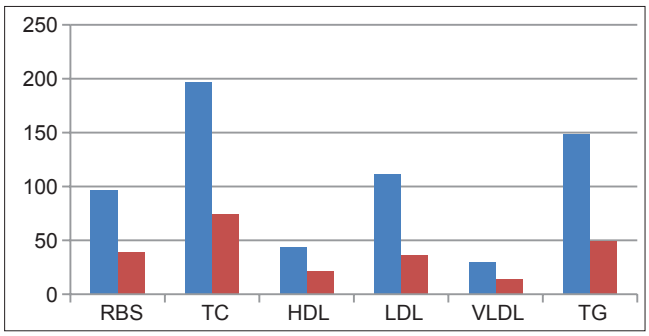

Fig. 2: Comparison of mean RBS and lipid profile parameters in maternal (blue) and cord blood (red). Significantly low lipid profile parameters and RBS were found in cord blood

Goldstein *et al.* observed that parents with high lipids or family history of CVD had their children with lipids in higher quartile [19]. Bellu *et al.* observed that neonates with family history of ischemic CVD had higher levels of TC and LDL-C, while there was no difference in TG levels [20]. Yusuf *et al.* noted a higher cholesterol and TG level in neonates with family history of CVD and suggested an early intervention for the prevention of CVD in such cases [21].

We also tried to determine mean sugar levels, and HbA1c levels at birth and these were significantly low when compared to adult reference ranges.

Schaefer Graf *et al.* studied the lipid profile parameters in mothers with gestational diabetes and suggested that maternal lipids as strong predictors for fetal lipids and fetal growth [15].

In the present study, lipid profile parameters LDL-C, TC, TG's were significantly altered in babies born to mothers with diabetes. While LDL-C and TG were significantly altered in babies born to mothers with hypertension, suggesting that maternal factors and inutero environment might directly impact neonatal lipid parameters. This can have a negative impact on future cardiovascular health.

The present study, though small, shows promising results that maternal factors could impact neonatal lipid profile; however, larger prospective

studies are required to validate these results. Bogalusa Heart Study cohort of children it was observed that higher cholesterol levels in neonates predicted high cholesterol levels in early and late childhood as well as greater coronary and aortic atherosclerosis [7,8].

Neonatal lipid levels serve a guide to know the physiological levels of lipids required for maintaining bodily metabolisms. Our findings suggests that LDL-C levels were significantly low (mean of 36.63 mg/dl) than adult reference range. This LDL-C may be required for maintenance of tissues and bodily metabolisms.

ATP III Guidelines for adult lipid lowering therapy suggest therapeutic option for LDL-C as <70 mg/dl in very high risk individuals with CVD [22]. Our data is consistent with this low LDL-C value, suggesting that further lowering of LDL-C in high risk individuals with coronary heart disease would be beneficial, however lowering LDL-C below 36.63 mg/dl could interfere with the normal cellular metabolism.

Future studies are required to dissect out the exact mechanisms involved in the lipoprotein transport from mother to fetus and mechanisms involved in initiating programming events inutero. Results of the present study indicate the need for further research in this field. Long term effects of low LDL-C in adults on various bodily metabolisms and its systemic effect are to be studied.

CONCLUSION

Roots for adult coronary vascular disease begin in early life, and these factors could be directly related to maternal factors and environment. In the present study, we confirmed lower lipid levels in cord blood when compared with maternal blood and adult reference values. Neonatal lipid levels may serve as an indirect guide for adult lipid lowering therapy in coronary vascular disease.

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REFERENCES

1. Antman EM, Selwyn AP, Braunwald E, Lascalzo J. Ischemic Heart Disease: Harrison's Principles of Internal Medicine. 18th ed. New York: McGraw-Hill Companies; 2012. p. 1998.
2. Rifai N, Backorik P, Albers J, Carl A, Edward R. Teitz Textbook of Clinical Chemistry. 3rd ed. Philadelphia: Saunders; 1999. p. 826-30.
3. McGill HC Jr, McMahan CA, Herderick EE, Malcom GT, Tracy RE, Strong JP. Origin of atherosclerosis in childhood and adolescence. Am J Clin Nutr 2000;72 (5 Suppl):1307S-15.
4. Cohen MS. Fetal and childhood onset of adult cardiovascular diseases. Pediatr Clin North Am 2004;51(6):1697-719, x.
5. Barker DJ. The intrauterine origins of cardiovascular disease. Acta Pædiatr 1993;82:9.
6. WHO Study Group. Prevention in childhood and youth of adult cardiovascular diseases: Time for action. Technical Report Series No. 792. Geneva: WHO; 1990.
7. Freedman DS, Srinivasan SR, Cresanta JL, Webber LS, Berenson GS. Cardiovascular risk factors from birth to 7 years of age: The Bogalusa Heart Study. Serum lipids and lipoproteins. Pediatrics 1987;80:789-96.
8. Berenson GS, Srinivasan SR, Bao W, Newman WP rd, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. N Engl J Med 1998;338(23):1650-6.
9. Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) Collaborative Group, Armitage J, Bowman L, Wallendszus K, Bulbulia R, Rahimi K, *et al*. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12,064 survivors of myocardial infarction: A double-blind randomised trial. Lancet 2010;376(9753):1658-69.
10. Bansal N, Cruickshank JK, McElduff P, Durrington PN. Cord blood lipoproteins and prenatal influences. Curr Opin Lipidol 2005;16(4):400-8.
11. Parker CR Jr, Simpson ER, Bilheimer DW, Leveno K, Carr BR, MacDonald PC. Inverse relation between low-density lipoprotein-cholesterol and dehydroisoandrosterone sulfate in human fetal plasma. Science 1980;208(4443):512-4.
12. McConathy WJ, Lane DM. Studies on the apolipoproteins and lipoproteins of cord serum. Pediatr Res 1980;14(5):757-61.
13. Pardo IM, Geloneze B, Tambascia MA, Barros-Filho AA. Atherogenic lipid profile of Brazilian near-term newborns. Braz J Med Biol Res 2005;38(5):755-60.
14. Esfarjani SV, Irvani E, Razzaghi Azar M. Determination of the lipid profile of cord blood in neonates and its correlation with maternal age in Iran. J Compr Pediatr 2012:3(2):71-6.
15. Schaefer-Graf UM, Graf K, Kulbacka I, Kjos SL, Dudenhausen J, Vetter K, *et al.* Maternal lipids as strong determinants of fetal environment and growth in pregnancies with gestational diabetes mellitus. Diabetes Care 2008;31(9):1858-63.
16. Jain R, Tripathi VN, Singh RD, Pandey K. Lipid profile & apolipoproteins in neonates in relation to birth weight and gestational maturity. J Pediatr Sci 2011;3(2):e80.
17. Kharb S, Singh V, Sangwan K. Correlation of birth weight and cord blood lipoprotein, apolipoprotein levels. Adv Med Dent Sci 2009;3(1):13-6.
18. Barker DJ. The intrauterine origins of cardiovascular disease. Acta Paediatr 1993;391:93-9.
19. Goldstein JL, Albers JJ, Schrott HG, Hazzard WR, Bierman EL, Motulsky AG. Plasma lipid levels and coronary heart disease in adult relatives of newborns with normal and elevated cord blood lipids. Am J Hum Genet 1974;26(6):727-35.
20. Bellù R, Ortisi MT, Agostoni C, Incerti P, Besana R, Riva E, *et al.* Familial history of cardiovascular disease and blood lipid pattern in newborn infants. Acta Paediatr 1992;81(1):21-4.
21. Yusuf S, Vaz M, Pais P. Tackling the challenge of cardiovascular disease burden in developing countries. Am Heart J 2004;148(1):1-4.
22. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285(19):2486-97.