

# Effect of Maturity and Birth Weight on Umbilical Cord Blood Lipid Profile: A Fetal Programming Phenomenon

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## ABSTRACT

**Background:** The recent research on "fetal programming hypothesis" has totally revived the mechanistic understanding of triggering factors responsible for development of cardiovascular diseases (CVDs). As deranged lipid profile is associated with increased predisposition to atherosclerotic CVDs, we planned to study effect of fetal maturity and birth weight on umbilical cord blood lipid profile. **Methods:** A hospital based cross sectional study including 200 neonates satisfying inclusion criteria was carried out. The umbilical cord blood samples of selected neonates were collected and analysed for lipid profile (Total Cholesterol (TC), Triglycerides (TG), High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C) and Very Low Density Lipoprotein Cholesterol (VLDL-C)) in order to be compared among groups of neonates based on maturity and birth weight. **Results:** The preterm neonates had statistically significant higher levels of umbilical cord blood TC, TG, LDL-C and VLDL-C (with P values of 0.025, 0.001, 0.045, 0.007 and 0.045 respectively) while lower but statistically insignificant (p value of 0.131) levels of HDL-C in as compared to full term neonates. The low birth weight neonates also had statistically significant higher levels of TC, TG, LDL-C and VLDL-C (P values of 0.001, 0.032, 0.00001 and 0.032 respectively) but statistically significant (P value of 0.034) lower levels of HDL-C in umbilical cord blood as compared to normal birth weight neonates. **Conclusion:** The results suggest that prematurity as well as low birth weight have deleterious effect on umbilical cord blood lipid profile resulting in more atherogenic lipid levels. This could be regarded a triggering factor responsible for development of CVDs in later life. This observation not only conciliates with fetal programming hypothesis but also indicates that its effect is evident (in the form of altered lipid profile) even at the birth in such programmed neonates.

**Keywords:** Umbilical cord blood lipid profile, Fetal programming, Neonatal dyslipidemia, Prematurity, Low birth weight.

## INTRODUCTION

Nowadays, Cardiovascular disease (CVDs) is the primary cause of adult mortality and morbidity especially in developing countries like India.<sup>[1]</sup> Obesity, insulin resistance and associated dyslipidemia are the well known risk factors for coronary artery disease.<sup>[2]</sup> However, the recent research on the "fetal programming hypothesis" has added a lot to our understanding of triggering factors responsible for development of these diseases.<sup>[3]</sup>

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roots traceable to fetal life itself. The adverse intrauterine environment during the critical phase of fetal development programmes the fetus and/or imprints the development of fetal tissues and organs.<sup>[3-5]</sup> This phenomenon is more relevant to developing countries, where women are chronically malnourished especially in rural areas.<sup>[6]</sup>

Lipid profile is a marker of the cardiovascular status.<sup>[7,8]</sup> Lipids and lipoproteins in the cord blood are supposed to reflect the status of plasma lipids and their metabolism during the fetal life and at the birth as most fetal lipids are synthesized de novo and only part of it is derived from the placental circulation.<sup>[9]</sup> Several studies suggested that preterm birth and low birth weight are linked with a higher prevalence of atherosclerotic CVDs in later life.<sup>[3-5]</sup> Therefore, this study was planned to explore the effect of fetal maturity and birth weight on umbilical cord blood lipid profile.

## MATERIALS AND METHODS

A hospital based cross sectional study was carried out at Kasturba Hospital, Mahatma Gandhi Institute of Medical Sciences, Sewagram, Wardha, Maharashtra from 1st July 2012 to 31st July 2014 after obtaining permission from institutional research committee. A total number of 200 neonates were enrolled after obtaining informed consent from parents.

**Inclusion criteria**

Neonates delivered with singleton pregnancy both males and females

**Exclusion criteria**

Neonates with one minute APGAR score < 7 and/or with congenital anomalies and/or maternal conditions like addictions, medical or obstetric diseases.<sup>[9,11]</sup>

Following definitions were used to classify neonates according to maturity (into preterm, full term and post term neonates) and birth weight [into low birth weight, normal birth weight and high birth weight neonates]:<sup>[12]</sup>

**Preterm neonates:** neonates delivered after 37 weeks of gestation

**Full term neonates:** neonates delivered between 37 to 40 weeks gestation

**Post term neonates:** neonates delivered after 40 weeks gestation

**Low Birth Weight (LBW) neonates:** neonates with birth weight less than 2.5 KG

**Normal birth weight neonates:** neonates with birth weight between 2.5 to 4 KG

**High birth weight neonates:** neonates with birth weight more than 4 KG

Umbilical cord blood sample of neonates were collected immediately after delivery and analysed for lipid profile at our Clinical Biochemistry Laboratory. Lipid profile estimation was done on ERBA EM360 Random Access fully automated analyzer using compatible reagent kits and protocols by ERBA Diagnostics Mannheim GmbH, Germany following the standard operating procedure of our laboratory.

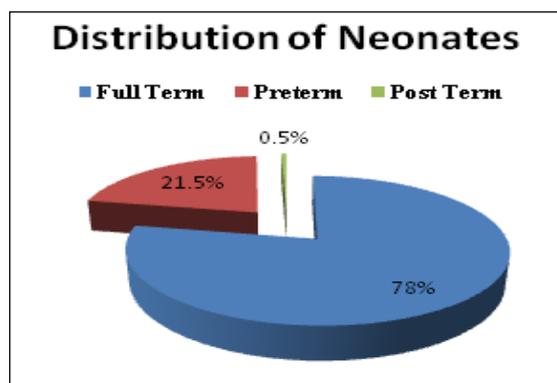
**Estimation of lipid profile of umbilical cord blood samples was done by following methods:**

- Total Cholesterol (TC) by CHOD-PAP method.<sup>[13]</sup>
- Triglyceride (TG) by GPO-Trinder method.<sup>[14]</sup>
- High Density Lipoprotein cholesterol (HDL-C) by Modified PVS and PGME coupled method.<sup>[15]</sup>
- Low Density Lipoprotein Cholesterol (LDL-C) and Very Low Density Lipoprotein Cholesterol (VLDL-C) levels were calculated using Friedwald equation.<sup>[16]</sup>

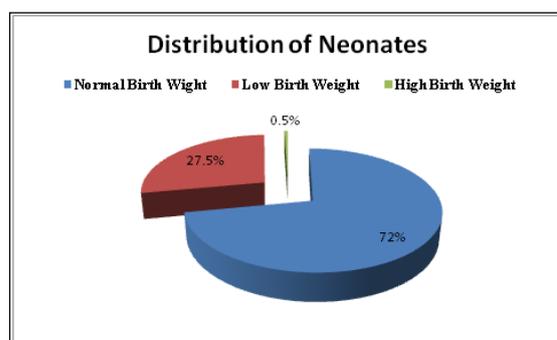
The statistical analysis was done by SPSS 23.0 using student unpaired t test for the difference between two

means and p<0.05 was considered as level of significance.

**RESULTS & DISCUSSION**



**Figure 1: Distribution of neonates according to their maturity**



**Figure 2: Distribution of neonates according to their birth weight**

The Figure 1 & 2 shows neonatal distribution of neonates according to their maturity and birth weight respectively. As the number of post term and high birth weight neonates were very few, these were exempted in further analysis.

**Table 1: Comparison of umbilical cord blood lipid profile between full term and preterm neonates.**

Lipid Profile*	Full term Neonates	Preterm Neonates	t- Value	p- Value**
TC	80.51±13.52	85.69±12.56	-2.258	0.025
TG	72.42±13.12	76.83±11.08	-2.016	0.045
HDL-C	29.05±5.60	27.69±3.37	1.516	0.131
LDL-C	36.97±12.04	42.63±11.65	-2.748	0.007
VLDL-C	14.48±2.62	15.36±2.21	-2.016	0.045

\* Values expressed as Mean±SD in mg/dL

\*\* P value (p<0.05) was considered as level of significance

As per the Table 1, the preterm neonates in our study had statistically significant higher (p value < 0.05) levels of umbilical cord blood TC, TG, LDL-C and VLDL-C while lower but statistically insignificant (p value > 0.05) levels of HDL-C as compared to full term neonates. Several studies (Avinash et al,<sup>[17]</sup> Pardo et al,<sup>[18]</sup> Tohmaz et al,<sup>[19]</sup> Jane et al,<sup>[17]</sup> Haridas et al.<sup>[18]</sup> and Mathur et al.<sup>[19]</sup>) have reported similar findings. The reason for this observation could be the

shorter intrauterine life associated with prematurity. The preterm neonates are deprived of opportunity of energy storage in late gestation and thus lack both hepatic carbohydrate (glycogen) and subcutaneous adipose tissue (triacylglycerol). Rise in cord blood cholesterol levels may reflect the metabolic adaptation to provide adequate energy.<sup>[20,21]</sup>

**Table 2: Comparison of umbilical cord blood lipid profile of normal birth weight and low birth weight neonates.**

Lipid Profile*	Normal birth weight neonates	Low birth weight neonates	t-value	p-value**
TC	79.65±13.17	86.90±12.93	-3.491	0.001
TG	72.20±13.77	76.56±9.35	-2.160	0.032
HDL-C	29.25±5.80	27.50±2.89	2.130	0.034
LDL-C	35.95±11.38	44.08±12.25	-4.411	0.000017
VLDL-C	14.44±2.75	15.31±1.87	-2.160	0.032

\* Values expressed as Mean±SD in mg/dL

\*\* P value (p<0.05) was considered as level of significance

As per the Table 2, the LBW neonates were found to have statistically significant higher (p value < 0.05) levels of umbilical cord blood TC, TG, LDL-C and VLDL-C but statistically significant lower (p value < 0.05) levels of HDL-C as compared to normal birth weight neonates. Authors like Kelishadi et al,<sup>[22]</sup> Hossain et al,<sup>[23]</sup> Jones et al,<sup>[24]</sup> Chandika et al,<sup>[25]</sup> Nayak et al,<sup>[26]</sup> and Aletayab et al,<sup>[27]</sup> have reported similar results. The proposed reason for this alteration may be the lack of glucose as fuel in these growth-restricted LBW neonates. As the glucose is not available, these neonates have to use alternative source as a fuel such as amino acid and lipids in order to synthesize glucose (gluconeogenesis) by activating lipid and other metabolism.<sup>[21]</sup> This results in increased hepatic generation of lipids (particularly VLDL-C and chylomicrons). The intrauterine growth retardation is also known to be associated with decreased lipoprotein lipase activity.<sup>[28]</sup> The increased hepatic lipogenesis coupled with decreased peripheral utilization of lipids (due to decreased lipoprotein lipase activity) explain the mechanism of higher concentration of plasma lipids in LBW neonates.

## CONCLUSION

From the results of this study we propose that maturity and birth weight have great impact on umbilical cord blood lipids. These fetal factors are responsible for atherogenic umbilical cord blood lipid levels (increased TC, TG, LDL-C and VLDL-C while decreased HDL-C). These observations suggest the role of fetal programming and resultant dyslipidemia in predisposition to adulthood CVDs. However these findings needs to be validated by further studies specifically planned to analyze the effect of prematurity and low birth weight on

umbilical cord blood lipid profile. Based on these observations we assume that cord blood lipid screening can be used to identify these high risk neonates. Theoretically, early diagnosis followed by prudent management of such high risk neonates seems provide an opportunity for the long term primary amelioration of risk factors and thus prevention of CVDs in adult life. However further studies are required to validate this assumption.

The findings of our study not only indicate that the processes responsible for predisposition to CVDs in the later life start early but also demonstrates that the effect of these processes in terms of atherogenic umbilical cord blood lipid profile can be evaluated during fetal life itself. The study highlights that dyslipidemia (a major risk factor for CVDs) could be diagnosed at the very birth by a cost effective and "theoretically non-invasive" investigation i.e. umbilical cord blood lipid profile analysis.

## REFERENCES

- Moran AE, Forouzanfar MH, Roth GA, et al. The global burden of ischemic heart disease in 1990 and 2010: the Global Burden of Disease 2010 study. *Circulation*. 2014;129:1493.
- Jha P, Gajalakshmi V, Gupta PC, Kumar R, Mony P, Dhingra N, et al. Prospective study of one million deaths in India: rationale, design, and validation results. *PLoS Med*. 2006 Feb;3(2):e18.
- Fall CHD, Barker DJP. The fetal origins of coronary heart disease and non insulin dependent diabetes in India. *Indian J Pediatr*. 1997;34(1):5-8.
- Kent L, Thornburg. Fetal Origins of Cardiovascular Disease. *Am Academy of Pediatrics*. December 2004;(5):527-34.
- Vaag AA, Grunnet LG, Arora GP, Brons C. The thrifty phenotype hypothesis revisited. *Diabetologia*. 2012;55:2085-8.
- Gopalan C. Low birth weights; Significance and implications. In: nutrition in children: Developing Country Concerns. Eds. Sachdev HPS, Choudhury P, New Delhi National Update on Nutrition.1994;1-33.
- Ross R. The pathogenesis of atherosclerosis: a perspective for the 1990s. *Nature*. 1993;362:801.
- Ginsberg HN. Lipoprotein metabolism and its relationship to atherosclerosis. *Med Clin North Am*. 1994;78:1-20.
- Herrera E, Amusquivar E, López-Soldado I, Ortega H. Maternal lipid metabolism and placental lipid transfer. *Horm Res*. 2006;65(3):59.
- Finster M, Wood M. The Apgar score has survived the test of time. *Anesthesiology*. 2005 May; 102 (4):855-857.
- Bachani D, Agarwal DK, Mathur HN. Maternal factors influencing birth weight in rural population. *Jr Obs Gyn Ind*. 1985;35:528-33.
- Cloherty JP, Stark AR. Manual of neonatal care. 7th edition. Lippincott;2011:74-89.
- Allain CC, Poon LS, Chan CSG, Richmond W, Fu PC. *Clin Chem*. 1974;20:470-475.
- Trinder P. Triglyceride estimation by GPO-PAP method. *Ann Clin Biochemistry*. 1969;6:24-7
- Burstein M, Scholnick HR, Morfin R. Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. *J Lipid Res*. 1970;11:583-95.
- Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18:499-502.

17. Jadhao AN, Tadas AK, Tadas SA. Lipid profile of umbilical cord blood of near term and term neonates International. J Current Med Applied Sci. 2014;2(2):01-11.
18. Pardo IMCG. Atherogenic lipid profile of Brazilian near-term newborns. Braz J Med Biol Res. 2005;38(5):755-60.
19. Tohmaz U, Raid MR. Cord blood lipid profile. Ir J Neonatol. 2013;4(4):8-10.
20. Misra PK, Tiwari DK, Sharma B, Kaul R. Free fatty acids and Triglycerides in normoglycemic low birth weight newborns in early neonatal period. Indian J Pediatr. 1984;51:637-641.
21. Kimura RE. Lipid metabolism in the fetal-placental unit In: Cowett RM. Principles of Perinatal-Neonatal Metabolism. New York: Springer-Verlag; 1991, p.291-303.
22. Kelishadi R, Badiie Z, Adeli K. Cord blood lipid profile and associated factors: baseline data of a birth cohort study. Paediatric and Perinatal Epidemiol. 2007;21:518 -524.
23. 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 Jul;15(2):180-182.
24. Jones J N, Taylor G, Taylor DD. Altered cord serum lipid levels associated with small for gestational age infants. J of Am College of Obstetricians and Gynecology. 1999 Oct; 93:527-531.
25. Chandrika D. Nayak, Agarwal V, Nayak DM. Correlation of Cord Blood Lipid Heterogeneity in Neonates with Their Anthropometry at Birth. Indian J Clinical Biochemistry. April 2013;28(2):152-157.
26. Nayak CD, Agarwal V, Nayak DM. Correlation of cord blood lipid heterogeneity in neonates with their anthropometry at birth. Indian J Clin Biochem. 2013;28:152-7.
27. Aletayeb SM, Dehdashtian M, Aminzadeh M, Moghaddam AR, Mortazavi M, Malamiri RA, et al. Correlation between umbilical cord blood lipid profile and neonatal birth weight. Pediaatria Polska. 2013;88(6):521-5.
28. Gauster M, Hiden U, Blaschitz A, Frank S, Lang U, Alvino G, Cetin I, Desoye G, Wadsack C. Dysregulation of placental endothelial lipase and lipoprotein lipase in intrauterine growth restricted pregnancies. J. Clin. Endocrinol. Metab. 2007;92(6):2256-2263.

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