International Journal of Contemporary Pediatrics
Yashodha HT et al. Int J Contemp Pediatr. 2018 Mar;5(2):542-546
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20180551

Original Research Article

Cord blood lipid profile in late preterm and term neonates

Yashodha H. T., Syeda Kausar Anjum*

Department of Pediatrics, Kempegowda Institute of Medical Sciences and Research Center, Bangalore, Karnataka, India

Received: 20 December 2017
Accepted: 25 January 2018

***Correspondence:**
Dr. Syeda Kausar Anjum,
E-mail: kausar.anjum86@gmail.com

ABSTRACT

Background: Atherosclerotic cardiovascular diseases are the major causes of mortality and morbidity both in developed and developing countries. High concentrations of lipids in neonates with low gestational age may increase the risk of cardiovascular diseases in the future. It has been suggested that early diagnosis along with appropriate diet and drug therapy may provide an opportunity for long term amelioration of risk factors that contribute to atherosclerosis and cardiovascular diseases in adult life. This study is conducted to compare lipid profile and atherogenic indices in late preterm and term neonates.
Methods: It is a prospective comparative study conducted over a period of 12 months in a tertiary care hospital, Bangalore. A total of 170 neonates between 34 to 42 weeks were included in the study. Umbilical cord blood was collected immediately after delivery and lipid values were measured. Atherogenic indices were calculated.
Results: Out of 170 neonates, 93 (54.7%) were male and 77 (45.3%) were female. 88 (55%) were late preterm and 72 (45%) were term. The cord blood lipid levels were not affected by the gender of the neonates. TG, TC, LDL, VLDL, LDL/HDL, TC/HDL were higher in late preterm babies compared to term babies ($p < 0.05$), HDL levels were not statistically significant. The mean serum lipid levels (TG, TC, LDL and VLDL) and atherogenic indices were higher in SGA babies than AGA, but HDL levels were not statistically significant.
($p > 0.05$)
Conclusions: Lipid levels are inversely correlated with the gestational age. This could be regarded as a risk factor for development of atherosclerosis and cardiovascular diseases in later life.

Keywords: Atherogenic indices, Cord blood lipid profile, Late preterm, Term

INTRODUCTION

Atherosclerotic cardiovascular diseases are the major causes of mortality and morbidity both in developed and developing countries. Cardiovascular diseases account for 31% of total global deaths which amounts to about 17.5 million people losing their lives every year. Over three quarters of cardiovascular deaths take place in low and middle-income countries. Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke.[1] The incidence of cardiovascular diseases depends on the prevalence of genetic and environmental risk factors.

According to Barker's hypothesis, atherosclerotic lesion may have its origin in the neonatal period and adverse intrauterine environment during fetal development, may lead to impaired intrauterine growth and cardiovascular diseases in later adult life.[2] Fetal lipid profile will be deranged either due to genetic programming or due to prepartum or intrapartum stress, and this deranged lipid profile can continue into adult life and result in cardiovascular diseases.[3] It is known that preterm neonates have lost the chance to complete their energy deposits in later part of pregnancy. Thus, many times these growth restricted neonates need to use endogenous reserves, thereby activating lipid metabolism that

generates energy and promote gluconeogenesis. Long term consequences of these metabolic adaptations will lead to an increased prevalence of cardiovascular diseases, hypertension and type 2 diabetes mellitus, with contributions from several other maternal and fetal factors such as obesity, hypertension.[4]

Studies have shown that small for gestational age babies have abnormal lipid profile when compared to those normal for gestational age and these are the ones who are at higher risk of developing cardiovascular diseases in the future.[5] Thus the overall nature of the progress of the atherosclerosis is age dependent, which begins in childhood and progresses with advancing age.[6,7] The serum lipid concentrations in new-born period may be associated with lifelong changes in the metabolic functions.[8] Hence this study aimed to determine the cord blood lipid levels in late preterm and term neonates.

METHODS

This was a prospective hospital based comparative study conducted at a tertiary care center, Bangalore from July 2016 to July 2017. A total of 170 neonates were included in the study, after obtaining informed consent from the mothers and ethical committee clearance.

Inclusion criteria

Neonates between 34 to 42 weeks.

Exclusion criteria

- Multiple births
- Congenital anomalies and syndromes
- APGAR score at 5 minutes below 7
- Sick neonates
- Maternal chronic pancreatitis, thyroid disorders, Cushing's disease, primary hypercholesterolemia
- Maternal intake of drugs which affect neonatal lipid levels

Neonates were divided into 2 groups: late preterm (34 weeks to 36 weeks 6 days) and term (37 weeks to 42 weeks). Birth weight was measured by using digital electronic weighing scale after uncovering i.e., removing clothes of the baby and before first feeding. AGA (Appropriate for gestational age) was defined as birth weight between 10^{th} and 90^{th} percentile for gestational age. SGA (small for gestational age) was defined as birth weight $<10^{th}$ percentile or <2 SD below the mean for gestational age.

About 2 ml of umbilical venous blood was collected in a clean, dry vial under aseptic precautions after cord clamping from maternal umbilical end and was allowed to clot at room temperature. Serum was separated by centrifugation and analyzed immediately for lipid levels i.e., total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein, very low-density lipoprotein by standard enzymatic methods.

Measurement of serum cholesterol by CHOD/PAP Trinder's method

Cholesterol esterase hydrolyses cholesterol esters in the specimen into free cholesterol and fatty acid. In the second reaction, cholesterol oxidase converts cholesterol to cholest-4-en-3-one and hydrogen peroxide. In presence of peroxidase, hydrogen peroxide oxidatively couples with 4-aminoantipyrine and phenol to produce red quinoneimine dye which has absorbance maximum at 510 nm. The intensity of red colour is proportional to the total cholesterol in the sample.

Measurement of HDL cholesterol by Phosphotungstate precipitation method

Phosphotungstate/Mg2+ precipitates chylomicrons, low density lipoprotein cholesterol and very low-density lipoprotein cholesterol fractions. After centrifugation, high density lipoprotein fraction remains unaffected in supernatant. Cholesterol content of HDL fraction is assayed using ready to use reagent supplied with cholesterol kit.

Measurement of Serum triglyceride by GPO-PAP Trinder's method

Glycerol released from hydrolysis of serum triglycerides by lipoprotein lipase of the kit is converted by glycerol kinase to glycerol 3 phosphate, which is oxidized by glycerol phosphate oxidase to dihydroxy acetonephosphate and H_2O_2. In presence of peroxidase, H_2O_2 oxidizes phenolic chromogen to a red coloured compound and intensity of the colour measured on auto analyzer.

Estimation of LDL and VLDL

LDL cholesterol was calculated by Friedewald formula

Serum LDL = Serum total cholesterol - (serum VLDL + Serum HDL)

VLDL Cholesterol in mg % = Serum Triglyceride / 5

The following atherogenic indexes were calculated: total cholesterol / HDL cholesterol, LDL cholesterol / HDL cholesterol

Statistical analysis

Data analysed using SPSS version 24.0

For statistical analysis students unpaired 't' test was used to compare the both groups and p value <0.05 was taken as statistically significant.

RESULTS

Out of 170 neonates, 93 (54.7%) were male and 77 (45.3%) were female as shown in Figure 1. 88 (55%) were late preterm and 72 (45%) were term (Figure 2). 67 (39.6%) were delivered by normal vaginal delivery and 103 (60.4%) were delivered by caeserian section. 69 (40.6%) had birth weight between 1.5-2.49 kg, 101 (59.4%) had weight between 2.5-3.9 kg.

Table 1: Lipid profile in male and female babies.

Parameters	Male	Female	p value
	Mean±SD		
Triglyceride	48.1±3.8	46.3±11.5	0.33
Cholesterol	74.6±18.8	73.1±16.7	0.54
HDL	24.4±6.7	24.5±4.7	0.84
LDL	41.2±17.1	40.1±14.4	0.63
VLDL	9.9±2.8	9.5±3.5	0.47
LDL/HDL	1.8±0.9	1.7±0.7	0.52
TC/HDL	3.2±1.1	3.1±0.9	0.38

P <0.01 Significant

The cord blood lipid levels were not affected by the gender of the neonates. Mean triglyceride in male babies was 48.1±3.8 and female babies was 46.3±11.5. Mean Cholesterol in male babies was 74.6±18.8 and female babies was 73.1±16.7. Mean LDL in male babies was 41.2±17.1 and female babies was 40.1±14.4. Mean VLDL in male babies was 9.9±2.8 and female babies was 9.5±3.5. Mean LDL/HDL in male babies was 1.8±0.9, female babies was 1.7±0.7. Mean TC/HDL in male babies was 3.2±1.1, female babies was 3.1±0.9. Mean HDL in male babies was 24.4±6.7 and female babies was 24.5±4.7. Mean triglyceride, cholesterol, LDL, VLDL, TC/HDL, LDL/HDL was higher in male than female, HDL was higher in female than male but were statistically not significant P >0.05, as shown in Table 1.

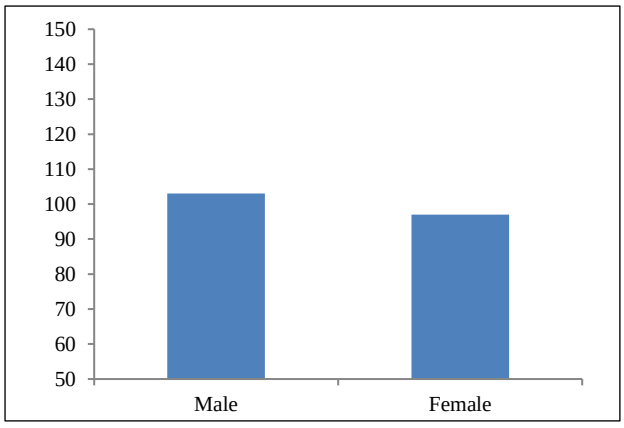

Figure 1: Gender of baby.

Triglyceride, cholesterol, LDL, VLDL, LDL/HDL, TC/HDL were higher in late preterm babies compared to term babies (p <0.05). Mean triglyceride in term babies was 45.6±12.6 and late preterm babies was 52.3±12.3. Mean Cholesterol in term babies was 71.5±16.3 and late preterm babies was 81.3±20.3. Mean LDL in term babies was 38.7±15.3 and late preterm babies was 46.7±15.8.

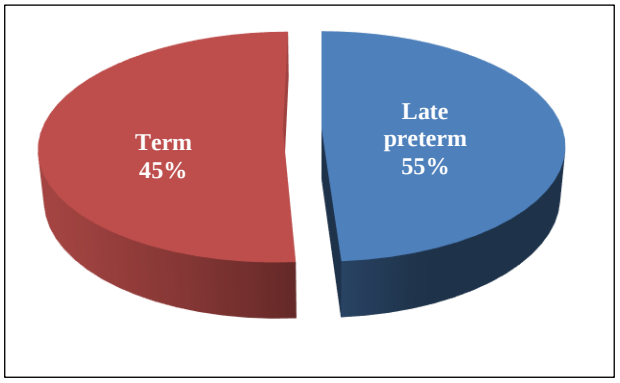

Figure 2: Distribution according to gestational age.

Mean VLDL in term babies was 9.3±2.6 and late preterm babies was 11.1±4.2. Mean LDL/HDL in term babies was 1.7±0.7, late preterm babies was 2.1±1. Mean TC/HDL in term babies was 3.1±0.8, late preterm babies was 3.5±1.3. Mean HDL in term babies was 24.5±5.7 and late preterm babies was 24.3±6.2. There was no statistically significant difference in HDL among term and late preterm babies as shown in Table 2.

Table 2: Distribution of Lipid profile according to Gestational age

Lipid	Term Mean±SD	Late preterm Mean±SD	P value
Triglyceride	45.6±12.6	52.3±12.3	0.001*
Cholesterol	71.5±16.3	81.3±20.3	0.001*
HDL	24.5±5.7	24.3±6.2	0.82
LDL	38.7±15.3	46.7±15.8	0.002*
VLDL	9.3±2.6	11.1±4.2	0.001*
LDL/HDL	1.7±0.7	2.1±1	0.002*
TC/HDL	3.1±0.8	3.5±1.3	0.003*

P <0.01 *significant

Table 3: Distribution of Lipid profile according to birth weight.

Lipid	SGA	AGA	P value
Triglyceride	51.1±10.2	39.9±7.3	<0.001*
Cholesterol	69.1±7.9	63.9±14.3	0.01*
HDL	23.8±2.8	26.0±7.2	0.14
LDL	34.1±5.6	30.9±13.5	0.01*
VLDL	10.2±1.8	8.5±1.8	<0.001*
LDL/HDL	1.5±0.3	1.2±0.5	<0.001*
TC/HDL	2.9±0.4	2.5±0.7	0.001*

P <0.01 *significant

Mean triglyceride in SGA babies was 51.1±10.2 and AGA babies was 39.9±7.3. Mean cholesterol in SGA babies was 69.1±7.9 and AGA babies was 63.9±14.3. Mean LDL in SGA babies was 34.1±5.6 and AGA babies

was 30.9±13.5. Mean VLDL in SGA babies was 10.2±1.8 and AGA babies was 8.5±1.8. Mean LDL/HDL in SGA babies was 1.5±0.3, AGA babies was 1.2±0.5. Mean TC/HDL in term babies was 2.9±0.4, late preterm babies was 2.5±0.7. Mean HDL in AGA babies was 23.8±2.8 and SGA babies was 26.0±7.2. Triglyceride, cholesterol, LDL, VLDL, LDL/HDL, TC/HDL were higher in SGA babies than AGA babies. There was no statistically significant difference in HDL between SGA and AGA babies as shown in Table 3 (p>0.05).

DISCUSSION

Dyslipidemia may cause complications such as atherosclerosis, coronary heart disease, stroke. Concentrations of the cord blood lipid is influenced by fetal malnutrition and prematurity.[8] More than 20 million are born as low birth weight (LBW) babies worldwide. India accounts for 40 per cent of the incidence of LBW babies in the world. In addition to genetic factors which are major determinants of lipid levels, fetal growth retardation may also establish a lifelong irreversible atherogenic profile. Low birth weight is associated with increased incidence of cardiovascular diseases, hypertension and type 2 diabetes in adult life.[9] Changes in blood lipids in LBW newborns with relative insulin intolerance can increase the risk of cardiovascular diseases in adulthood. Given the early life origin of adult diseases, primordial and primary prevention should be emphasized. Our values were similar to Nayak et. al, Pratinidhi et al, but lower than Piyush et al.[10] Yip PM et al showed pediatric reference intervals for plasma lipid biomarkers for males and females for 0-12 months infants.[11]

Present study showed that lipid values were higher in latepreterm than term babies which was similar to other studies like Avinash et al, Pardo et al and Tohmaz URMR et al[12-14] It has been reported that the plasma depletion of cholesterol that occurs at term is due to a decrease in HDL and LDL levels. In the present study, higher levels of triglycerides, total cholesterol and LDL in late preterm infants could be explained by the fact that preterm newborns lack both hepatic carbohydrate and subcutaneous adipose stores. Increase in cord blood cholesterol level may reflect the metabolic adaptation to provide adequate energy, especially to vital organs like brain.

The lower value of cholesterol in serum is probably the cause of fall in plasma LDL concentration due to increase in its uptake by fetal adrenal gland for steroid hormone production, as postulated by Parker et al.[15] Since HDL is not metabolized efficiently by the adrenals, fall in HDL levels may be associated with an increase in the activity of the lectin acetyl cholesterol transferase enzyme.[16] It is suggested that the decreasing activity of the lipoprotein lipase, hepatic lipase and lecithin cholesterol acyltransferase enzymes in preterm may lead to high concentrations of lipoproteins.

Chandrika et al reported that abnormal intrauterine milieu created by maternal changes during gestation may bear an impact on lipid metabolism in neonates, which may account for their differences in lipid profile and anthropometry at birth. In our study lipid values were higher in SGA babies than AGA babies which was similar to other studies like Nayak et al, Aletayab et al.[17,18]

This study showed no statistically significant gender difference for lipid profile, atherogenic indices which is similar to Kenchappa et al, Pratinidhi et al.[19,20] But Kelishadi et al had shown that in female newborns, TC, LDL and HDL were significantly higher compared to male.[21]

From the results, it is observed that lipid profile values in the neonate are much different from adults. All the values were lower than the adult's lipid profile values. In new born, liver cells and its enzyme are not well developed for lipid metabolism and so can contribute to lower values in lipid profile.

CONCLUSION

To reduce the burden of cardiovascular diseases, various influences on atherogenesis should be investigated both early and late in its development. There may be a primary influence of prenatal factors on the atherosclerotic process itself from early in the disease. The primary prevention of risk of developing cardiovascular diseases in future therefore may depend on strategies that promote fetal growth in utero. Present study showed that lipid levels and atherogenic indices were significantly higher in late preterm neonates and SGA neonates. Therefore, in these high-risk neonates, early diagnosis and appropriate intervention may provide an opportunity for a long term primary amelioration of risk factors that contributes for atherosclerosis and cardiovascular diseases in adult life. Hence these susceptible neonates require regular long term follow up.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organization. Cardiovascular Diseases (CVDs): Factsheet. 2016. Available at http://www.who.int/mediacentre/factsheets/fs317/en
2. Barker DJP. Fetal and infant origins of adult disease. Monatsschr Kinderheilkd. 2001;149(1):S2-6.
3. 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. Pediatr. 1987;80:789-96.

4. Barker DJ, Hales CN, Fall CH, Osmond C, Phipps K,Clark PM. Type 2 (non-insulin-dependent) diabetes mellitus, hypertension and hyperlipidemia (syndrome X): relation to reduced fetal growth. Diabetol.1993;36(1):62-7.
5. Molina M, Casanueva V, Cid X, Ferrada MC, Pérez R. Lipid profile in newborns with intrauterine growth retardation. Rev Med Chil. 2000;128:741-8.
6. Orchard TJ. Dyslipoproteinemia and diabetes. Endocrinol Metab Clin North Am. 1992;19:361-80.
7. Basavaraju SR, Jones TD. Atherosclerotic risks from chemicals: Part 1. Toxicological observations and mechanisms of atherosclerosis. Arch Environ Contam Toxicol. 1998;35(1):152-64.
8. Parker CR Jr, Carr BR, Simpson ER, MacDonald PC. Decline in the concentration of low-density lipoprotein-cholesterol in human fetal plasma near term. Metabol. 1983;32:919-23.
9. Meas T. Fetal origins of insulin resistance and the metabolic syndrome: a key role for adipose tissue? Diabetes Metab. 2010;36:11-20.
10. Tailor PB, Patel SM, Shah CJ, Upadhyay N. Reference range for lipid profile in healthy newborn, infant and LBW newborn. JPSI. 2012;1(4):34-6.
11. Yip PM, Chan MK, Nelken J, Lepage N, Brotea G, Adeli K. Pediatric reference intervals for lipids and apolipoproteins on the VITROS 5,1 FS chemistry system. Clin Biochem. 2006; 39:978-83.
12. 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.
13. Pardo IMCG. Atherogenic lipid profile of Brazilian near-term newborns. Braz J Med Biol Res. 2005;38(5):755-60.
14. Tohmaz U, Raid MR. Cord blood lipid profile. Ir J Neonatol. 2013;4(4):8-10.
15. Parker Jr CR, Fortunato SJ, Carr BR, Owen J, Hankins GD, Hauth JC. Apo lipoprotein A-1 in umbilical cord blood of newborns: relation to gestational age and high-density lipoprotein cholesterol. Pediatr Res. 1988;23:348-51.
16. Hamosh M. Lipid metabolism in premature infants. Biol Neonate. 1987;52:50-64.
17. 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.
18. 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. Pediatria Polska. 2013;88(6):521-5.
19. Kenchappa Y, Behera N. Assay of neonatal cord blood lipid levels and its correlation with neonatal gestational age, gender and birth weight: a single center experience. Int J Contemp Pediatr. 2016;3(3):718-24.
20. Pratinidhi SA, Darawade SP, Seema G, Hegde MV, Naphade PR, Ghadage DP, et al. Study of correlation of cord blood lipids and neonatal anthropometry. Int J Sci Stud. 2015;3(1):99-103.
21. Kelishadi R, Badiee Z, Adeli K. Cord blood lipid profile and associated factors: baseline data of a birth cohort study. Paediatr Perinat Epidemiol. 2007;21:518-24.
22. Badiee Z, Kelishadi R. Cord blood lipid profile in a population of Iranian term newborns. Pediatr Cardiol. 2008;29:574-9.

Cite this article as: Yashodha HT, Anjum SK. Cord blood lipid profile in late preterm and term neonates. Int J Contemp Pediatr 2018;5:542-6.