

Research Article**One Week Post Natal Changes in Neonatal Lipid Profile Values and Its Association with Gestational Age: A Prospective Study in North India****Pushpendra Magon¹, R.S Bharatwaj^{2*}**¹Professor, Dept. of Paediatrics, Sri Lakshminarayana Institute of Medical Sciences, Pondicherry, India²Associate Professor, Dept. of Community Medicine, DM Wayanad Institute Of Medical Sciences, Wayanad, Kerala, India***Corresponding author**

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Abstract: Adult serum lipid disorders have their root in childhood. Most of the past studies have measured lipid profiles at birth and the next measure earliest at 6 months after birth. The aim of this study was to estimate the neonatal lipid profile values at birth and 1 week of age & look for association of these values with birth weight and gestational age. 504 singleton live-borns from a tertiary care centre were studied. Lipid profiling was done using standard procedures. Data was compiled and analyzed using SPSS-15 for significance of difference in means by unpaired t-test. There was no significant difference in mean lipid values based on birth weight. The preterms had an unhealthier lipid profile. The overall change in mean lipid values over one week was highly significant. The increase in values for pre-terms was more sluggish. In conclusion, there is a rapid change in lipid profile post birth even as early as one week. Pre-terms are at greater atherosclerotic risk due to unhealthier lipid profile.**Keywords:** Gestation, India, Lipid profile, Neonate.

INTRODUCTION

It was exactly a century ago that cord lipids were measured for the first time by Herrman and Neuman in 1912 AD who found them to be considerably lower than those found in normal women. Recently interest in cord lipids has increased because it is thought that adult serum lipid disorders have their roots in childhood and atherogenic changes are postulated to originate early in life [1]. Observations from both epidemiological and clinical studies have suggested that the pathological process of coronary artery disease begins in childhood. The aortas of children as young as 3-4 years age often contain intimal lipid deposits, commonly called "fatty streaks" [2]. These aortic fatty streaks increase in extent rapidly during the second decade of life and similar lesions begin to appear in the coronary arteries in the latter part of second decade. Risk reduction would likely be of greatest importance if appropriate intervention were to begin early in life because there is compelling evidence that atherosclerosis has its origins in childhood [3]. A relatively small reduction in mean cholesterol levels for a population of children, if continued into adult life could significantly reduce the incidence of risk of coronary heart disease.

For men results from the cohort studies have shown that a decrease of serum cholesterol concentration of 0.6 mmol/l (about 10%) was associated with a decrease

in incidence of ischaemic heart disease of 54% at age 40 years, 39% at age 50, 27% at 60, 20% at 70, and 19% at 80. The data for women are limited but indicate a similar effect [4].

The significant physiological change in lipid profile values post birth is well documented. Previous studies on tracking of lipid profile among newborns have at the earliest observed changes only 6 months post birth. We wanted to find out the lipid parameters of neonates from an urban background in northern India and look for differences in lipid parameter values based on gestational age and also to track how the values change over the first week of life to see how fast the lipid profile parameters are altered after birth.

MATERIALS AND METHODS

The selection criteria was all the 504 live born singleton babies of mothers with no history of diabetes, hypertension, fetal growth restriction and other pregnancy complications and who were born at a tertiary care teaching hospital over a 2 year period. After obtaining the mother's informed consent routine examination was performed for all of these babies at birth. Cord blood samples were collected from the placental side of the umbilical cord at birth and analyzed for the lipid profile which included Serum cholesterol, Low density lipoprotein [LDL], Very Low

density lipoprotein [VLDL], High density lipoprotein [HDL], Low density lipoprotein cholesterol [LDL-C], Triglycerides and Apo lipoprotein-B [Apo-B]. The same tests were repeated when the neonate reached one week of age by collecting venous samples from a peripheral vein.

For the estimation of Total Cholesterol and HDL the CHOD-PAP method was used and for Triglycerides GPO-PAP method was used. The Apo-B levels were estimated by immune-turbidometric method using kits from Boehringer Mannheim that were adapted for the auto analyzer (RA XT). Estimation of differential lipids was done by nephelometry. Mean plus or minus two standard deviation was calculated for all the different parameters and used in our analysis. Tests for “significance of difference in means” were used for the statistical work that was accomplished with the statistical software SPSS 15.

RESULTS

There were a total of 504 new borns in the two year period, who were our study subjects, out of which the proportion of males was more: 286 (56.7%). Considering the gestational age, 462(91.9%) were term babies and 42 were preterm [below 36 weeks gestation]. Looking at the birth weights, 92(18.25%) of the neonates were of a low birth weight (<2.5Kg). Overall the mean values of all the lipid parameters increased from birth to one week of age (Table 1). This increase for all the parameters was statistically highly significant

($p < 0.001$). The value of VLDL showed the widest variation. Comparing between genders, at birth the mean values for all the parameters was higher in the female neonates compared to their male counterparts though the difference was statistically significant only in the values of Total cholesterol and Low density lipoprotein [LDL]. This difference of values between genders continued up to one week of age but at one week only a higher value of HDL was statistically significant (Table 2).

Examining the gestational age and its association with lipid profile, at birth the pre term neonates had statistically significant higher values of all the lipid parameters except Triglycerides, HDL, total cholesterol/HDL ratio and Apo-B though these values were still higher than that of the term neonates (Table 3). On measuring after one week it was interesting to observe that the differences in the mean values of the different lipid fractions between the term and pre term neonates had almost disappeared except for the higher values of LDL, and Apo-B in the pre term though not statistically significant (Table 3). Further taking the pre terms as a group and evaluating them based on the gestational age, as, above and below 34 weeks we found that, at birth among the pre term neonates those lesser than 34 weeks gestation had a higher value of all the lipid parameters. The difference was statistically significant for the Total cholesterol and triglycerides, but by one week of age this difference in the values was either totally lost or reduced considerably (Table 4).

Table 1: Overall Mean Lipid Profile Values, At Birth and at One Week of Age

	Mean ± 2 SD, At Birth	Mean ± 2 SD, At 1 st Week	p-value
Total Cholestrol	83.8 ± 28.1	158.1 ± 39.0	<0.0001
HDL	32.5 ± 15.2	41.2 ± 15.4	<0.0001
Triglycerides	64.8 ± 43.6	160.4 ± 80.0	<0.0001
Chylomicrons	28.0 ± 27.4	57.9 ± 41.03	<0.0001
VLDL	192.8 ± 175.0	337.9 ± 217.4	<0.0001
LDL	150.5 ± 66.5	252.2 ± 99.9	<0.0001
APO –B	28.1 ± 16.9	68.2 ± 59.2	<0.0001

Table 2: Mean Lipid Profile Values Based on Gender at Birth and at One Week Age

	At Birth			At 1 Week		
	Males Mean ± 2 SD	Females Mean ± 2 SD	p value	Males Mean ± 2 SD	Females Mean ± 2 SD	p value
Total Cholestrol	81.8 ± 27.6	86.5 ± 28.6	0.06	155.0 ± 40.6	161.0 ± 36.7	0.07
HDL	31.8 ± 15.5	33.4 ± 14.5	0.21	40.3 ± 13.2	43.6 ± 17.7	0.02
Triglycerides	63.4 ± 44.5	66.5 ± 42.4	0.41	155.7 ± 81.1	166.6 ± 78.3	0.13
Chylomicrons	26.9 ± 27.3	29.6 ± 27.5	0.29	60.0 ± 42.4	55.2 ± 39.8	0.28
VLDL	187.9 ± 177.4	199.2 ± 172.2	0.48	336.4 ± 214.3	339.9 ± 222.2	0.88
LDL	147.6 ± 97.2	154.4 ± 103.6	0.27	249.4 ± 97.2	256.1 ± 103.6	0.54
APO –B	27.9 ± 16.0	28.4 ± 18.0	0.73	67.1 ± 53.5	69.8 ± 66.1	0.61
TC/HDL	2.9 ± 1.4	2.8 ± 1.9	0.71	3.8 ± 3.1	3.7 ± 2.1	0.7

Table 3: Mean Lipid Profile Values Based On Gestational Age, at Birth and At One Week Age

	At Birth			At 1 Wk		
	Preterm Mean ± 2 SD	Term Mean ± 2 SD	p value	Preterm Mean ± 2 SD	Term Mean ± 2 SD	p value
Total Cholestrol	101.6 ± 34.1	82.2 ± 26.9	<0.001	159.7 ± 45.1	158.0 ± 38.5	0.57
HDL	33.8 ± 14.0	32.4 ± 15.2	0.57	41.9 ± 13.3	41.7 ± 15.5	0.94
Triglycerides	67.9 ± 53.0	64.5 ± 42.7	0.63	163.1±47	160.4±51	0.16
Chylomicrons	42.9 ± 31.7	26.6 ± 26.6	0.003	59.1 ± 34.5	57.8 ± 41.7	0.89
VLDL	340.0 ± 237.3	179.0 ± 162.3	<0.001	363.0 ± 233.4	336.0 ± 216.5	0.56
LDL	172.1 ± 87.5	148.6 ± 64.0	0.03	281.8 ± 152.2	249.5 ± 194.7	0.27
APO –B	30.3 ± 15.2	27.9 ± 17.1	0.39	80.9 ± 74.2	67.2 ± 57.8	0.14
TC/HDL	2.9 ± 1.4	2.8 ± 1.9	0.007	3.8 ± 3.1	3.7 ± 2.1	0.68

Table 4: Mean Lipid Profile Values Based Among Pre-terms based on degree of pre-maturity, At Birth And At One Week Age

	At Birth			At 1 Wk		
	Upto 34 Wks Mean ± 2 SD	>34 Wks Mean ± 2 SD	p value	Upto 34 Wks Mean ± 2 SD	>34 Wks Mean ± 2 SD	p value
Total Cholestrol	113.4 ± 35.8	89.4 ± 27.9	0.03	167.6 ± 57.3	153.0 ± 32.1	0.49
HDL	33.7 ± 16.8	32.3 ± 8.4	0.72	44.1 ± 15.0	37.9 ± 7.5	0.11
Triglycerides	82.8 ± 69.6	51.5 ± 13.5	0.04	156.1 ± 81.8	126.3 ± 45.3	0.15
Chylomicrons	45.9 ± 24.1	38.3 ± 40.6	0.47	58.5 ± 37.9	59.6 ± 33.4	0.92
VLDL	387.6 ± 237.4	266.9 ± 224.0	0.11	368.1 ± 273.9	329.0 ± 170.1	0.71
LDL	185.9 ± 106.7	159.9 ± 55.9	0.37	323.5 ± 184.9	260.8 ± 75.5	0.28
APO –B	32.3 ± 16.0	27.5 ± 14.0	0.32	80.1 ± 83.7	81.8 ± 63.8	0.90

DISCUSSION & CONCLUSIONS

Atherosclerosis originates during childhood and serum lipid levels are a key factor in the process. The observations on a new born cohort offer an opportunity to study the risk factor variables in the earliest stage of their lives. The observations in infancy provide a background for studies in older children and adults. The neonates in our study all belonged to parents of the upper socio economic strata of society. The values found for the different lipid parameters at birth is consistent with the reports from other studies from India and as well as the west [5-7]. There were no significant differences observed in the lipid parameters between low birth weight and normal birth weight babies. This is supported by observations from other studies in the past [8].

Out of the Apo lipoproteins the type B is most strongly associated with ischemic heart disease. The pre terms had a higher Apo-B at birth as well as at one week age compared to the term babies. Apo B is the major apo-lipoprotein component of the atherogenic lipoproteins (VLDL, LDL, IDL). Each atherogenic particle contains 1 molecule of apoB, and therefore plasma apoB represents the total atherogenic particle number [9]. Apolipoprotein-related Mortality Risk (AMORIS) study showed that the age-adjusted values of apo B was strongly and positively related to increased risk of fatal myocardial infarction in men and

women. In multivariate analyses, apo B was a stronger predictor of risk than LDL-cholesterol in both men and women [10].

ApoB is more closely associated with increased body mass index, abdominal obesity, hyperglycemia, insulin resistance, and prothrombogenic and proinflammatory markers [9]. In our study the mean Apo-B values among pre-terms when compared to term, which was 8.6% higher at birth, became 20.36% higher at the end of one week. Keeping in consideration the results from a previous study that, a decrease in Apo-B by 10% is associated with 22% lowered risk of ischemic heart disease, it is plausible for us to state that pre-terms by the virtue of a much higher apo-B are at a far greater risk [6]. Our study results point to the fact that the more premature the baby is the un-healthier the lipid parameters.

There is a major increase in the various lipid values between birth and seven days of life, approaching closer to the adult values. The magnitude of rise in the values of total cholesterol, triglycerides, and apo-B from baseline values at birth, in one week duration was similar to what was observed in a previous study for six month duration. This past study also found no major rise in the values from six months of age to three year of age [11].

Another past study concluded that mean levels of all serum lipids and lipoproteins increased greatly in the first 6 months of life, and by 2 years of age, levels approached those seen in adolescents. Serum lipid and lipoprotein levels at age 7 years were associated with previously measured levels as early as 6 months of age, and infants with unfavorable levels were likely to have similar adverse levels at 7 years of age. In addition, increases in obesity between 6 months and 7 years of age were positively associated with increases in levels of serum triglycerides suggesting that certain persons at increased risk for cardiovascular disease can be identified in infancy [12].

In all prior studies that we could find after extensive search, the earliest a second measure of lipid parameters was done was not before six months of age and hence the trend of lipid profile in between birth to six months may not have been as yet accurately documented. Our study which measured the parameters one week after birth helps bridge the gap. Since the magnitude of increase in major atherogenic lipid parameters is nearly as much as it would be expected at six months based on previous studies, it might imply that the lipid values after birth increase quite rapidly even as fast as one week and remain more or less stable for many years at least into early childhood. Thus lipid profiling as early as one week post birth could be a good indicator of future cardiovascular risk as well as predict likely trend of future lipid profile giving us extra inputs to plan our follow up for the same.

This rise in values was significantly higher for the term babies as compared to the pre term babies. Thus at one week age the serum cholesterol and HDL values of both term and pre term babies were almost equal. However the LDL and Apo-B in pre terms still continued to be higher though at a statistically non-significant level.

The postnatal rise in various lipids reflects the metabolic adaptation to provide adequate energy supply especially to organs like the brain. The rise in pre terms of the various values is sluggish as compared to the term babies. This sluggish rise is probably due to the low lipid stores in the pre term babies as well as the immaturity of the various metabolic processes involved in fat metabolism. As the products of fat oxidation form a valuable fuel for the neonatal brain the preterm infants are at a higher risk for this fuel shortage and may suffer cerebral damage.

In the normal infant, fat accounts for 16% of the total body weight at birth serving as the largest store of energy within the body. As the carbohydrate stores are being rapidly depleted following the delivery, there is a rapid conversion from the utilization of carbohydrate in utero to that of fat. This is further established by the fact that during the first few hours of life the respiratory quotient falls from 1.0 to 0.7 signifying a transfer to fat

as the principal source of energy. Considering the formation of LDL from VLDL, several lines of evidence have suggested that the addition of core lipids to apoB to form a lipoprotein particle within the endoplasmic reticulum (ER) may involve two steps: first, the addition of small amounts of core lipids to membrane-bound apoB, generating a lipid-poor, small apoB-containing particle, and second, the fusion of that particle with a larger, independently formed triglyceride-rich and apoB-free "lipid particle." to form VLDL. Thus, the ability to modulate the size of lipid particles allows an organism to increase the size of apoB-containing TG-rich lipoproteins when nutrients are plentiful and to decrease their size during periods of fasting [13].

In the event of a fat deficiency as in case of pre-terms, this could lead to formation of smaller VLDL and hence a greater conversion of the same into small dense LDL. The smaller VLDL are more prone to getting converted to LDL because they are deficient in Apo-E as well as cholesteryl esters and so poorly taken up by the hepatocytes [14]. Small, dense LDL has a higher affinity for CS-PGs than large buoyant particles, probably because they expose more of the segments binding the glycosaminoglycans (GAGs) than larger LDL. The fat deficit in pre-terms coupled with higher Apo-B in the form of LDL of a smaller size due to the fat deficit (more atherogenic) promotes binding to proteoglycans (PGs) of the intima, by association of specific positive segments of the apo B-100 with the negatively-charged GAGs. PGs cause irreversible structural alterations of LDL that potentiate hydrolytic and oxidative modifications. These alterations also increase LDL uptake by macrophages and smooth muscle cells thus acceleration atherosclerosis [15]. This in turn would make the pre-terms more vulnerable to the atherosclerosis.

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REFERENCES

1. Kannel WB, Mass F, Dawber TR; Atherosclerosis as a pediatric problem. *The Journal of pediatrics*, 1972; 80(4): 544-554.
2. Holme I; An analysis of randomized trials evaluating the effect of cholesterol reduction on total mortality and coronary heart disease incidence. *Circulation*, 1990; 82(6): 1916-1924.
3. Newman TB, Browner WS, Hulley SB; The case against childhood cholesterol screening. *JAMA*, 1990; 264(23): 3039-3043.
4. Law MR, Wald NJ, Thompson SG; By how much and how quickly does reduction in serum cholesterol concentration lower risk of

- ischaemic heart disease. *BMJ*, 1994; 308(6925): 367-372.
5. Barnes K, Westel PJ, Payne ES; Neonatal plasma lipids. *Medical journal of Australia*, 1972; 28: 1002.
 6. Darmady J M, Fosbrooke AS, Lloyd JK; Prospective study of serum cholesterol levels during first year of life. *British Medical Journal*, 1972; 2(5815): 685-688.
 7. Potter JM; Perinatal plasma lipid concentrations. *Aust NZJ Med.*, 1977; 7(2): 155-160.
 8. Brody S, Carlson LA; Plasma lipid concentrations in the newborn with special reference to the distribution of the different lipid fractions. *Clin Chim Acta*, 1962; 7:694-699.
 9. Sniderman AD, StPierre A, Cantin B, Dagenais GR, Despres JP, Lamarche B; Concordance/discordance between plasma apolipoprotein B levels and the cholesterol indexes of atherosclerotic risk. *Am J Cardiol.*, 2003; 91(10): 1173–1177.
 10. Walldius G, Jungner I, Holme I, Aastveit AH, Kolar W, Steiner E; High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): a prospective study. *Lancet*, 2001; 358(9298):2026-2033.
 11. Srinivasan SR, Sharma C, Foster TA, Berenson GS; Longitudinal changes of serum lipid and apoB levels in a newborn-infant cohort. *JAMA*. 1982; 31(2): 167-171.
 12. 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. *JAMA*. 1987; 80(5 Pt 2): 789-796.
 13. Hamilton RL, Wong JS, Cham CM, Nielsen LB, Young SG; Chylomicron-sized lipid particles are formed in the setting of apolipoprotein B deficiency. *J Lipid Res.*, 1998; 39(8):1543-1557.
 14. Havel RJ; Lipoproteins and lipid transport. *Adv Exp Mcd Biol.*, 1975; 63: 37-59.
 15. Camejo G, Hurt-Camejo E, Wiklund O, Bondjers G; Association of apo B lipoproteins with arterial proteoglycans: pathological significance and molecular basis. *Atherosclerosis*, 1998; 139(2): 205-222.