Determination of cord blood lipid profile in neonates and its correlation with birth weight and maternal anthropometry

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ABSTRACT

Introduction: Serum lipid disorders have their roots in childhood and atherogenic changes are postulated to originate early in life. Cord lipid profile is a useful tool in the earlier detection of babies at a higher risk. **Objectives:** The objectives of the study were to assess the early onset dyslipidemia by determining cord blood lipid profile in healthy term newborns and to compare the cord blood lipid profile between terms small for gestational age (SGA) and appropriate for gestational age (AGA) newborns. **Materials and Methods:** This prospective observational study was conducted from October 2013 to October 2014 in the Department of Pediatrics of a Tertiary Care Institution of Central India. All normal term newborns with gestational age between 37 and 42 weeks were included in the study. After thorough examination, their weight, length, and ponderal index (PI) were recorded. Cord blood was collected immediately after the delivery and cord lipid profile was measured. Data were recorded and correlated statistically. **Results:** Of 114 neonates, 71 were AGA, 40 were SGA, and three were large for gestational age. There were 59 (51.8%) female and 55 (48.2%) male neonates. Birth weight, length, gestational age, head circumference, and PI were significantly higher in AGA neonates than SGA neonates ($p<0.001$, 0.013, 0.022, 0.02, and <0.001, respectively). Total cholesterol (TC), triglycerides (TGs), low-density cholesterol (LDL), and very low-density cholesterol (VLDL) levels were significantly higher in term SGA than term AGA neonates. **Conclusion:** Birth weight correlated negatively with LDL, VLDL, TC, and TG. Lipid profile parameters were also higher in babies with maternal body mass index ≥25 kg/m^2.

Key words: *Lipid profile, Cord blood, Ponderal index, Small for gestational age*

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. Recent animal experiments and human studies have shown the influence of the intrauterine environment on the development of risk factors for cardiovascular disease [1]. Low birth weight (LBW), thinness, and short body length are now known to be associated with increased rates of cardiovascular diseases and non-insulin-dependent diabetes mellitus (IDDM) in adult life. The fetal origin hypothesis proposes that these diseases originate through adaptations that a fetus makes when it is undernourished. These adaptations may be cardiovascular, metabolic, or endocrine. They permanently change the structure and function of the body. Prevention of the diseases may depend on the prevention of imbalances in fetal growth or imbalances between prenatal and postnatal growth, or imbalances in nutrient supply to the fetus [2].

Primarily cord blood screening has been utilized to detect the population at greater risk of developing atherosclerosis, a pathological hallmark of coronary heart disease. Its utility is further recognized for lipid fractional analysis, which also has been employed for screening and diagnostic evaluation of various other disorders [3]. Although blood cholesterol and lipid profile have been extensively studied in adults, limited studies are available in pediatric population. There are scanty data on serum lipid levels in preterm and term newborns. This study was undertaken to find out the influence of LBW and growth restriction on cord lipid levels and to compare the cord blood lipid levels in term small for gestational age (SGA) and term appropriate for gestational age (AGA) newborns [4]. The present study was undertaken for early detection of abnormalities in the lipid profile at the earliest (at birth) in the term newborns 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 amelioration of risk factors that contribute to the development of cardiovascular diseases in adult life.

Objectives of our study was to assess to compare the cord blood lipid profile between term SGA and AGA newborn and to correlate it with postpartum maternal anthropometry body mass index (BMI).

MATERIALS AND METHODS

This prospective observational study was conducted from October 2013 to October 2014 in the Department of Pediatrics of a Tertiary Care Institution of Central India. Prior approval from the Institutional Ethics Committee was obtained. All normal term newborns with gestational age between 37 and 42 weeks were included in the study. Newborn babies, delivered in the Department of Obstetrics and Gynecology during this period, fulfilling the inclusion criteria were enrolled in this study. Sample size was calculated by the formula 4 pq/L, where p is prevalence, q is 1–p, and L is level of error, which was 5% in the study.

Following neonates were excluded from the study: Neonates with any congenital malformations; neonates born to mother with maternal illness such as diabetes mellitus (DM) including insulin-dependent DM and gestational diabetes, tuberculosis, asthma, pregnancy-induced hypertension, and thyroid disease; neonates with family history of coronary heart disease/hypercholesterolemia; any maternal medication, except iron and vitamin supplements; drug abuse in mother and antenatal medication; instrumental delivery including extraction; and neonates with 1 min Apgar score <7.

All the subjects were included after obtaining written informed consent from parents/guardian. 5 ml of cord blood was collected from the umbilical cord immediately after the delivery from the placental end of the cord just after the delivery of the baby in a plain dry test tube. Cord blood was allowed to clot and then immediately sent to laboratory where the samples were centrifuged at 400× for 10 min, and then serum was separated and stored at −20°C until analysis.

A thorough clinical examination of the newborn was done and weight of the baby was recorded by electronic weighing scale. Length was recorded with the help of infantometer, head circumference (HC), chest circumference, and other relevant anthropometric data were recorded using non-stretchable measuring tape. Classification of infants was done based on gestational age as term and preterm newborn based on New Ballard's scoring [5]. Intrauterine growth charts developed at AIIMS were used to assess the weight for gestational age. Any baby whose weight was <10th percentile for the respective age was classified as SGA and neonates who were between 10th and 90th percentiles were classified as AGA. Babies were also divided into two groups, first with ponderal index (PI) <2 and second with PI >2. PI was calculated using the formula [6], Ponderal index (PI)=Weight (g)/Length (cm)^3 × 100.

Lipid profile was done using autoanalyzer (Erba Mannheim, Transasia Bio-Medicals Ltd.). Total cholesterol (TC) estimated using modified Roeschlau method, triglycerides (TG) estimated using Wako and the modification by McGowan *et al.* and Fossati *et al.,* high-density lipoprotein (HDL) and low-density lipoprotein (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. Very low-density lipoprotein (VLDL) estimated by TC/5 and atherogenic index (AI) by TC/HDL. Postpartum maternal BMI was calculated using formula - weight/ht^2 (kg/m^2).

Results were expressed as mean ± standard deviation for continuous variables and as number and proportion (%) for categorical data. Microsoft Excel was used for data entry as well as to generate graphs and tables and statistical software SPSS version 20 was used to analyze the data. Unpaired Student's test and Chi-square test are used to find out association and significance p<0.05 was considered statistically significant.

RESULTS

In the present study, the total number of cases was 114, of which 55 were male and 59 were female. 71 (62.3%) were AGA, 40 (35.1%) were SGA, and 3 (2.6%) were large for gestational age.

As shown in Table 1, BW, length, GA, HC, and PI were significantly higher in AGA neonates than SGA neonates.

As shown in Table 2, TC, TG, LDL, VLDL, and AI were significantly higher in term SGA than term AGA babies. HDL levels were also higher in SGA than AGA, but the difference was not statistically significant (p=0.47).

Table 1: Neonatal parameter distribution

Parameters	AGA (n=71)	SGA (n=40)	p value
	Mean±SD	Mean±SD	
Birth weight	2.9±0.3	2.0±0.2	<0.001
Length	47.6±1.4	47.0±1.0	0.013
Gestational age	38.4±1.2	37.9±1.0	0.022
Head circumference	33.5±1.2	33.0±0.9	0.02
Ponderal index	2.9±0.3	2.0±0.0	<0.001

SGA: Small for gestational age, AGA: Appropriate for gestational age, SD: Standard deviation

Table 2: Comparison of cord blood lipid profile between term AGA and term SGA

Lipid profile	Term/AGA	Term/SGA	Total	p value
	Mean±SD	Mean±SD	Mean±SD	
Total cholesterol	71.7±21.3	101.1±27.0	82.6±27.2	<0.001
Triglycerides	66.3±20.0	81.8±22.6	71.2±22.3	0.0006
High-density lipoprotein	28.0±5.3	29.0±7.9	28.4±6.3	0.47
Low-density lipoprotein	34.8±16.7	45.9±8.6	39.3±15.5	<0.001
Very low-density lipoprotein	13.3±4.0	16.6±4.4	14.3±4.5	<0.001
Atherogenic index	2.6±0.9	3.8±1.8	3.0±1.4	<0.001

SGA: Small for gestational age, AGA: Appropriate for gestational age, SD: Standard deviation

As shown in Table 3, TC, TG, LDL, and VLDL levels were significantly higher in babies with PI <2 than PI >2. HDL levels and AI were also higher in babies with PI<2, but the difference was not statistically significant (p = 0.56 and 0.065, respectively).

As shown in Table 4, TC, TG, HDL, LDL, VLDL, and AI were higher in babies with postpartum maternal BMI >25 kg/m^2 than babies with maternal BMI <25 kg/m^2; however, the differences were not statistically significant.

As shown in Table 5, cord lipid profile values were approximately equal in males and females.

DISCUSSION

Recently, interest in cord lipids has increased because serum lipid disorders have their roots in childhood and atherogenic changes are postulated to originate early in life. Lipid profile is a marker of an underlying cardiovascular status, and there is direct correlation between the abnormalities in lipid profile and occurrence of cardiovascular morbidities and mortality.

Levels of lipids and lipoproteins in the cord sera should be a reflection of the status of plasma lipid metabolism in the infant at birth because the most fetal lipids are synthesized *de novo* through the conversion of glucose to various fatty acid-containing compounds. Only part of it is derived from placental circulation, so measurement of cord blood lipid profile will be like measuring lipid metabolism during fetal life and at birth.

Among various factors theorized in the development of atherosclerosis, increased plasma levels of cholesterol and/or triglycerides are considered to be most important. In the present study, among term males and females, the cord blood lipid values were approximately equal with no statistically significant p value. AI values were higher in females which were not statistically significant (p=0.6450). Badiee *et al.* [7] found that irrespective of gestational age, female neonates had significantly higher TC and HDL (p≤0.05 and p≤0.05, respectively); TG and LDL values were also higher in females, but it was not statistically significant.

Magon *et al*. [8] found statistically higher LDL values in females (p<0.005). TC, TG, and HDL values were also higher in females, but the difference was not statistically significant (p>0.05 for all). They also found AI was higher in males (p>0.05). Esfarjani *et al*. [9] found significantly higher TC and LDL in females (p=0.016 and 0.007). In the present study in SGA neonates, cord blood TG, TC, LDL, and VLDL were significantly elevated compared to AGA term neonates. HDL levels were also elevated, but there was no significant difference (p=0.47).

Wang *et al.* [10] also found similar results in their study. SGA neonates had higher TG, TC, and LDL levels than in AGA infants, both among full-term and preterm neonates. There was significant difference between the two groups (p<0.01, 0.04, and 0.01, for TG, TC, and LDL, respectively). Of 93 babies with PI ≥2, 71 were AGA and 19 were SGA. 21 babies had PI <2, all were SGA. There was a significant difference between the PI of both the study groups (p<0.0001). These findings were consistent with other studies conducted by Ramy *et al.* [11] and Arora *et al.* [12], where cord blood LDL, TC, and TG levels showed strong negative correlation with PI.

In our study, cord blood lipid profile was higher in babies with postpartum maternal BMI ≥25 kg/m^2 than babies with maternal BMI <25 kg/m^2; although the results were not statistically significant. In the present study, cord blood lipid profile values in SGA were elevated than in AGA neonates. 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), whereby activating lipid and other metabolisms, 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 [13].

Oba *et al.* [14] in their study concluded that term SGA had significantly higher values of TC, TG, LDL, and HDL compared to term AGA neonates. Kumar *et al.* [15] in their study concluded that term AGA and preterm AGA infants had higher values of TC compared to term SGA and preterm SGA, but values were not statistically significant. Term SGA and preterm SGA had higher

Table 3: Correlation of cord blood lipid profile with ponderal index

Cord blood lipid profile	<2 (n=21)	>2 (n=93)	p value
	Mean±SD	Mean±SD	
Total cholesterol	97.05±18.699	79.37±27.788	0.007
Triglycerides	92.14±17.522	66.43±20.533	<0.0001
High-density lipoprotein	29.10±7.536	28.20±6.012	0.56
Low-density lipoprotein	46.00±9.370	37.73±16.274	0.027
Very low-density lipoprotein	18.52±3.544	13.37±4.133	<0.001
Atherogenic index	3.52±1.632	2.90±1.319	0.065

Table 4: Comparison of cord blood lipid profile with postpartum maternal BMI

Lipid profiles	BMI<25 kg/m^2 (n=79)	BMI >25 kg/m^2 (n=35)	p value
	Mean±SD	Mean±SD	
Total cholesterol	79.7±27.6	89.1±25.3	0.09
Triglycerides	71.1±21.3	71.4±24.8	0.93
High-density lipoprotein	28.3±6.4	28.6±6.1	0.79
Low-density lipoprotein	37.8±15.5	42.5±15.4	0.14
Very low-density lipoprotein	14.3±4.2	14.3±5.1	0.96
Atherogenic index	3.0±1.5	3.1±1.2	0.52

BMI: Body mass index, SD: Standard deviation

Table 5: Comparison of cord blood lipid profile between male and female

Lipid profiles	Males (n=55)	Females (n=59)	p value
	Mean±SD	Mean±SD	
Total cholesterol	82.81±24.1	82.46±29.93	0.94
Triglycerides	72.25±23.22	70.23±21.66	0.6323
High-density lipoprotein	28.65±6.65	28.10±5.98	0.643
Low-density lipoprotein	40.21±16.36	37.57±13.92	0.354
Very low-density lipoprotein	14.45±4.64	14.03±4.33	0.6237
Atherogenic index	2.98±0.98	3.10±1.54	0.645

TG value compared to term AGA and preterm AGA values which were statistically significant ($p \leq 0.05$).

LBW infants are born with intrauterine malnutrition. Such circumstances favor fetal adipose tissue break down liberating free fatty acids, which escapes oxidation for energy, are synthesized in the liver into triglyceride, which causes elevated levels of TG in LBW babies. Intrauterine malnutrition could be the result of placental insufficiency. The prevalent concept is, having bad habits in adult life, such as being sedentary, eating a high-fat diet and smoking causes coronary heart disease. The fetal hypothesis does not deny the importance of these adult factors, it simply adds another layer to the complex and multifactorial etiology of the disease, suggesting that in addition to genetic factors and lifestyle factors fetal nutrition needs to be considered a risk factor. There have been studies to show that coronary heart disease has its roots traceably to infancy. Hyperlipoproteinemia at birth is one of the risk factors for developing coronary artery disease later in life. In our study, there are an elevated TG levels in SGA term newborns. This suggests that a fetus receiving inadequate nutrition has to make adaptations to survive and may be prone to hyperlipidemia [16].

Thus, strategy to prevent coronary heart disease must include measures to improve fetal growth and early detection of hyperlipidemia with dietary intervention during infancy and later childhood. These high-risk babies need vigilant monitoring for prevention of coronary heart diseases in future.

CONCLUSION

TC, TG, LDL, VLDL, and AI were found to be significantly higher in term SGA neonates compared to term AGA neonates. These values were also higher in babies with PI <2 than PI ≥2. Studying for the association of prenatal factors with cord blood lipid profile can serve as a beginning point for studying lipid changes during early life and for correlating them with the cardiovascular diseases later.

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