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ORIGINAL ARTICLE

Lipid Profile & Apolipoproteins in Neonates in relation to Birth Weight and Gestational Maturity

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Abstract:
Background : Cardiovascular disease is a common cause of death in developed countries and also is a rising trend in developing countries. **Aim:** The objective of this study was to study lipid profile& apolipoproteins in neonates in relation to birth weight and gestational maturity. **Methods:** A total of 150 neonates were selected which were grouped on the basis of gestational age and birth weight.Umbilical venous blood was collected from them. Lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, VLDL cholesterol, triglycerides), apolipoproteins (apo B and apo A-I) and atherogenic index were evaluated and compared. Student- t test(unpaired) was applied to test the significance. **Results:** Total cholesterol (TC) and LDL were significantly higher in preterm small for gestational age(SGA) newborns as compared to term SGA neonates (P<0.05). VLDL and apolipoprotein B were increased highly significantly in preterm SGA newborns than in term SGA group(P<0.001) . TC/HDL and LDL/HDL were significantly increased in preterm SGA newborns than in term SGA group (P<0.05) and preterm AGA babies than term AGA group(P<0.05).Apo B/Apo A-I was highly significantly increased in preterm neonates in comparison to term group(0.71v/s 0.54,P<0.001). Gestational age and birth weight were inversely correlated with TC, LDL , VLDL, apolipoprotein B , TC/HDL, LDL/HDL and Apo B/Apo A-I. **Conclusions:** These findings demonstrate a trend towards worse lipid profile in preterm SGA newborns. There is an inverse correlation between a bad lipid profile and birth weight & gestational age. There is a need to investigate if this atherogenic lipid profile is a marker for future cardiovascular diseases.

Keywords: lipid profile, apolipoproteins, gestational age, newborn
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Introduction

The fetal origins hypothesis [1] states that fetal undernutrition in middle to late gestation, which leads to disproportionate fetal growth, programmes later coronary heart disease. Studies in humans have shown that men and women whose birth weights were at the lower end of the normal range, who were thin or short at birth, or who were small in relation to placental size have increased rates of coronary heart disease. The programming of blood pressure, insulin responses to glucose, cholesterol metabolism, blood coagulation, and hormonal settings are all areas of active research. The platform for fetal origins hypothesis is that like other living beings in their early life, human beings are 'plastic' and are able to adapt to their environment but unlike adults, these adaptations made in fetal life have permanent effects on body's structure and function referred to as programming- a critical period when a system is plastic and sensitive to environment followed by loss of plasticity and a

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fixed functional capacity. Barker et al [2,3] demonstrated that low birth weight is correlated with increased prevalence of cardiovascular diseases, hypertension and type 2 diabetes mellitus. This was in synchronization with 'fetal origins' hypothesis and reflects the phenomenon 'programming' whereby a stimulation or insult during critical period of intrauterine life could result in alteration of physiology and metabolism during adult life. The objective of this study is to study lipid profile and apolipoproteins in neonates and their relation with birth weight and gestational maturity.

Material and methods

Setting

It is a hospital based study conducted in a tertiary care hospital.

Study design

A total of 150 cases were selected from neonates attending Neonatal Intensive Care Unit either for monitoring or routine care. Neonates were selected on the basis of gestational age ranging from 32 – 42 weeks and birth weight ranging from 1200 – 3800 grams. Birth weight was taken within 24 hrs of birth on an electronic weighing machine. Gestational age was confirmed by New Ballard et al [4] scoring system done within 24 hrs of birth. Newborns were divided into two groups- term and preterm. Babies less than 37 completed weeks of gestation were taken as preterm and those with 37 completed weeks of gestation up to 42 weeks were taken as term. These were further divided as small for gestation age (SGA) and appropriate for gestational age(AGA) according to birth weight. Babies with birth weight < tenth percentile were SGA and those with birth weight > tenth and < ninetieth percentile were AGA.

Neonates with congenital malformations, congenital heart diseases, mothers having diabetes mellitus, hypertension and myocardial diseases, hypoxia, respiratory distress syndrome, sepsis, Meconium Aspiration Syndrome (MAS), Persistent pulmonary Hypertension (PPHN) and large for gestational age were not included in the study. Informed consent was taken from the parents of newborns included in the study. Umbilical venous blood was collected in a clean, dry vial under full aseptic precautions. Quantity of blood taken was 2 ml. The collected blood was allowed to clot at room temperature and centrifuged to obtain serum. This was used for estimation of Total cholesterol (Total Chol), LDL cholesterol, HDL cholesterol, VLDL cholesterol, Triglycerides (TG) by photometry. Apolipoprotein B (Apo B), Apolipoprotein A-I (Apo A-I) by nephelometry [5,6] TC/HDL, LDL/HDL and Apo B /Apo A-I were calculated as the ratio of these parameters.

Statistical Analysis

Mean values and standard deviation have been used to define data in each group. These values were compared between preterm and term babies of AGA group and preterm and term newborns of SGA group. Student unpaired 't' test was used to test the significance between the data.

Results

Total cholesterol (Total Chol.) was significantly higher in preterm as compared to term newborns in AGA and SGA groups ($p<0.05$, Table-I). LDL and VLDL were higher in preterm neonates as compared to term newborns and this difference was statistically significant ($p<0.05$, $p<0.001$). Apo B level was higher preterm than in term babies both in AGA and SGA group ($p<0.001$). TC/HDL, LDL/HDL, Apo B/Apo A-I were significantly higher in preterm SGA and preterm AGA group as compared to corresponding term groups ($p<0.05$, $p<0.05$, $p<0.001$, Table-II).

Gestational age was inversely correlated to TC, LDL, VLDL,TG,Apo B , TC/HDL, LDL / HDL, Apo B/Apo A-I (Table III).

Birth weight was inversely correlated with TC,LDL VLDL,TG,Apo B ,TC/HDL, LDL/ HDL, Apo B/Apo A-I (Table IV).

Table I. LIPID PROFILE IN TERM AGA AND PRETERM AGA BABIES

	Preterm AGA (n=7) (Mean ± SD)	Term AGA (n=67) (Mean ± SD)	p
TOTAL CHOL.	146.5± 30.7	94.2±34.9	<0.05
LDL	69.8±30.81	36.4±20	<0.05
HDL	30.68±11.72	29±10.7	NS
VLDL	45.8±26.57	28.6±17.5	<0.05
TG	119±26.30	118.5±9	NS
APO B	32.9±21.62	60.8±4.5	<0.001
APO A-I	87.6±14.3	85.8±5.5	NS
TC/HDL	5.37±2.35	3.52±1.4	<0.05
LDL/HDL	2.51±1.26	1.41±0.8	<0.05
APO B/APO A-I	0.75±0.06	0.53±0.08	<0.001

Table II. LIPID PROFILE IN TERM SGA AND PRETERM SGA BABIES

	Preterm SGA (n=62) (Mean ± SD)	Term SGA (n=14) (Mean ± SD)	p
TOTAL CHOL.	162.68±43	132.5±37.8	<0.05
LDL	107.11±31.8	75.51±27	<0.05
HDL	28.45±11.09	27.71±6.3	NS
VLDL	49.8±18.5	27.66±8.3	<0.001
TG	184.13±66.6	133.70±50	<0.05
APO B	65±8. 5	44.64±3.6	<0.001
APO A-I	83.07± 20.8	87.39±11.6	NS
TC/HDL	5.89±2.09	4.90±1.6	<0.05
LDL/HDL	3.9±1.3	2.98±1.4	<0.05
APO B/APO A-I	0.76±0.11	0.54±0.11	<0.001

Discussion

Since total cholesterol increases after birth, it might be presumed that the total cholesterol levels of preterm neonates are similar to or lower than those observed in term infants. The cholesterol levels detected in umbilical cord blood were lower than those found in plasma of adults. This was in agreement with Hellmuth (1926) [7]. However, our results demonstrated that the cholesterol levels of the premature group were substantially higher than those of the term group, in agreement with a previous report [8].

In our study, total cholesterol levels were significantly higher in preterm babies in both AGA and SGA groups (mean 146.50, 162.68 mg/dl) in comparison to term newborns of corresponding groups (mean 94.20, 132.50, $p<0.05$). LDL cholesterol was significantly higher in preterm AGA and SGA groups (mean 69.80, 107.11 mg/ dl respectively) in comparison to term AGA and SGA groups (mean 36.39, 75.51 mg/ dl, $p < 0.05$). This was similar to the result of the study done by Pardo et al, 2005 and by Diaz et al [8,9].

VLDL levels were significantly higher in preterm AGA and SGA (mean 45.80, 49.8 mg/dl) in comparison to term AGA and SGA groups (mean 28.59, 27.68 mg / dl respectively, p is <0.001). HDL cholesterol levels in preterm newborns, both SGA and AGA were not significantly different than term group. Triglycerides level in preterm SGA (mean 184.13 mg/dl) were higher in comparison to term SGA (mean 133.70 mg/dl, $p <0.05$). This was similar to the study done by Badiee, 2007 [10]. Higher TG levels were also seen in growth retarded newborn babies in the study by Koklu et al. [11] and suggested that prenatal events might predispose to later cardio vascular risk.

TC/HDL and LDL / HDL were higher in preterm, both AGA and SGA group than corresponding term groups ($p < 0.001$). Apo B/Apo A-I levels were higher in preterm SGA

Table III. CORRELATION COEFFICIENTS BETWEEN LIPID PROFILE AND GESTATIONAL AGE

	Correlation coefficient (r)	p
Gestational age vs TC	- 0.35	<0.05
Gestational age vs LDL	- 0.37	<0.05
Gestational age vs HDL	0.15	NS
Gestational age vs VLDL	- 0.35	<0.05
Gestational age vs TG	- 0.08	<0.05
Gestational age vs Apo B	- 0.53	<0.05
Gestational age vs ApoA-I	0.01	NS
Gestational age vs TC/HDL	- 0.45	<0.05
Gestational age vs LDL/HDL	- 0.40	<0.05
Gestational age vs ApoB /ApoA-I	- 0.35	<0.05

Table IV. CORRELATION COEFFICIENTS BETWEEN LIPID PROFILE AND BIRTH WEIGHT

	Correlation coefficient (r)	p
Birth weight Vs TC	- 0.53	<0.05
Birth weight Vs LDL	- 0.54	<0.05
Birth weight Vs HDL	0.03	NS
Birth weight Vs VLDL	- 0.45	<0.05
Birth weight Vs TG	- 0.29	<0.05
Birth weight Vs ApoB	- 0.65	<0.05
Birth weight Vs ApoA-I	0.083	>0.05
Birth weight Vs TC/HDL	- 0.56	<0.05
Birth weight Vs LDL/HDL	- 0.56	<0.05
Birth weight Vs ApoB /ApoA-I	- 0.58	<0.05

and preterm AGA (mean 0.76, 0.75 respectively) in comparison to corresponding term groups (mean 0.54, 0.53, p<0.001).

Spear et al. [12] demonstrated that lectin acetyl cholesterol transferase activity was lower in preterm neonates compared with the term infants. However, we found that the decrease of total cholesterol was due to LDL-cholesterol, whereas HDL-cholesterol remained constant. This finding is in conflict with the results of Spear et al [12]. This discrepancy might be explained by the group selection for study or by differences in the design of the studies. Although the concentrations of apolipoprotein A-I were not significantly different, our findings show a trend towards a worse lipid profile in the preterm group, with higher apolipoprotein B levels, related to low-density lipoproteins, and lower apolipoprotein A-I levels, related to the inverse cholesterol transport, that protect against atherosclerotic lesions [13-15]. Moreover the apolipoprotein B/apolipoprotein A-I index, considered to be one of the best markers of risk for cardiovascular disease even during the first year of life [16] was significantly higher in the preterm neonate group compared with the term group, demonstrating that this index is altered even in umbilical blood cord. Future studies could elucidate the reasons and the consequences of these differences between preterm and term neonates.

The gestational age of the newborns correlated inversely with total cholesterol, LDL-cholesterol, VLDL, Apo B and total cholesterol/HDL-cholesterol and LDL-cholesterol/HDL-cholesterol index, confirming the difference in lipid distribution between preterm and term infants. Preterm birth [17] and low birth weight [18] have been described as factors for cardiovascular risk in adult life. Koklu et al found increased aorta intima thickness in IUGR babies [11]. Although the atherogenic process has been recognized as a pediatric problem since 1965, the reversibility of the injuries in this early

phase of life is highly questionable. A new study published by the same authors [19,20] demonstrated the existence of lipid accumulation in the extracranial arteries of aborted fetuses and preterm newborns, demonstrating the atherogenic response to a hypercholesterolemic environment. Our findings demonstrate that total cholesterol, LDL-cholesterol fraction, VLDL and apolipoprotein B are significantly higher in preterm neonates compared with term infants, showing a trend to a worse lipid profile in Indian preterm infants.The present study suggests that worse lipid profile and atherogenic indices were seen in small for gestational age newborns. This, too, can be an area of interest for further research. Therefore, we remark that both gestational age and birth weight were inversely correlated with TC, LDL, VLDL, TG, Apo B, TC / HDL, LDL/HDL and Apo B / Apo A-I. There is also a need to study the outcome of high risk newborns in view of early onset cardiovascular diseases in future.

Conclusions

Hence, it was clearly visible that lipid profile and atherogenic indices were worse in preterm newborns, both AGA and SGA groups than babies of corresponding term groups. It was observed during the study that these parameters were higher in babies of small for gestational age as compared to AGA babies, this need to be studied further. It may be interesting to see whether these susceptible neonates are at increased of developing cardiovascular diseases in future. The study also hints towards the role of adverse maternal conditions in origin of early onset cardiovascular diseases. There is an inverse correlation between a bad lipid profile and birth weight & gestational age. Lesser the latter two, worse the former.

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Competing interests

The authors declare that there are no competing interests.

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