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Original Article

Paediatrics Section

Comparison of Cord Blood Lipid Profile in Preterm Small for Gestational Age and Appropriate for Gestational Age Newborns

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ABSTRACT

Introduction: Coronary heart disease is one of the major causes of morbidity and mortality in current era. The roots of this epidemic have been traced to as early as foetal life by foetal origin hypothesis. There are a few studies which have compared the cord blood lipid profile of preterm and term babies and thereby leading a path to primordial prevention of chronic diseases.

Aim: To study cord blood lipid profile of preterm appropriate for gestational age and preterm small for gestational age neonates and compare atherogenic index of both groups.

Materials and Methods: This cross-sectional study was conducted in 109 preterm infants. Cord blood samples were collected from placental side of umbilical cord at birth and analyzed for lipid profile which includes serum cholesterol, triglycerides, Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL) and apolipoproteins which include ApoA1, Apo B.

Results: Preterm Small for Gestational Age (SGA) neonates had statistically significant higher values of triglycerides, Apo B and atherogenic index compared to preterm Appropriate for Gestational Age (AGA) neonates. Other measured lipid levels were not statistically significant, though the values were higher than reference ranges for term babies.

Conclusion: Prematurity as a factor associated with a more atherogenic lipid profile is re-affirmed and SGA as an additional risk factor has been proven giving scope for future research and primordial prevention.

Keywords: Apolipoprotein B, Atherogenic index, Preterm neonate

INTRODUCTION

Preterm birth, is defined as delivery prior to 37 completed weeks or 259 days of gestation. It is a major challenge for maternal and perinatal care providers worldwide and a leading cause of neonatal morbidity and mortality. Children born pre-maturely have higher rate of learning disability, cerebral palsy, sensory deficits and respiratory illnesses compared to children born at term [1]. These negative health and developmental effects of preterm birth often extend to later life, resulting in enormous medical, educational, psychological and social costs [2]. Premature newborns do not have the opportunity to complete their energy deposits, so they need to use their endogenous reserves basically activating lipid metabolism. The long term consequences of these adaptations have not been explained.

Barker DJ et al., investigated that low birth weight is correlated with an increase in prevalence of cardio vascular diseases, hypertension and Type 2 diabetes mellitus [3]. Researchers recommended that this association is due to programming, a phenomenon where a stimulation and/or insult during a critical period in intra uterine life could result in changes of physiology and metabolism during adult life [4]. Apo A1, Apo B and atherogenic index are regarded as markers of risk for cardiovascular diseases. Recent studies showed that detection of these markers in the umbilical cord blood from the term newborn could recognize neonates at a higher risk for coronary heart disease.

The current study was conducted to evaluate the possible relationship between preterm SGA and AGA and risk of future atherosclerosis by determining umbilical cord serum lipid profile and apolipoproteins and thereby calculating atherogenic index.

MATERIALS AND METHODS

The present study was conducted in the Department of Paediatrics, KMC, Mangaluru, India from November 2012 to March 2014. The study protocol was approved by institutional ethics committee. The study group consisted of 109 preterm newborns who were delivered during the study period and satisfied both inclusion and exclusion criteria.

Inclusion Criteria: Neonates born preterm (28 to 37 weeks) by normal vaginal delivery and caesarean section in Government Lady Goschen hospital Mangaluru, Karnataka, India.

Exclusion Criteria: Out born babies, one-minute Apgar score < 7, babies with congenital anomalies, multiple pregnancies. Newborns were divided into two groups, AGA and SGA, based on birth weight. After taking informed and written consent from parents, 5 ml umbilical venous blood was collected at the time of delivery from placental side of the cord right after cord is clamped and centrifuged to separate the serum. Serum was analyzed for total cholesterol, HDL, LDL, triglycerides, Apo A1, Apo B. Atherogenic index was calculated as ratio of Apo B to Apo A1.

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS version 13.0. The data was represented as mean+standard deviation. Mean values were compared using student t-test. p-value < 0.05 was considered as significant.

RESULTS

Of 109 preterm newborns, 52.2% were AGA and 47.7% were SGA. [Table/Fig-1] shows the relationship of cord blood lipid profile with birth weight. Mean values of total cholesterol, HDL and LDL were higher in AGA newborns compared to SGA newborns. However, the difference was not statistically significant. Serum triglyceride levels were significantly high in SGA newborns ($p<0.05$).

[Table/Fig-2] shows SGA neonates having higher levels of Apo B and atherogenic index than AGA neonates ($p<0.05$ for Apo B and $p<0.01$ for atherogenic index) and the levels of Apo A1 in both

Parameter	AGA	SGA	p-value
Total cholesterol	85.404±22.982	83.654±31.656	0.74
HDL	36.382±12.139	32.575±13.316	0.121
LDL	39.684±15.931	38.885±23.819	0.836
Triglycerides	55.509±26.756	74.596±39.927	0.004

[Table/Fig-1]: Comparison between various lipid parameters.

Parameter	AGA	SGA	p-value
Apo B	40.228±11.650	47.610±21.236	0.025
Apo B / Apo A1	0.494±0.110	0.619±0.264	0.001
Apo A1	81.579±14.754	77.654±19.137	0.231

[Table/Fig-2]: Comparison between apolipoproteins and atherogenic index.

the groups were not statistically significant, implying a worsening trend in the lipid profile of preterm SGA newborns.

DISCUSSION

India ranks among the top 10 countries with highest incidence of preterm births along with Brazil, the United States and Nigeria, demonstrating that preterm birth is truly a global phenomenon [5]. It has been proven in previous studies that preterm birth is a risk factor for future coronary heart disease and other non-communicable diseases. This study was done to see if SGA adds as an additional factor to preterm in the development of these diseases.

Of the 109 newborns studied, 52.2% were AGA and 47.7% were SGA. Preterm birth and low birth weight have been described as factors for cardiovascular disease in adult life. Koklu E et al., found increased aorta intimal thickness in IUGR babies [6]. Study done by Napoli C et al., demonstrated existence of lipid accumulation in the extra cranial arteries of aborted foetuses and preterm newborns, pointing out to the detrimental effects of hypercholesterolemic environment in such an early stage [7].

In the present study, the mean values of total cholesterol, triglycerides and LDL fall between 50th to 95th percentile of reference standards for term babies as per "prevention of coronary and heart disease – 1983" and hence, was higher than observed by earlier researchers, Ophir E et al., and Fosbrooke AS et al., whereas high-density lipoproteins were within fifth to 50th percentile of reference standards [8,9]. The cholesterol levels in umbilical cord blood were lower than those in adults. Since total cholesterol increases after birth, it is possible that the total cholesterol levels of preterm neonates are similar to or lower than those in full term newborns. However, our results showed the cholesterol levels of the premature group were substantially higher than those of the full term group, similar to a previous report by Kherkrulidze P et al., [10].

The mean cholesterol level in the present study was 84.5±27.3 mg/dl which was higher than observed in study done by Kharb S et al., (78.9±24.6) and Tohmaz U et al., (74.8±20.7) in term babies [11,12]. Our study also showed that AGA babies are found to have a higher mean cholesterol levels compared to SGA babies though the difference is not statistically significant.

The mean LDL level in the present study was 39.3±19.9mg/dl which was lower than that found by Magon P et al., (56.5±28.4) in preterm infants [13]. AGA babies had a higher mean LDL levels compared to SGA, a finding similar to that of others done in term babies.

The mean HDL level in the present study was 34.5±12.7mg/dl which was similar to that observed in preterm babies by Tohmaz U et al., (33.1±8) and Magon P et al., (33.8±14.0) [12,13]. AGA babies had a higher mean HDL levels compared to SGA babies which is in agreement to that of Nayak CD et al., in term babies [14].

The mean triglyceride level in the present study was 64.6±34.8mg/dl, which was higher than that observed in study done by Nayak CD et al., in term babies (43.06±15.2) and also a significantly higher value was observed in SGA babies compared to AGA babies [14] [Table/Fig-1] which was in accordance with study done by Huter O et al., [15].

The mean value of HDL cholesterol was similar to that done by Magon P et al., [13] whereas mean LDL value was lower than that found in the same study. The total cholesterol, HDL and LDL levels are found to be higher in AGA babies compared to SGA babies. However, these changes are found to be statistically insignificant and are in accordance to study done by Nayak CD et al., [14].

The mean level of Apo A1 in our study 79.7±17.0 mg/dl was slightly lower than that found by Pardo IM et al., in late preterm Brazilian newborns (89.0±5.48) [16]. This difference can be attributed to different ethnic backgrounds in which the studies were conducted. Whereas, the mean Apo B levels in the present study (43.7±17.2) mg/dl were higher than those observed by Magon P et al., in preterm newborns (30.3±15.2) [13]. The ratio of Apo B to Apo A1 in the current study was slightly higher than that observed in term babies by Kharb S et al., [11], But was similar to that observed by Pardo M et al., in term babies [16].

It is well documented that low Apo A1 and/or increased Apo B are associated with increased cardiovascular risk. Elevated LDL and Apo B levels in young adults are linked with cardiovascular disease in later life. In present study SGA newborns had low Apo A1 levels and higher Apo B and atherogenic index compared to preterm AGA newborns which was statistically significant [Table/Fig-2]. These findings were in accordance to that of Radunovic N et al., who reported a significant difference in Apo B concentrations and the ratio of Apo B to A1 in growth-retarded foetuses when compared with normally grown [17].

LIMITATION

The main limitation of our study is its cross-sectional nature. Future longitudinal studies with long term follow up will be necessary to verify the clinical implications of the current findings.

CONCLUSION

Findings in our study show a trend towards altered lipid profile in the preterm SGA group, with higher Apo B levels and lower Apo A1 levels, related to the reverse cholesterol transport, that protect against atherosclerotic lesions. Moreover, the Apo B/Apo A1 index, considered to be one of the best markers of risk for cardiovascular disease even during the first year of life, was significantly higher in the preterm SGA neonate group compared with the preterm AGA group, demonstrating that this index is altered even in umbilical blood cord. Hence, further studies on preterm cord blood are required to elucidate the consequences of these differences in preterm SGA and AGA newborns and thereby following an approach of primordial prevention to prevent long term consequences.

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