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RESEARCH ARTICLE

CORD BLOOD LIPID PROFILE IN LOW BIRTH WEIGHT BABIES

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ABSTRACT

Introduction: The incidence of metabolic syndrome is increasing, evidence is accumulating that adaptive responses made by the fetus in-utero to malnutrition can result in increased susceptibility to adult onset diseases.

Aim and objective: The objective of the study was to find out the cord blood lipid profile in low birth weight babies so that vigilant monitoring of these high risk babies can be done in future.

Material and method: All babies delivered at Subharti hospital during the one year time frame who fitted the inclusion criteria were enrolled and their cord blood lipid profile was sent. Cord blood was investigated for TC(total cholesterol), TG(triglyceride), HDL(high density lipoprotein), LDL (low density lipoprotein), VLDL(very low density lipoprotein), and AI(atherogenic index which was calculated as TC/HDL). 80 Babies were enrolled and classified according to the weight and gestation age into four categories TAGA, TSGA, PTAGA and PTSGA. Cord blood in these four categories were compared and analyzed.

Conclusion: Preterm and SGA babies had deranged lipid profile at birth and are at higher risk for developing metabolic syndrome later in life. Thus we must be cautious and judicious while fortifying feeds for preterm (PT) and small for gestation age (SGA) babies and life style modifications need to be made right from the start.

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INTRODUCTION

The incidence of metabolic syndrome, type II diabetes and cardiovascular disease is increasing both in the developed and developing countries. This has imposed an economical burden on society and has led to intensive efforts in detection and treatment of these diseases. While the cause of this phenomenon is likely to be multifactorial, evidence is accumulating that adaptive responses made by the fetus in-utero to malnutrition can result in increased susceptibility to adult onset diseases (Kent, 2004). The fetal origins hypothesis (Barker, 2001), in synchronization with BARKER *et al* (Barker, 1993 and Barker, 1993). states that fetal under nutrition in middle to late gestation, leads to disproportionate fetal growth and is associated with increased susceptibility to development of coronary heart disease and allied conditions later in life. It is known that premature and growth restricted newborns have lost the chance to complete their energy deposits in later part of pregnancy.

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Barker and his colleagues showed that abnormalities in cholesterol concentrations were linked to disproportionate size at birth i.e. short body in relation to size of head (sparing of brain growth at cost of other vital organs like liver) (Barker, 1993 and Barker, 1993). Impaired liver growth results in reprogramming of liver metabolism which leads to raised levels of atherogenic lipids Thus, many times these growth restricted neonates need to use these endogenous reserves, there by activating lipid metabolism that generates energy and promotes gluconeogenesis, and also due to the limited supply of the nutrients, the development of essential organs (brain) is favored when compared to non essential organs, such as kidney (nephron mass) and pancreas (beta cell mass). The long-term consequences of these metabolic adaptations will lead on to an increased prevalence of cardiovascular diseases, hypertension and type 2 diabetes mellitus in this group of babies (Rasa *et al*., 2006). This present study was undertaken to find out the influence of intra-uterine growth retardation on cord blood lipid levels in term and preterm, so that vigilant monitoring of these high risk babies can be done in the future. It has been an age old practice in neonatal care units to fortify the feed of a low birth weight baby (preterm or SGA) with

energy dense MCT oils (medium chain triglyceride). But if these babies are prone to cardiovascular diseases, hypertension and type 2 diabetes in future, it is better to make judicious use of feed fortifiers so as to prevent these diseases 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 development of cardio vascular diseases in adult life.

Aims and Objectives

- To find out cord blood lipid profile (TC, TG, HDL, LDL and VLDL) in low birth weight babies.
- To estimate and compare lipid profile (TC, TG, HDL, LDL, VLDL) in term and low birth weight babies.
- To estimate and compare cord blood lipid profile (TC, TG, HDL, LDL, VLDL) among the two subclasses:
- a)LBW-SGA (low birth weight small for gestation age)
- b)LBW-AGA (low birth weight appropriate for gestation age)

MATERIALS AND METHODS

Setting

This study was conducted in the neonatal unit in the department of Pediatrics at Subharti Medical College, Meerut.

Study Design: Hospital based prospective study.

Source of Data

Babies born in June 2013 to June 2014 who fulfilled the inclusion criterion were included. Study subjects included 80 babies in which 33 were full term babies which were considered as the control group and 47 were low birth weight babies. Among the low birth weight babies 15 were Preterm small for gestation age (PT-SGA), 16 were preterm appropriate for gestation age (PT-AGA) and 16 were term small for gestation age (T-SGA) babies.

Inclusion criteria

All neonates who were delivered at Subharti Medical College during the given time frame.

Exclusion criteria

- Neonates with any Congenital malformations.
- Neonates born to mother with maternal illness like Diabetes mellitus (DM) including Insulin dependent diabetes mellitus (IDDM) & gestational diabetes, Tuberculosis, Asthma, Pregnancy induced hypertension, thyroid disease.
- Neonates with family history of coronary heart disease / hypercholesterolemia.
- Any maternal medication, except iron & vitamin supplements.
- Drug abuse in mother and antenatal medications.
- Instrumental delivery including extraction
- Neonates with one minute Apgar score <7
- LGA babies.

Method of the study

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 in a plain dry test tube. Cord blood was allowed to clot and then immediately sent to lab where the samples were centrifuged at 400×for 10 minutes, and then serum was separated and analyzed. The babies were examined, weight was recorded on electronic weighing scale, length was recorded with the help of infantometer, head circumference, chest circumference and other relevant anthropometric data were recorded using non stretchable measuring tape. Gestational age was calculated from the first day of the last menstrual period and in its absence confirmed by clinical assessment using modified New Ballard's score. Babies were classified as AGA and SGA with the help of intrauterine growth charts and Ponderal Index using the Intrauterine growth charts developed at AIIMS.

Any baby whose weight was less than the 10th percentile for the respective age was classified as SGA and neonates who were between 10th and 90th percentiles were classified as AGA. Ponderal Index was computed as, PI = Weight (GM)/Length (CM)3 x 100. Ponderal Index of <2.0 between 29 and 37 weeks of gestation and <2.25 beyond 37 weeks of gestation was taken as a cut off value to classify SGA babies. Lipid profile was done by using VITROS 250 Auto analyzer (Johnson and Johnson Company). TC estimated by using enzymatic method using the kit CHOL-slides [CHE/CHO/POD], TG estimated by using enzymatic method [lipase/GK/GPO/POD] using the kit TRIG- slides. HDL was estimated by phosphotungstic acid MgCl2- without correction for free glycerol enzymatic method. LDL estimated based on Friedmal's Formula (VLDL+HDL-TC).VLDL estimated by TG/5.

Statistical Analysis

Results were expressed as mean ± standard deviation for continuous variables and as number and proportion (%) for categorical data. Since all data are known to be normally distributed, the parametric tests were used for statistical analyses. Differences between SGA, AGA neonates and Preterm, Term neonates and lipid profile in the category PI<2 & PI>2.25 were determined by Student's t test. Chi-square test was applied to test the association between two categorical factors. All the tests of significance were applied at 5% level of significance. Anova test was applied to calculate the relation amongst the four classes.

Statistical software

SPSS software was used for the analysis of the data and Microsoft Excel was used for data entry as well as to generate graphs, tables etc.

Table 1. Comparison of mean values, standard deviation & AI of cord blood lipid profile among term AGA with term SGA, preterm AGA &preterm SGA neonates

lipid Profile	TC Mean±sd	TG Mean±sd	Hdl Mean±sd	Ldl Mean±sd	Vldl mean±sd	AI
T AGA N=31	59.84±17.67	39.03±12.01	19.18±8.46	31.10±15.58	7.83±2.39	2.3±1.07
T SGA N=15	77.06±27.42	41.24±12.72	19.83±4.74	48.44±26.13	8.11±2.53	2.1±0.61
PT AGAN=16	82.28±25.62	59.06±22.62	19.93±10.20	50.47±22.20	11.83±4.49	4.88±5.36
PT SGAN=16	97.80±24.50	48.10±19.14	23.07±6.34	59.63±24.95	9.61±3.82	2.13±0.7

ANOVA						
		Sum of Squares	Df	Mean Square	F	Sig.
TC	Between Groups	16858.062	3	5619.354	10.827	.000
	Within Groups	39445.910	76	519.025		
	Total	56303.972	79			
TG	Between Groups	4700.299	3	1566.766	5.937	.001
	Within Groups	20057.603	76	263.916		
	Total	24757.902	79			
HDL	Between Groups	169.489	3	56.496	.899	.446
	Within Groups	4776.350	76	62.847		
	Total	4945.839	79			
LDL	Between Groups	10368.530	3	3456.177	7.707	.000
	Within Groups	34084.075	76	448.475		
	Total	44452.605	79			
VLDL	Between Groups	191.262	3	63.754	6.080	.001
	Within Groups	796.956	76	10.486		
	Total=	988.218	79			

Table 2. Comparison of mean values, standard deviation& AI of cord blood lipid profile among TERM and PRETERM neonates

LIPID Profile	TC MEAN±SD	TG MEAN±SD	HDL MEAN±SD	LDL MEAN±SD	VLDL MEAN±SD	AI
TERM N=48	65.22±22.40	39.72±12.14	19.38±7.45	36.52±20.85	7.92±2.41	2.25±0.94
PRETERM N=32	90.07±25.93	53.58±21.35	21.50±8.50	55.05±23.70	10.72±4.26	3.5±4.02
P VALUE	<0.001	0.0004	0.2423	0.0004	0.0003	0.04

Table 3. Comparison of mean values, standard deviation & AI of cord blood lipid profile among AGA & SGA neonates

LIPID PROFILE	TC MEAN±SD	TG MEAN±SD	HDL MEAN±SD	LDL MEAN±SD	VLDL MEAN±SD	AI
AGA N=49	67.17±22.94	45.57±18.60	19.42±8.97	37.42±20.01	9.14±3.70	3.15±3.35
SGA N=31	87.80±27.65	46.78±16.46	21.50±5.77	54.22±25.73	8.89±3.30	2.11±0.66
P VALUE	0.0005	0.8472	0.2544	0.0016	0.7599	0.09

Table 4. Comparison of cord blood lipid profile according to ponderal index

LIPID PROFILE	PONDERAL INDEX		P VALUE
	≤2(n=32)	≥2.25(n=38)	
TC	88.96±26.35	60.90±18.51	<0.001*
TG	49.88±19.10	38.84±12.38	0.0049*
HDL	20.99±7.91	18.44±6.59	0.145
LDL	56.54±24.25	33.13±16.40	<0.001*
VLDL	9.92±3.83	7.79±2.47	0.0049*
AI	3.32±4.0	2.33±1.04	0.146

RESULTS

After comparison of lipid profile among the various subclasses the following results were seen.

- From Table 2-Preterms had statistically higher values of TC($p<0.001$), TG($p<0.001$), LDL($p<0.001$), VLDL ($p<0.001$) & AI($p<0.05$) in comparison to term babies.
- From Table 1-PT AGA had significantly higher levels of TC($p<0.001$), TG ($p<0.001$), LDL($p<0.001$), VLDL ($p<0.001$)& AI ($p=0.01$) in comparison to T AGA.
- From Table 1-PT SGA had significantly higher level of TC ($p<0.001$), TG ($p<0.05$). LDL ($p<0.001$) & VLDL ($p=0.05$) in comparison to T AGA.
- Concluding that preterm babies have higher cord blood lipid profile at birth.

- From Table 3-SGA babies had significantly higher values of TC ($p<0.001$) & LDL ($p<0.001$) in comparison to AGA babies.
- From Table 1-T SGA had significantly higher value of TC ($p=0.05$) & LDL ($p< 0.01$) in comparison to T AGA.
- From Table 4-Babies with PI<2.0 had significantly higher values of TC ($p<0.001$), TG ($p <0.01$), LDL ($p<0.001$) & VLDL ($p<0.01$) in comparison to babies with PI ≥2.25.
- None of the studies done up till now (Pardo, 2005; Jane Oba, 2006; Hossain *et al*., 2006; Kelishadi *et al*., 2007; Jain, 2011 and Hetal Jeeyani, 2012) have used Ponderal index to define true small for gestation age babies. Estimation of gestation age is fraught with problems thus Ponderal index is a more reliable marker to find out any intra uterine growth retardation.
- Thus making preterm and SGA babies at higher risk for developing metabolic syndrome later in life.
- ATHEROGENIC INDEX was significantly higher in preterm babies in comparison with term babies and in PT AGA in comparison with T AGA.

This suggests that a fetus receiving inadequate nutrition has to make adaptations in order to survive and may be prone to hyperlipidemia. Thus we must be cautious and judicious while fortifying milk for PT and IUGR babies. Since PT and IUGR babies have deranged lipid profile at birth and are prone to cardiovascular diseases later in life, diet restrictions and life style modifications need to be made right from the start. Measures for early detection of hyperlipidemia with dietary intervention during infancy and childhood need to be taken for these high risk babies along with vigilant monitoring.

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