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STUDY OF CORD BLOOD LIPID PROFILE IN NEWBORNS ACCORDING TO THEIR WEIGHT AND GESTATIONAL AGE

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KEYWORDS :

Introduction:

Cardiovascular diseases are the largest single contributor to global mortality now and will continue to dominate the mortality trends in future. 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 environment risk factors. Recent animal experiments and human studies have shown the influence of intrauterine environment on the development of risk factors for cardiovascular diseases.[1]

In India, the incidence of coronary artery disease (CAD) has increased during the last 30 years, whereas declining trends have been noticed in developed Western Countries. India is in the midst of such demographic transition. The average life expectancy at birth in India is 63.7 years, being 63.1 years, being 63.1 for males and 64.4 for females, compared with the natural average of 41.2 years in 1951-1961. There has been a decline in death rate from 1941 to 1971, followed by sharp decline in birth rate from 1971 onwards. This rise in life expectancy in India is attributed to a decrease in infectious, parasitic, and nutritional disorders and this itself, is a remarkable achievement.[2]

The present study was undertaken for the detection of abnormalities in lipid profile at the earliest (at birth), especially in the preterm and SGA babies, 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 term primary amelioration of risk factors that contribute to development of cardio vascular diseases in adult life.

Materials and Method

STUDY DESIGN: Hospital based prospective observation study.
SOURCE OF DATA:
This study was conducted at Shadan Hospital, Hyderabad from July 2014 to Jan 2016.
Study subjects included 125 babies in which 78 are term babies, 45 are pre term babies and 80 are AGA, 42 are SGA babies.

Method of the study:

This hospital based prospective study was carried out at Shadan Hospital, Hyderabad from July 2014 to Jan 2016. Newborn babies delivered at Shadan Hospital during this period who fulfilled the inclusion criteria were enrolled in this study.

All the subjects were included after obtaining written informed consent from parents/ guardian.

METHOD OF DATA COLLECTION

Data was collected in a predesigned proforms which included socio-demographic profile, obstetric history and cord blood lipid profile values of the neonates.

SPECIMEN COLLECTION AND ANALYSIS

5 ml of cord blood was collected from the umbilical cord immediately after the delivery from placental end of the cord just after delivery of the placenta and cord clamping in a plain dry test tube. Cord blood was allowed to clot and then immediately sent to lab where the samples were centrifuged at 30000rpm for 30 minutes and then serum was separated and stored at -20 ^{0}C until analysis.

From the serum sample total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoprotein(VLDL) were calculated as follows:
1. Serum Cholesterol was measured by CHOD (cholesterol oxidase)-POD (peroxidase) enzymatic method.

2. Serum triglycerides measured by GPO(Glycerol Phosphate Oxidase)-POD (peroxidase) method.
3. Serum HDL measured by homogenous enzymatic calorimetric test.

4. Serum LDL measured by direct enzymatic homogenous calorimetric test.

5. Serum VLDL calculated by TG/5.

After the delivery, 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 confirmed by clinical assessment using New Ballard's score.

Babies were classified as SGA, AGA and LGA with the help of intrauterine growth charts and Ponderal index. Fenton's intrauterine growth charts were used to assess the weight for gestational age. Any baby whose weight was less than the 10th percentile for the respective age and sex was classified as SGA, more

than 90th percentile was classified as LGA 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 29and 27 weeks of gestation and <2.2 beyond 37 weeks of gestation was take as a cut off value to classify SGA babies.

RESULTS

Gestational Age Distribution

Gestational Age Distribution	Number	%
Term	78	62.40
Preterm	45	36.00
Post Term	2	1.60
total	125	100

As per the table in our study of the 125 neonates studied, 78 were term, 45 were preterm and 2 were post term.

Birth Weight Distribution

Birth Weight Distribution	Number	%
AGA	80	64.00
SGA	42	33.60
LGA	3	2.40
TOTAL	125	100

As in table the total number of cases were 125 of which 80 were AGA, 42 were SGA and 3 were LGA.

Gender Distribution

Gender Distribution	Number	%
Male	64	51.20
Female	61	48.80
total	125	100

As per table, Majority of our study subjects belonged to the male gender status (n=64, 51.20%) followed by female gender status (n=61, 48.80%).

Gender Distribution According to Gestational Age

Gender Distribution – Gestational Age	Term	%	Preterm	%	Post Term	%
Male	43	55.13	20	44.44	1	50.00
Female	35	44.87	25	55.56	1	50.00
Total	78	100	45	100	2	100
P Value (fishers Exact Test)				0.6321		

As per table in the present study total number of cases were 125 out of which term males were 43 and term females were 35, preterm males were 20 and preterm females were 25, post term male was 1 and post term female was 1. There was no statistically significant difference between them according to gender (p>0.05).

Gender Distribution According to Birth Weight

Gender Distribution – BirthWeight	AGA	%	SGA	%	LGA	%
Male	44	56.41	19	43.18	1	33.33
Female	36	43.59	23	56.82	2	66.67
Total	80	100	42	100	3	100
						0.3649

As per table in our study the total number of cases were 125 out of which AGA males were 44 and AGA females were 34, SGA males were 19 and SGA females were 25, LGA male was 1 and LGA females was 2. There was no statistically significant difference among them according to gender (p>0.05).

Gestational Age And Birth Weight Distribution

Gestational Age and Birth Weight	Number	%
Term AGA	68	54.40
Term SGA	9	7.20
Preterm AGA	11	8.80
Preterm SGA	34	27.20
Others	3	2.40
Total	125	100

As per table the total study population was 125vout of which term AGA were 68, term SGA were 9, preterm AGA were 11, preterm SGA were 34 and others were 3. The majority were term Appropriate for Gestational Age neonates(54.4%).

NOTE : Since the number of post term and LGA neonates was very small we excluded them from further statistical analysis.

Gestational Age Distribution in Weeks

Gestational Age Distribution in weeks	Term	%	Preterm	%	Combined	%
<37 weeks	0	0.00	45	100.00	45	36.59
37-40 weeks	77	98.72	0	0.00	77	62.60
41 weeks	1	1.28	0	0.00	1	0.81
Total	78	100	45	100	123	100
Gestational Age Distribution in weeks		Term (n=78		Preterm (n=45)		Combined (n=125)
Mean ± SD		38.59 ± 1.02		34.38 ± 1.63		

As per table majority of the term study subject belonged to 37-40 weeks gestational age group (n=77, 98.72%) with a mean gestational age of 38.59 weeks. In the preterm study subjects, all belonged to the <37 weeks gestational age group (n=45, 100%) with a mean gestational age of 34.38 weeks.

Birth Weight Distribution According to Gestational Age

Birth Weight Distribution Vs Gestational Age	Term	%	Preterm	%	Combined	%
≤ 1.5 kgs	1	1.28	10	22.22	11	8.94
1.51-2.0 kgs	5	6.41	25	55.56	30	24.39
2.01-2.5 kgs	8	10.26	10	22.22	18	14.63
2.51-3.0 kgs	44	56.41	0	0.00	44	35.77
>3.0 kgs	20	25.64	0	0.00	20	1626
Total	78	100	45	100	123	100
Birth Weight Distribution Vs Gestational Age		Term (n=78)		Preterm (n=45)		Combined (n=125)
Mean ± SD		2.77 ± 0.45		1.78 ± 0.36		2.42 + 0.64

As per the table in the present study majority of the term neonates had birth weight in the range of 2.52-3.0 kgs (44%) and majority of the preterm neonates had birth weight in the range of 1.51-2.0 kgs (55.56%). Mean birth weight for term babies was 2.77 ± 0.45 and for preterm babies the mean birth weight was 1.78 ± 0.36.

Neonatal Parameter Distribution According to the Gestational Age

Neonatal Parameters Distribution – Gestational Age		Gestational Age in kgs	Birth weight in kgs	Lenth in cms	Head circumference in cms	Ponderal Index in gm/cm^3
Term (n=78)	Mean	38.59 ± 1.02	2.77 ± 0.45	47.42 ± 1.45	33.73 ± 1.05	2.60 ± 0.32

Preterm (n=45)	Mean	34.38 ± 1.63	1.78 ± 0.36	45.67± 1.86	32.84 ± 1.71	1.85 ± 0.24
P value Unpaired t Test		<0.0001*	<0.0001*	<0.0001*	0.0024*	<0.0001*

As per table in the present study there was a statistically significant correlation between neonatal parameters (gestational age in weeks, birth weight, length, head circumference and PI values) and gestational age (term and preterm) with P-value <0.05.

Neonatal parameters Distribution According to Birth weight

Neonatal Parameters Distribution – Fetal Maturity	Gestational Age in Weeks	Birth Weight in kgs	Length in cms	Head Circumference in cms	Ponderal Index in gm/cm³
AGA(n=80)	37.75 ± 2.25	2.72 ± 0.46	47.28 ± 1.47	33.78 ± 1.06	2.55 ± 0.36
SGA (n=42)	35.67 ± 2.09	1.8 ± 0.37	45.79 ± 2.01	32.67 ± 1.65	1.87. ± 0.22
P value Unpaired t Test	<0.0001*	<07.0001*	<0.0001*	<0.0002*	<0.0001 *

According to table in the present study there was a statistically significant correlation between neonatal parameters (gestational age in weeks, birth weight, length, head circumference and PI values) and birth weight (SGA and AGA) with p value < 0.05.

Ponderal Index Distribution

Ponderal Index Distribution	AGA	%	SGA	%	Combined	%
< 2	8	10.00	35	83.33	43	35.25
>2.0	72	90.00	7	16.67	79	64.75
Total	80	100	42	100	122	100
Ponderal Index Distribution		**AGA (n=80)**		**SGA (n=42)**		**Combined (n=125)**
Mean + SD		2.55 + 0.36		1.87 + 0.22		2.33 + 0.46
P value Unpaired t Test				<0.0001*		

As per table in the present study majority of the AGA neonates had PI> 2 and the SGA neonates had PI < 2. The mean PI in AGA was higher (2.55 ± 0.36) when compared to SGA (1.87 ± 0.22) with statistical Significance (p<0.05)

Ponderal Index Distribution Among SGA Neonates

Ponderal Index Distribution - SGA	Term	%	Preterm	%	Combined	%
< 2	6	66.67	29	87.88	35	83.33
>2.0	3	33.33	4	12.12	7	16.67
Total	9	100	33	100	42	100
Ponderal Index Distribution - SGA		**Term (n=9)**		**Preterm (n=33)**		**Combined (n=42)**
Mean + SD		2.02 + 0.13		1.83 + 0.22		1.87 + 0.22
P value Unpaired t Test				0.0031*		

As per table in the present study total number Sga neonates were 42 out of which 35 neonates had P < 2 and 7 neonates had PI > 2. The mean PI in term was higher (2.02 ± 0.13) when compared to preterm (1.83 ± 0.22) with statistical significance. (p< 0.05)

Comparison of the Cord Lipid Profile According to the Gestational Age

Lipid Profile Vs Gestational Age	TC	TG	HDL	LDL	VLDL
Term (n=78)	73.69 + 19.86	68.44 + 20.52	27.23 + 5.21	36.65 + 16.28	13.73 + 4.21
Preterm (n=45)	97.56 + 21.94	83.80 + 21.37	33.16 + 11.72	51.51 + 16.88	16.76 + 4.27
P value Unpaired t Test	<0.001*	<0.0002*	<0.0022*	<0.001*	<0.0003*

As per table in the present study 78 neonates were term and 45 neonates were preterm neonates. The preterm neonates had higher TC, TGL, HDL, LDL, and VLDL compared to term neonates which was statistically significant with P value < 0.05.

Comparison of the Cord lipid Profile According to the Birth Weight

Lipid Profile Vs Gestational Age	TC	TG	HDL	LDL	VLDL
AGA (n=80)	75.29 + 23.35	65.40 + 19.69	29.85 + 7.71	38.30 + 18.95	13.13 + 4.05
SGA (n=42)	96.36 + 17.32	90.55 + 16.54	28.57 + 10.35	49.76 + 12.95	18.11 + 3.31
P value Unpaired t Test	<0.001*	<0.001*	<0.4837	<0.0001*	<0.001*

As per table in the present study there were 80 AGA neonates and 42 SGA neonates.

The SGA neonates had higher TC, TG, LDL and VLDL compared to AGA neonates which was statistically with P value < 0.05. The SGA neonates had lower HDL compared to the AGA neonates which was not statistically significant (P >0.05)

DISCUSSION :

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. There are many studies showing direct relationship between the abnormalities in lipid profile among the preterm and SGA neonates and occurrence of cardiovascular diseases. The present study was undertaken for early detection of abnormalities in the lipid profile at the earliest (at birth), especially in the preterm and SGA neonates, so that these high risk babies can be vigilant monitoring in future.

GENDER :

TABLE 24: COMPARISION OF INFLUENCE OF THE GENDER OF NEONATE ON CORD LIPID PROFILE

Lipid Profile	Present Study		Jagadish Singh et al.[13]		Badiee Zet al.[16]		Khalid Mirza et al.[19]	
	Male	Female	Male	Female	Male	Female	Male	Female
TC	78.11 + 22.25	86.95 + 24.26*	88.70 + 19.10	91.10 + 17.20*	75.20 + 21.10	81.40 + 28.10*	166.03 06.99	166.80 06.64*
TG	70.81 + 20.69	77.47 + 23.05	-	-	61.00 + 02.00	62.00 + 02.00	56.30 06.83	59.29 06.16
HDL	29.10 + 8.75	29.72 + 8.62	-	-	28.80 + 08.70	31.18 + 09.97*	74.68 07.11	75.14 05.83*
LDL	38.22 + 14.50	46.15 + 20.28*	-	-	32.10 + 16.30	35.90 + 22.40	-	-
VLDL	14.15 + 4.14	15.57 + 4.71	-	-	-	-	-	-

As per the table in the present study, statistically significant higher TC and LDL were observed in female neonates. While TG, HDL and VLDL were higher in female neonates with respect to male, it was not statistically significant.

In studies by Badiee z et al.[16] Khalid Mirza et al.[19] female neonates had significantly higher TC and HDL. LDL value was higher in females in study done by Badiee Z et al but it was not statistically significant[16]. In a study by Jagadish Singh et al.[13] among term males and females the cord lipid profile values were approximately equal with no statistically significant p value.[13]

N.Haridas and P.T. Acharya et al.[8] In their study concluded that preterm neonates have higher TG and TC levels but statistically significant difference was found only in TC levels.
Mathur et al.[9] in their study concluded that in preterm neonates TC value was significantly high.

Jane Oba et al.[14] in their study concluded that TC LDL, HDL values were significantly higher in preterm neonates, TG values were significantly lower in preterm neonates.

Pardo et al.[4] in their study concluded that TC, LDL, HDL were higher in preterm neonates compared to term neonates with statistically significant difference in TC and LDL levels, but HDL had no statistically significant difference. A1 values were more in preterm compared to term which was not statistically significant.

A K Kalra et al.[10] in their study concluded that all Cord lipid profile values were lower in preterm neonates compared to term neonates but statistically significant difference was found with TC levels and no statistically significant difference was found with HDL and LDL levels.

Jagadish Singh et al.[13] in their study concluded that term neonates had higher TC compared to preterm neonates with statistically significant difference.

P.K Mishra et al.[7] in their study concluded that TG levels were more compared to preterm with no statistically significant difference.

In our study higher cord lipid levels in preterm babies could be explained by the fact that preterm babies lack both hepatic carbohydrate and subcutaneous adipose stores, with a result that circulating fuel are low and may run out. Rise in cord blood Cholesterol levels may reflect the metabolic adaptation to provide adequate energy, especially to organs like brain.
Jone et al.[11] Danial et al.[6] Wang et al.[12] and Hossain et al.[5] in their studies had similar results.

In the present study cord blood lipid profile values in SGA were elevate when compared to AGA, the reason is that, there is lack of glucose fuel in SGA babies , so these babies use alternative source as a fuel (amino acid and lipids) are generate glucose (gluconeogenesis), where by activating lipid and other metabolism , so there there will be increased hepatic generation of lipids (particular VLDL and cylomicrons) also, there is decreased activity of lipoprotein lipase enzyme in growth restired babies. These two facts explain higher concentration of plasma lipid in SGA babies.[3,4,12]

Barker hypothesis demonstrated that low birth weight correlated with an increased prevalence of cardiovascular disease, hypertension and type 2 diabetes mellitus and suggested that this association reflects the phenomenon known as programming, whereby a stimulation or insult during a critical period of intrauterine life could also result in alterations of physiology and metabolism during adult life.[17,18]

Jane Oba et al.[14] in their study concluded that Preterm SGA had higher values of TC, TG, LDL, HDL compared to preterm AGA which was statistically significant with P values <0.0001, <0.01, <0.0001, <0.0001 respectively and Term SGA had higher values of TC, TG, LDL, HDL compared to term AGA which was statistically significant with P values <0.0001, <0.01, <0.0001, <0.0001, respectively.
In our study there is an increase in the cord blood levels of total cholesterol in preterm newborns and an elevated TG levels in low birth weight newborns. This suggests that a fetus receiving inadequate nutrition has to make adaptations in order to survive and may be prone to hyperlipidemia. Thus strategy to prevent coronary heart disease must include measures to improve fetal growth and ear;y detection of hyperlipidemia with dietary intervention during infancy and later childhood.

NEONATAL PARAMETERS :

Birth Weight :

In the present study the average birth weight was 2.42 $\pm$ 0.64. Average birth weight of SGA was 1.78 $\pm$ 0.37 with statistical significance. Similarly study conducted by Pardo et al.[4] and Jones et al.[3] found the birth weight to be 2.04 $\pm$ 0.76 and 2.07 $\pm$ 0.53 respectively, which was also statistically significant. But in studies done by Kelishadi et al.[15] and Wang et al.[12] mean birth weight was 2.34 and 2.22 $\pm$ 0.55 respectively which was higher when compared to present study because they have used only term SGA babies as cases where as in present study and Pardo et al.[4] study both term and preterm SGA were included in the study group.

Ponderal Index :

in the present study average Ponderal index was 1.87 $\pm$ 0.22 which was statistically significant and in study by Kelishadi et al.[15] It was 2.18, and it was not significant statistically.

Gestational Age :

In the present study mean Gestational age was found out to be 37.13 $\pm$ 2.46 Weeks. In the study by Pardo et al.[4] which included both term and preterm SGA neonates in the study group, mean gestational age is 35.57 $\pm$ 0.11 wks, as both studies Other studies like Kelishadi et al.[15] and Wang et al.[12] had higher gestational age as they had included only term SGA neonates in the study group.

CONCLUSION :

The following conclusions were drawn from this study:

GENDER :

Statistically significant higher TC and LDL were observed in female neonates. While TG, HDL AND VLDL were higher in female neonates with respect to male, it was not statistically significant.

GESTATIONAL AGE :

Preterm had significantly higher values of TC, TG, HDL, LDL, VLDL compared to term neonates.

BIRTH WEIGHT :

In SGA neonates cord blood triglycerides, total cholesterol, LDL, VLDL were significantly elevated and HDL levels were decreased with no statistical significance compared to AGA neonates.

GESTATIONAL AGE & BIRTH WEIGHT:

TGL, HDL and LDL were significantly higher in term SGA compared to term AGA. HDL was found to be statistically higher in preterm SGA when compared to preterm AGA. All cord lipid profile parameters were found to be significantly higher in preterm AGA when compared to term AGA . TGL, HDL AND VLDL were found to be significantly higher in preterm SGA when compared to term SGA.

PONDERAL INDEX:

All cord blood lipid profile parameters were significantly higher in neonates with PI $\leq$ 2.

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