Research Paper Medical Science

Cord Blood Lipid Profile at Birth Among Normal Indian Newborns and Its Relation to Gestational Maturity and Birth Weight- A Cross Sectional Study

* Pushpendra Magon ** R.S Bharatwaj*** Manorama Verma **** Jugesh Chatwal

* Associate Professor, Dept Of Paediatrics, Punjab Institute Of Medical Sciences C-25, Silver heights apartments, Nakodar Road, Jalandhar City- 144001

** Associate Professor, Dept Of Community Medicine, Sri Lakshminarayana Institute Of Medical Sciences, Pondicherry- 605502

*** Former Prof & HOD, Dept Of Paediatrics, Christian Medical College, Brown Road, Ludhiana-141008

**** Prof, Dept of Paediatrics, Christian Medical College, Brown Road, Ludhiana-141008

ABSTRACT

Background: Coronary heart disease has its roots from the earliest phase of life as the fetal origin of atherosclerosis is a known fact. This study undertook estimation of the lipid values for an Indian cohort of newborns at birth.

Methods: This cross sectional study comprised of 504 singleton live healthy Indian newborns, whose mothers had no history of diabetes, hypertension and other pregnancy complications. . Cord blood samples were collected from the placental side of the umbilical cord at birth and analyzed for the lipid profile which included Serum cholesterol, Low density lipoprotein [LDL], Very Low density lipoprotein [VLDL], High density lipoprotein [HDL], Low density lipoprotein cholesterol [LDL-C], Triglycerides and Apo lipoprotein-B [Apo-B].

Result: Cord blood of female newborns had higher mean levels of T.Cholesterol, LDL, VLDL, Triglycerides, Chylomicrons, HDL, Apo-B and LDL-C where the greater LDL-C was statistically significant. Only the T.Cholestrol/HDl was lower in the females. The pre term neonates had a statistically significant higher value of all the lipid parameters except Triglycerides, HDL and Apo-B compared to the term neonates. The mean cholesterol/HDL ratio was also significantly higher among the preterm babies.

Conclusions: Prenatal environment as a determining factor in neonatal lipid profile is brought forth. Prematurity as a factor associated with a more atherogenic lipid profile is re-affirmed. The need to consider these findings in the light of lipid transport system changes during early life, opens up scope for further research.

Keywords : Newborn, Lipid profile, Gestation, India

Introduction

Observations from both epidemiological and clinical studies have suggested that the pathological process of coronary artery disease begins in childhood. The aortas of children as young as 3-4 years age often contain intimal lipid deposits, commonly called “fatty streaks”.[1] Studies have shown an enhanced rate of coronary heart disease among men and women whose birth weights were at the lower end of the normal range and who were thin or short at birth. Under-nutrition in the middle to late gestation leading to disproportionate fetal growth programmes later coronary heart disease as per the ‘Fetal origins hypothesis’. Barker et al demonstrated that low birth weight is correlated with increased prevalence of cardiovascular hypertension and type 2 diabetes [2]. The objectives of this study were to estimate the lipid profile including apolipoprotiens in neonates and look for an association with birth weight and gestational age.

Methods

After obtaining informed consent from the mothers all the 504 singleton live babies, whose mothers had no history of diabetes, hypertension and other pregnancy complications, born at a tertiary care teaching hospital over a 2 year period in the Department of Obstetrics and Pediatric Medicine were the study subjects. . Routine examination was performed for all of these babies at birth.Gestational age was assessed from the history of the mother and the clinical examination of the new born according to the criteria of Dubowitz et all[3], the latter being given more weightage in case of discrepancy. Cord blood samples were collected from the placental side of the umbilical cord at birth and analyzed for the lipid profile which included Serum cholesterol, Low density lipoprotein [LDL], Very Low density lipoprotein [VLDL], High density lipoprotein [HDL], Low density lipoprotein cholesterol [LDL-C], Triglycerides and Apo lipoprotein-B [Apo-B]. For the estimation of Total Cholesterol and HDL the CHOD-PAP method was used and for Triglycerides GPO-PAP method was used. The Apo-B levels were estimated by immunoturbidometric method using kits from Boehringer Mannheim that were adapted for the auto analyzer (RA XT). Estimation of differential lipids was done by nephalometry. Mean plus or minus two standard deviation was calculated for all the different parameters and used in our analysis. Tests for “significance of difference in means” were used for the statistical work that was accomplished with the statistical software SPSS 15.

Results

There were a total of 504 new borns who were our study subjects out of which the proportion of males was more: 286 (56.7%). Considering the gestational age, 462(91.9%) were

term babies and 42 were preterm [below 36 weeks gestation]. Looking at the birth weights, 92(18.25%) of the neonates were of a low birth weight [<2.5Kg].Of the 462 term babies, 20 (4.3%) were small for gestational age (SGA), 383 (82.9%) were appropriate for gestational age and 59(12.7%) were large for gestational age. Among the 42 preterms 1(2.3%) was SGA, 37(88.9%) were AGA and 4(9.5%) were LGA babies.

Comparing between genders, at birth, the mean values for all the parameters was higher in the female neonates compared to their male counterparts though the difference was statistically significant only in the values of Low density lipoprotein[LDL-C].[Table 1]

When lipid parameter values were compared based on the birth weight, we found that there was no statistically significant difference in any of the values except for VLDL and chylomicrons, between low birth weight and normal birth weight neonates [Table 2]

Examining the gestational age and its role in the lipid profile, at birth the pre term neonates had a statistically significant higher value of all the lipid parameters except Triglycerides, HDL and Apo-B compared to the term neonates. The mean cholesterol/HDL ratio was also significantly higher among the preterm babies [Table 3].

Considering the mean lipid values at different gestational ages week wise among the pre term deliveries there was no consistent trend observed for the parameters. Further taking the pre terms as a group and evaluating them based on the gestational age, as, above and below 34 weeks we found that, at birth among the pre term neonates those lesser than 34 weeks gestation had a higher value of all the lipid parameters. The difference was statistically significant for the Total cholesterol and triglycerides.[Table 4]

Among the term babies when we compared the lipid values based on intrauterine growth at birth we found that in SGA babies the cholesterol, LDL, LDLC, Apo B were low but HDLC was high indicating that term SGA infants have a more favorable lipid profile compared to AGA babies.[Table 5]

Discussion

Atherosclerosis originates during childhood and the serum lipid levels are a key factor in the process. The observations on a newborn cohort offer an opportunity to study the risk factor variables in the earliest stage. The observations in infancy provide a background for the studies in older children and adults.

In the present study 8.1% of the neonates were preterm. This is much lower than what was observed in other studies in India where the proportion of pre terms was 25% and 36.9% Also the proportion of low birth weight in our study was 18.3% which is lower than the values of 32.1% and 23% found in past studies [4,5].This could be due to a better antenatal care at the tertiary care centre where health care was not free and all the parents belonged to the upper socio economic status.

The mean values for all the parameters was higher in the female neonates compared to their male counterparts. Gender based differences in lipoprotein metabolism have been reported to be implicated in lipoprotein differences.[6]

The mean cholesterol in this study was 83.3±28.1 mg/dl which is similar to various other reports from India as well as the west. Where the values were, 76±19[7], 94±32 [8], 79±17[9]. Lower values ranging from 64±19 to 72±have been noted in other studies[10]. Higher value upto 105.6±17.1 has also been noted [3]

The mean triglyceride levels noted in the present study were much lower as compared to standard adult values. Perhaps the quiescent state of fat utilization in the fetus and the absence of need for fat mobilization is responsible for low serum triglycerides at birth. The values of HDLC and LDLC were similar to those reported in other studies[7,8]. A lot of variability in the value of VLDL was noted (Mean ± 175 mg/dl) which reduces the significance of this parameter.

Out of the apolipoproteins, the type B (Apo B) is most strongly associated with ischemic heart disease risk. A decrese in Apo B of 10% was associated with 22% reduction in risk of ischemic heart disease [11]. In our study the Apo B levels in the cord blood were found to be 28.1±16.9 which is similar to the value of 25.4±1.2 reported by a past study[10]

It was noted in our study that the more premature the baby is , higher are the lipid parameters significantly so for cholesterol, chylomicrons, VLDL, LDL and LDLC. No Significant difference was observed in the triglyceride and Apo B values between terms and preterms.This is in contrast to a past study that reports a higher triglyceride value among the preterms[5]. Also contrary to the present findings lower levels of cholesterol and other lipids in preterms compared to term babies was noted in studies by Kalra and Mathur. [4,12]. An interesting observation in our study was that the levels of VLDL in the preterms were significantly higher than their term counterparts. This may partly be due to the fact that VLDL is not adequately metabolized by the immature system of the pre term infants.

Birth weight is a measure of fetal growth which summates head size, body length and subcutaneous fat. Studies in preston have shown that babies who have a reduced birth weight in relation to gestation tend as adults to develop syndrome “X” a combination of hypertension, non-insulin dependent diabetes mellitus, disordered lipids, hyperinsulinemia, obesity and abdominal fatness.[2]. The present study demonstrated that cord blood cholesrol levels do not have a singnficant association with the birth weight as has been reported by kumar et al [5]. Birth weight (below and above 2.5 Kg) did not find any significant association with any of the other lipid parameters except VLDL and chylomicrons. In studies by Desai also no association was found between the birth weight and lipid levels [9] but in a study by Mathur a significantly lower cholesterol was found among babies weighing lower than 2.5 Kg [4].

‘Small for gestational age babies are more often hypertriglyceridemic and hyper cholestrolemic when compared to those of normal size’ [13]. The present study showed that mean cholesterol was lower in SGA babies compared to AGA. Even other lipid values except for HDLC were found to be lower though not statistically significant. Total cholesterol/HDL ratio of term SGA was also found to be significantly lower.

Preterm birth and low birth weight have been described as factors for cardiovascular disease in adult life[14,15]. Koklu et al found increased aorta intimal thickness in IUGR babies[16]. A study in the not so distant past has demonstrated existence of lipid accumulations in the extra cranial arteries of aborted fetuses and preterm newborns pointing out to the damaging effects of a hypercholesterolemic environment at such an early stage. [17]

In this study birth weight with a cut off point of 2.5 Kg did not influence the lipid values much which is in agreement with a few past studies but at the same time there has been a variability where in other study results have shown that birth weight does influence the lipid values. Studies have found that fetal growth retardation establishes a life-long irreversible atherogenic profile and that those adults with history of a low birth weight are reported to have an atherogenic profile[18]. Barker et al have reported an inverse correlation of birth weight and neonatal abdominal circumference with adult serum cholesterol, LDLC and Apo B levels suggesting that the association between aberrant lipoprotein metabolism and low birth weight is present by the time intrauterine growth restriction is clinically evident[2] . Other reports have demonstrated that abnormal lipoprotein profiles in childhood persist into adult life.

[19]. At best we cant make any definite conclusions from our study concerning birth weight as a predictor of neonatal lipid profiles at birth but in the light of these previous studies we may suggest that the cut off point of 2.5 Kg as a guideline for assessment could be masking the actual situation and by altering the cut off to a lower value we might be in a better situation to predict the atherogenicity of the lipid profile at birth as a risk for health implications in adulthood.

Though atherogenesis as a pediatric process has been known for decades, the reversibility of the injuries in this early phase of life is open to speculation. However since many adult studies have shown a beneficial effect in maintaining cholesterol values within limits it is not difficult for us to see that even at the early stage of life knowing the lipid parameters is of value as it might help in controlling the damage already caused by atherogenesi

Conclusions:

The findings in this study again reaffirm the link between prenatal factors and cord blood lipid profile. The points of interest in the present study are that there is a significantly unhealthy lipid profile among the preterms when compared to terms where in, with the values noted at birth, we might safely say that the preterms are exposed to a more hypercholestrolemic and potentially more atherogenic environment than their term counterparts. Also the more the prematurity greater were the cholesterol values. Since this process of vessel damage is not a onetime event and needs the blood environment for a long term to be promotive to the process, this opens up scope for further research to track the lipid values as the neonate grows and note the natural trend.

Conflict of interest:

The authors have no conflicts of interest.

Financial Support:
Nil

Table 1-Lipid Parameters At Birth For Male And Female Neonates

LIPIDS	**MALES**	**FEMALES**	P VALUE
TOTAL CHOLESTROL	81.8 ± 27.6	86.5 ± 28.6	> 0.05
HDL	31.8 ± 15.5	33.4 ± 14.5	> 0.05
TRIGLYCERIDES	63.4 ± 44.5	66.5 ± 42.4	> 0.05
CHYLOMICRONS	26.9 ± 27.3	29.6 ± 27.5	> 0.05
VLDL	187.9 ± 177.4	199.2 ± 172.2	> 0.05
LDL	147.6 ± 97.2	154.4 ± 103.6	> 0.05
LDL-C	39.2 ± 23.2	45.3 ± 24.8	<0.005
APO -B	27.9 ± 16.0	28.4 ± 18.0	> 0.05
TC/HDL	2.9 ± 1.4	2.8 ± 1.9	> 0.05

Table 2-Lipid Parameters At Birth based on birth weight

LIPIDS	Birth Weight less than or equal to 2.5 Kg	Birth Weight more than 2.5 Kg	P VALUE
TOTAL CHOLESTROL	83.2±32	83.3±26.9	> 0.05
HDL	33±14.8	32.2±15.2	> 0.05
TRIGLYCERIDES	65.5±44.8	64.8±43.5	> 0.05
CHYLOMICRONS	33.2±31.5	26.3±25.6	< 0.05
VLDL	237.2±212.6	165.3±165.8	< 0.05
LDL	149.1±72.6	149.8±64.8	> 0.05
LDL-C	42.7±25.6	41±23.3	> 0.05
APO -B	26.8±19.2	28.3±17.3	> 0.05

Table 3-Lipid Parameters At Birth Based On Maturity

LIPIDS	**PRETERM**	**TERM**	P VALUE
TOTAL CHOLESTROL	101.6 ± 34.1	82.2 ± 26.9	<0.001
HDL	33.8 ± 14.0	32.4 ± 15.2	>0.05
TRIGLYCERIDES	67.9 ± 53.0	64.5 ± 42.7	>0.05
CHYLOMICRONS	42.9 ± 31.7	26.6 ± 26.6	<0.01
VLDL	340.0 ± 237.3	179.0 ± 162.3	<0.001
LDL	172.1 ± 87.5	148.6 ± 64.0	<0.05
LDL-C	56.5 ± 28.4	40.5 ± 23.3	<0.001
APO -B	30.3 ± 15.2	27.9 ± 17.1	>0.05
TC/HDL	2.9 ± 1.4	2.8 ± 1.9	<0.01

Table 4-Lipid Parameters At Birth among preterms below and above 34 weeks gestation

LIPIDS	**UPTO 34 WKS**	**>34 WKS**	P VALUE
TOTAL CHOLESTROL	113.4 ± 35.8	89.4 ± 27.9	< 0.05
HDL	33.7 ± 16.8	32.3 ± 8.4	> 0.05
TRIGLYCERIDES	82.8 ± 69.6	51.5 ± 13.5	< 0.05
CHYLOMICRONS	45.9 ± 24.1	38.3 ± 40.6	> 0.05
VLDL	387.6 ± 237.4	266.9 ± 224.0	> 0.05
LDL	185.9 ± 106.7	159.9 ± 55.9	> 0.05
LDL-C	61.7 ± 27.8	53.1 ± 26.7	> 0.05
APO -B	32.3 ± 16.0	27.5 ± 14.0	> 0.05

Table 5-Lipid Parameters At Birth among term neonates based on intrauterine growth

LIPIDS	TAGA	TSGA	TLGA	P Value TAGA VS TSGA	P Value TAGA VS TLGA
TOTAL CHOLESTROL	83.4±27.4	68.6±20.2	78.9±24.8	**< 0.05**	> 0.05
HDL	32.6±15.7	35.8±18.7	29.9±10	> 0.05	> 0.05
TRIGLYCERIDES	64.8±43.4	61.2±43.4	62.2±43.4	> 0.05	> 0.05
CHYLOMICRONS	59.9±43	22.8±17.4	22.1±21.4	> 0.05	> 0.05
VLDL	183.1±163.8	143±146.2	177.7±167.5	> 0.05	> 0.05
LDL	149.3±65.5	135±56.5	145±56	> 0.05	> 0.05
LDL-C	41.1±22.9	35.7±20.3	37.1±26.3	> 0.05	> 0.05
APO -B	27.9±17.6	23.3±9.1	29.8±14.9	> 0.05	> 0.05
TC/HDLC	2.6±1.7	1.9±1.1	2.6±2.5	< 0.05	> 0.05

TAGA(Term Appropriate for gestational age), TSGA (Term Small for gestational age), TLGA Term Large for gestational age)

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