

## CORRELATION OF UMBILICAL CORD LIPID LEVELS AND ANTHROPOMETRY AT BIRTH IN TERM NEW BORN

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**Abstract** : This study was conducted to assess the cord blood lipid profile and its correlation with anthropometric measurement in newborns. One hundred (100) newborns delivered by spontaneous vaginal route and elective LSCS at term gestation were included in study. Umbilical cord blood was evaluated for cholesterol, low density lipoprotein (LDL-C), high density lipoprotein (HDL-C) and triglycerides. Present study showed no correlation of LDL with either abdominal girth, birth weight and head circumference in term newborns ( $p=0.221$  and  $p=0.978$  respectively). Similarly no correlates were found for total cholesterol, HDL, triglycerides and VLDL with weight, length, abdominal, girth, ponderal index or head circumference respectively of term newborns at birth in present study.

### INTRODUCTION

The imprints programmed during fetal growth in mothers womb manifest as substantial behavioral and metabolic findings in childhood. Many longitudinal studies have now established the interest in programmed changes during fetal life as origins of many diseases<sup>1</sup>. The hypothesis of such imprinting was put forward by DJP Barker and numerous studies have evaluated various parameters in fetal and neonatal life and subsequent emergence of adult diseases<sup>2,3</sup>. Many human fetuses have to adapt to limited supply of nutrients and in doing so they permanently change their physiology and metabolism<sup>4</sup> Though fetus behaving as a parasite extracts the required nutrients from mother and certain part of metabolic needs fulfilled by placenta itself, yet a shortfall of nutrients may impair fetal growth and low birth major Species, which are relatively heavy at birth such as guinea pigs and humans, have placentas, which are relatively permeable to fatty acids and related molecules in late gestation. Fatty acids may thus form a small but important component of fetal diet in these species at end of pregnancy<sup>5</sup>.

The initial epidemiological studies linked birth weight to subsequent disease risk. Later studies examined these risks in relationship to various body proportions at birth such as Ponderal Index [thinness], abdominal circumference etc<sup>6,7,8,9</sup>. This appears to have occurred because in many cases these measures are more closely related to disease risk than the actual birth weight itself. A fetus can reach a given birth weight via a variety of possible different growth trajectories.

Among various body proportions that can be studied *Ponderal Index* is important. It is defined as statistically, babies, may be divided as those having ponderal index more or less than 10<sup>th</sup> percentile. Another variable used in studies is abdominal circumferences at birth. Reduced abdominal circumference has been assumed to reflect reduced liver size<sup>10,11,12</sup> one has been used as possible explanation of relationship observed between abdominal circumference at birth and lipid metabolism in childhood. Studies in Sheffield showed that the neonate with a small body in relation to head size and the neonate with small abdominal circumference, though within the normal range of birth weight, have persistent disturbances of cholesterol metabolism and blood coagulation<sup>11</sup>. These results suggest that certain persons at increased risk for cardiovascular disease can be identified in infancy

and that early stages of atherosclerosis begin in childhood<sup>13</sup>.

More corroboration of liver programming during fetal life comes from animal experiments where it has been shown that under nutrition in rat fetuses in utero can permanently alter balance of two liver enzymes phosphoenolpyruvate carboxykinase and glucokinase. In support of fetal programming hypothesis most studies till date have been done in growth restricted fetuses or IUGR babies correlating the body proportions with cord blood lipid levels<sup>15,16</sup>. Studies have also shown racial and gender variabilities in cord lipid concentration<sup>17</sup> Studies to determine correlation in lipid profile at birth and abnormal body proportions in normal birth weight babies i.e. birth weight more than 2.5 kg are rarer<sup>15</sup> A study done in Israel has shown dysanthropometry at birth in correlation with cord blood lipid levels<sup>18</sup>. The aims of the present study were to determine relationship of umbilical cord lipid levels with anthropometry of baby at birth as measured by Ponderal index, abdominal circumference, head circumference, birth weight and length of baby at birth in babies born appropriate for gestational age between 37 to 40 weeks of gestation.

### MATERIAL & METHODS

One hundred new borns delivered by spontaneous vaginal route and elective LSCS at 37-40 weeks of gestation would be included in study. Umbilical cord blood will be collected for measurement of lipid profile. Exclusion criteria were congenital anomalies, chromosomal disorders, chronic congenital infections, major placental lesions, multiple births, infant of diabetic mothers, maternal hypertension, mothers with polyhydramnios, or oligohydramnios, maternal hypertension, toxemia of pregnancy, birth asphyxia [defined by Apgar Score<7 at 1 minute, persistent fetal heart rate abnormalities during labour]. Standardized records were kept for study group. Maternal and neonatal data were collected which included relevant maternal history and neonatal birth data including neonatal anthropometry and cord blood lipid profile. Mixed umbilical arterial and venous blood was obtained after clamping of umbilical cord post delivery and prior to delivery of placenta {5ml of cord blood in plain tube}. The lipid profile was done by centrifugation. The lipid fractions cholesterol, low density lipoprotein (LDL-C), high density lipoprotein (HDL-C) and triglycerides were measured using fully automatic BECKMAN-SYNCHRON CX5 PRO. The

method used for measurement was ELIMINATION METHOD using enzymes and subsequent COLORIMETRIC analysis of lipid fraction isolated. For statistical analysis Subject were segregated as per sex and PEARSON COEFFICIENT was used to analyze relationship between lipid concentration and anthropometric measurements. Each variable would be evaluated and a p value < 0.05 was considered significant. To study any correlation between abdominal girth and lipid fractions ANOVA was used after dividing abdominal girth into subgroup.

This study was conducted after clearance from hospital ethics committee and the written consent of the parents/guardians.

## RESULTS

Mean values of various lipid fractions in term newborns found in present study are shown in: Table-1

Table-1: Lipid profile of present study in term newborns

	Mean Value	Std Deviation
Total Cholesterol	62.31 mg/dl	19.15
LDL Fraction	27.46 mg/dl	10.79
HDL Fraction	26.98 mg/dl	11.57
Triglycerides	32.50 mg/dl	19.34
VLDL Fraction	7.460 mg/dl	4.77

Further to study any difference in male and female newborns, they were segregated and sex wise lipid parameters studied, which were as: Table -2 and Table-3.

Table-2 Data showing Lipid profile characteristics in female newborns.

	Minimum	Maximum	Median	Mean	Std Dev.
Total Cholesterol (mg/dl)	29	102	63.5	61.95	16.29
LDL fraction (mg/dl)	4.8	49.5	26.4	26.45	9.09
HDL Fraction (mg/dl)	10.6	64	26.1	29.03	11.5
Triglyceride (mg/dl)	2.0	49.8	28	28.01	12.23
VLDL fraction (mg/dl)	0.4	16	5.8	6.2	3.25

Table -3: Data showing Lipid profile characteristics in male newborns

	Minimum	Maximum	Median	Mean	Std Dev.
Total Cholesterol (mg/dl)	32	120.73	57	62.56	20.98
LDL fraction (mg/dl)	91	58.6	26.05	28.20	11.84
HDL Fraction (mg/dl)	8	68.4	22.1	25.61	11.47
Triglyceride (mg/dl)	5	118	31	35.49	22.49
VLDL fraction (mg/dl)	1	32.4	7.3	8.25	5.44

Except slight triglyceride fraction all other lipid fractions were similar in both males and females. To look for correlation of lipid fractions with different fraction the tests of correlation were used. Pearson's coefficient was used to determine any strength of correlation and p values 18 had shown a negative correlation of LDL, cholesterol with abdominal circumference, birth weight and head circumference. Barker<sup>6</sup> originally noted 14 that smaller abdominal circumference at

birth is associated with higher lipid levels. Based on this observation he suggested that, since abdominal circumference at birth is thought to reflect liver size, and cholesterol metabolism is regulated by the liver, impaired liver growth in uterus re-sets present study showed no correlation of LDL with either abdominal girth, birth weight and head circumference in term newborns (p=0.875, p=0.221 and p=0.978 respectively). Similarly no correlates were found for total cholesterol, HDL, triglycerides and VLDL with either weight, length, abdominal girth, Ponderal Index or head circumference respectively of term newborns at birth in present study (Table 4)

Table-4: Correlation of anthropometry variables with lipid fractions

WEIGHT	r	.049	.124	-.140	.013	.056
	p	.625	.221	.164	.900	.583
O.F.C	r	-.033	-.003	-.019	.015	.032
	p	.743	.978	.855	.879	.749
LENGTH	r	.059	.078	0.35	.061	-.004
	p	.557	.439	.729	.544	.971
POND INDEX	r	-.007	.050	-.160	-.042	.052
	p	.943	.623	-.113	.677	.604
ABD. GIRTH	r	.179	-.016	.163	.002	-.014
	p	.074	.875	.104	.985	.892

To further test the hypothesis of variability of lipid fractions as per abdominal girth, which was purported to correlate with liver size, lipid fractions were correlated to abdominal girths after dividing subjects into 4 groups based on abdominal girth (table 5).

Table-5 Lipid fractions distribution based on abdominal girth

Abd Girth	Total cholesterol	LDL fraction	HDL fraction	Triglycerides	VLDL fraction
>30 cm	58.94	27.91	24.15	33.60	8.07
30-30.5 cm	58.10	24.79	26.64	29.48	6.69
30.5-31 cm	70.00	27.71	34.71	31.69	7.07
>31 cm	64.85	28.58	26.29	33.54	7.47

ANOVA test was used to find significance of lipid fraction distribution within the 4 groups divided as per abdominal circumference (Table-6).

Table -6: ANOVA test

	p value
Total cholesterol	0.163
LDL fraction	0.662
HDL fraction	0.023
triglycerides	0.877
VLDL fraction	0.762

To study the seemingly significant HDL distribution (p value 0.023) as per abdominal girth groups Bonferroni multiple comparison test (post hoc) was used to find HDL fractions distribution across the abdominal girth groups and each group was compared with 3 other groups to find whether the distribution of HDL fraction was significant. In this analysis the distribution was not found to be behaving significantly across all the groups.

## DISCUSSION

The magnitude of association between birth parameters and later disease risk, requires assessment in comparison with those attributed to behaviors and lifestyle. A WHO paper in 2002<sup>22</sup> concluded that intrauterine programming is likely a third underlying factor of cardiovascular disease and major markers of risk, along with genetic predisposition and lifestyle. Studies have previously demonstrated altered lipid profiles in small for gestational age or IUGR newborns. Though such association has not been seen in term babies. Mainly by work of Barker and colleagues the lipid profile in newborn and possible risk of adult diseases has been brought to fore<sup>14</sup>. The study in full term newborns in Israel<sup>18</sup> showed disproportionate body size at birth in full term newborns is associated with disturbance of

cholesterol metabolism. It is known that many factors are associated with lipid characteristics in new born. In a study of 303 newborns and their mothers at the mean value of cholesterol was 72 mg/100 ml for the newborns and 253 mg/100 ml in the mothers. By multiple regression analysis it was shown that a significant independent correlation exists between cord blood cholesterol and the cholesterol of the mothers, birth weight, sex and the blood group of the ABO system of both the newborn and the mother. This demonstrates that several factors known to influence cholesterol in adult life are already operating at birth. Lipid profile in newborns has been studied in ethnically diverse populations and similar distribution has been noted in various populations. (table 7)

Table -7: Comparison of studies from different countries

	CHILE(20)	CHINA(19)	INDIAN(21)	ISREAL(18)
Total Cholesterol	64 mg/dl	65.91 mg/dl	76.6 mg/dl	88.4 mg /dl
LDL Cholesterol	30 mg/dl	31.59 mg/dl	20.7 mg/dl	61.7 mg/dl
HDL Cholesterol	27 mg/dl	22.62 mg/dl	22.5 mg/dl	21.6 mg/dl
Triglycerides	35 mg/dl	20.47 mg/dl	---	31.09mg/dl

Table 7 clearly shows that despite diverse ethnic backgrounds the metabolic milieu of newborn remain constant across the globe. The correlation of lipid profile with anthropometric measurement, however, showed no correlation in present study. A study of term newborns in Israel 18 had shown a negative correlation of LDL cholesterol with abdominal circumference, birth weight and head circumference. However present study showed no correlation of LDL with either abdominal girth, birth weight and head circumference in term newborns (p=0.875, p=0.221 and p=0.978 respectively.) Similarly no correlates were found for Total Cholesterol, HDL, Triglycerides and VLDL with Weight, Length, Abdominal Girth, Ponderal Index or Head Circumference respectively of term newborns at birth in present study.

Barker<sup>14</sup> originally noted that smaller abdominal circumference at birth is associated with higher lipid levels. Based on this observation he suggested that, since abdominal circumference at birth is through to reflect liver size, and cholesterol metabolism is regulated by the liver, impaired liver growth in uterus re-sets cholesterol concentration towards more atherogenic profile. This view is supported by one other study that shows a negative association between abdominal circumference and TG in growth-retarded human fetuses<sup>23</sup>. However, more research is needed to show whether the association between abdominal circumference and lipids exists in other populations, and how accurately measurement of abdominal circumference reflects the size of the liver in a new-born baby. The concordance between the size of the liver and abdominal circumference in humans is so far weak 10. Present study also shows no significant correlation between abdominal girth with lipid fractions in cord blood sera. A statistically significant correlation was found to be emerging after ANNOVA analysis of HDL among four abdominal girth groups (p=0.023), however the HDL values which seemingly behaved positively with abdominal girth as it increased from 30cm to 31cm fell as girth rose above values of 31cm. However, larger study with inclusion of maternal lipid profile, maternal anthropometry, maternal macro and

micronutrient intake with placental weight and neonatal anthropometry may prove useful in studying the concept of fetal programming and impact of maternal variables in this context.

Moreover, study of atherogenic lipoprotein fractions mainly Apo E, other fractions Apo B & Apo C may probably elucidate more interesting data. More important studies is long-term follow up; to study whether those with altered lipid profiles at birth manifest the chronic disease of adulthood independent of lifestyle variables.

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**REFERENCE**

1. **Barker DJP, Martyn CN.** Maternal and Fetal origins of cardiovascular disease. *Journal Epidemiology Health* 1992;46:8-11.
2. **Barker DJP.** *Mother, Babies and Relation in later life.* 2<sup>nd</sup> Edition; Churchill Livingstone 1998.
3. **Forsdahl A.** Are poor living conditions in childhood and adolescence an important risk factor for arteriosclerotic heart disease? *Br J Prev Soc Med* 1977;3:91-5.
4. **Desai M, Crowther NJ, Ozanne SE, Lucas A, Hales CN.** Adult glucose and lipid metabolism may be programmed during fetal life. *Biochem Soc Trans* 1995; 23:331-35.
5. **Fowden AL.** Fetal metabolism and energy balance. In: *Thorburn GD Harding R (eds). Textbook of Fetal Physiology.* Oxford: Oxford University Press, 1994, pp. 70-82.
6. **Barker DJP, Osmond C, Simmonds SJ, Wield GA.** The relation of small head circumference and thinness at birth to death from cardiovascular disease in adult life *BMJ* 1993;306:422-26.
7. **Law CM, Gordon GS, AW, Barker DJP, Hales CN.** Thinness at birth and glucose tolerance in seven-year-old children. *Diabetic Med* 1995;12:24-29.
8. **Philips DJ.** Birthweight and future development of diabetes, a review of evidence. *Diabetes Care* 1998;21:B1 150-5.
9. **Law CM, Shiell A.W.** Is blood pressure inversely related to birth weight? The strength of evidence from systemic review of literature. *Journ Hypertension* 1996;14:935-41
10. **Roberts AB, Mitchell JM, McCowan LM, Barker S.** Ultrasonographic measurement of liver length in the small-for gestational-age fetus. *Am J Obstet Gynecol* 1999;180:634-38.
11. **Barker DJP, Martyn CN, Osmond C, Wield GA.** Abnormal liver growth in utero and death from coronary heart disease. *BMJ* 1995;310:703-04.
12. **Harding J.E.** The nutritional basis of fetal origins of adult disease *International Journal Epidemiology* 2001;30:15-23.
13. **Srinivasan S.R, Cusanta J.L, Freedman D.S, Webber C.S et al.** Serum lipids and lipoproteins. *Pediatrics* 1987;80:789-96.
14. **Barker DJP, Martyn CN, Osmond C, Hales CN, Fall CHD.** Growth in utero and serum cholesterol concentration in adult life. *BMJ* 1993;307:524-7
15. **Kumar A, Gupta A, Malhotra V.K, Agarwal P.S et al.** Cord blood lipid levels in low birth weight newborns. *Indian Pediatrics* 1989;26:571-74
16. **Jones J.N, Taylor C.G** Altered cord serum lipid levels associated with small for gestational age infants. *Obstetrics and Gynaecology* 1999;93:527-3
17. **Rifai N, Heiss G.** Gender and race differences in cord blood lipoprotein, *Circulation* 1988;2:481.
18. **Ophir E, Oettinger M, Nisimov J, Hirsch Y et al** Cord blood lipids concentration and their relation to body size at birth : possible link between intrauterine life and adult disease, *American Journal of Perinatology* 2004;21:35-40
19. **Zhao WH, Liu YJ, Shou HC, Chen LJ.** Cholesterol concentrations I cord blood of newborn infants. *Zhonghua Er Ke Za Zhi* 2003;41(2):107-9
20. **Casaneuva V, Cid X, Chiang MT, Molina M, Ferrada MC, Perez R, Casaneuva P.** Lipids, Lipoproteins and apolipoproteins in normal newborns. *Rev Med Chil* 1998;126(9):1073-8.
21. **Kalra A, Kalra M, Agarwal MC, Pant MC.** Serum Lipid profile in term and preterm infants in early neonatal period. *Indian Pediatrics* 1998;25:977
22. **WHO .**Programming of chronic disease by impaired fetal nutrition: Evidence and implication for policy and intervention strategies. Department of Nutrition for Health and Development, Department of Noncommunicable Disease Prevention and Health Promotion World Health Organization, Switzerland. 2002.
23. **Roberts A, Nava S, Bocconi L, Salmona S, Nicolini U.** Liver function tests and glucose and lipid metabolism in growth-restricted fetuses. *Obstet Gynecol* 1999;94:290-94

**ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH**

The need for uniform ethical guidelines for research on human subjects is universally recognized. It has acquired a new sense of urgency as the ethical issues in the area of biogenetic research involving human subjects have become acute. Apart from the mandatory clinical trials on new drugs, a number of diagnostic procedures, therapeutic interventions and preventive measures including the use of vaccines, are being introduced which involve human subjects. Further the advent of new medical devices and radio-active materials and therapeutic benefits of recombinant DNA products have added a new dimension to the ethical issues that need to be considered before evaluating these for their efficacy, utility and safety.

Any research using the human beings as subjects shall bear in mind the following principles of: (i) essentiality, (ii) voluntariness, informed consent, (iii) non exploitation, (iv) privacy and confidentiality, (v) precaution and risk minimization, (vi) professional competence, (vii) accountability & transparency, (viii) maximisation of public interest and distributive justice (ix) institutional arrangements (x) public domain (xi) totality of responsibility and (xii) compliance.

Recent advances in the field of Assisted Reproductive technologies, organ transplantation, human genome analysis and gene therapy promise unprecedented benefits to mankind. At the same time, they raise many questions of law and ethics, stimulating public interest and concern.

(Source : ICMR Publication 2000)