Original Research Paper

Volume - 11 | Issue - 04 | April - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Biochemistry

HUMAN UMBILICAL CORD BLOOD BIOCHEMICAL VALUES IN TERM AND PRETERM NEONATES

Om Prakash Jha*	Research scholar, Department of Biochemistry Santosh Medical College and Hospital Ghaziabad (UP), India. *Corresponding Author
Dr.Preeti Sharma	Associate Professor, Department of Biochemistry Santosh Medical College and Hospital Ghaziabad (UP), India.
Jay prakash Jha	PhD scholar Department of Biochemistry, Indra Gandhi Institute of Medical Science, Patna.
Dr. T K Mohapatra	Ex Professor & HOD, Department of Biochemistry Santosh Medical College and Hospital Ghaziabad (UP), India.

ABSTRACT **Background:** The major causes of death both in developed and developing countries are diabetic mellitus, jaundice, cardiovascular disorders. Higher concentration of cord blood glucose, total cholesterol Triglyceride, LDL and VLDL, in pre term neonates may increase their future risk of cardiovascular diseases in diabetic mellitus. Early diagnosis and dietary modifications and proper management may rectify the risk factors and prevent future risk of disease. Our aim of Study to do biochemical profiling in human Umbilical cord blood as preterm and term Neonates.

Methods: It is retrospective and observational study conducted for a period of two years from October 2018 to November 2020 in the Departments of Biochemistry and Gynecology of Santosh Medical College and Hospitals, Ghaziabad.

Results: Among 300 neonates including 150 (50%) term and 150 (50%) preterm, Umbilical Cord blood serum blood Sugar, Total Cholesterol ,Triglyceride, LDL and VLDL were higher in preterm as compared to term babies while baby weight was significantly increased (<0.05) in term as compared to preterm babies.

Conclusion: There is inverse relationship between gestational age and different biochemical parameters and this deranged biochemical profile preterm group could be a risk factor for future development of diabetic mellitus, and cardiovascular disorders in their later part of life.

KEYWORDS : Newborn, Preterm neonates, Umbilical cord blood study, Low birth weight

INTRODUCTION

The neonatal period spans the first 28 days of life, and it is the time with the highest rate of mortality in childhood. Appropriate feeding and care will maximize the child's chances of survival (1).

Preterm birth is defined as a delivery occurring at less than 37 completed weeks or 259 days of gestation and is a major determinant of neonatal morbidity and mortality with short and long-term adverse consequences for health. Etiology of preterm birth is not completely understood, although it is thought to be multifactorial and the result from the interaction of several pathways (2-5).

Humane Umbilical Cord blood has been shown to be a source of stem cells for transplantation. The first Umbilical cordblood transplantation was performed for a 5year old child with fanconis anaemia, by Dr.Gluckman and colleagues (6). Also the first cord blood transplant for haemoglobinopathy was in 1995 by Issaragris. As at 2007, at least 350,000 to 400,000 Umbilical cord blood (UCB) units have been banked with over 6000 UCB transplant performed worldwide. UCB has become a fully established source of stem cell for transplanting malignant and non malignant disorders with reduced incidence of graft versus host disease(7,8,9,10)

Analysis of umbilical cord blood gases is widely used to describe the neonate's metabolic status at birth, and it has improved our knowledge about the fetal physiological and biochemical milieu. Umbilical cord blood gases change with advancing gestational age,1–5 and a mixed respiratory and metabolic fetal 'acidaemia' develops progressively.

Of the 20.6 million low birth weight (LBW) infants born every year, about 8 million are born in India(11). Low birth weight is the most important risk factor for neonatal mortality, contributing to about three quarters of neonatal deaths in India(12). In order to survive through infancy, LBW infants need additional care particularly with regard to breathing, temperature maintenance, feeding, hygiene and early recognition and treatment of infections. LBW infants are a heterogeneous group -born too early, born too small, or both - and the spectrum varies for developing and developed countries. In India, over two thirds of LBW infants are term.

The study of the biochemical parameters of Human Umbilical cord blood act as a mirror, which usually reflects the neonatal status. The measurement of lactate in the cord blood of neonates is helpful in the assessment of fetal distress. The umbilical cord blood leptin and adiponectin act as the predictors of adiposity in children. The detection of certain infections can also be done in the cord blood samples (13,14,15).

A fetus needs a considerable amount of total cholesterol for development of neonates tissues and organs. After birth lipid transport system is transformed from one containing low VLDL and LDL levels to adult system with a relatively high LDL levels which continues to increase with age. Cord blood contains all adult lipoproteins and apo-lipoproteins(16). Concentrations of lipids in neonates with low gestational age may increase the high risk of cardiovascular diseases and chronic diseases in the future. It has been suggested that early diagnosis and drug therapy along with appropriate diet may provide an opportunity for long term amelioration of risk factors that contribute to atherosclerosis and cardiovascular diseases in adult life. This study is conducted to compare lipid profile and atherogenic indices in late preterm and term neonates(17).

It is evident that the total cholesterol and LDL cholesterol in near term group is higher than term, triglyceride and VLDL is higher in term neonates as compared to near term neonates. Low HDL-cholesterol in term neonates as compared to near term neonates but the value is not statistically significant(18).

Very few studies were done in this area that's why we thought of choosing this study. This study was undertaken to compare neonate's weight, serum blood sugar and Umbilical cord blood lipid profile in term and preterm babies so as to pick up high risk babies for future monitoring.

MATERIALS AND METHODS:

The present study was conducted in the Department of Biochemistry in collaboration with Department of Obstetrics and Gynecology, Santosh Medical College and hospital, Ghaziabad (UP) India. The study was conducted in sample size of 300 of which a control group and experimental groups was divided. Total 300 neonates will be included in this study. Neonates were divided into two groups. Group A- 150 preterm neonates (31 weeks to 36 weeks) and group B- 150 full term neonates (37 weeks to 41weeks). Birth weight was measured by using digital electronic weighing scale.

Each patient was randomly selected. The clinical conditions of the selected full term and preterm delivery patients were carefully monitored throughout all the stages of labor. Human Umbilical Cord blood will be collected in plain and fluoride vial, about 5ml of Human Umbilical Cord blood will be collected from the placental end of umbilical vein (Fig.-1)Serum will be deep freeze at -20^0 C till further analysis.

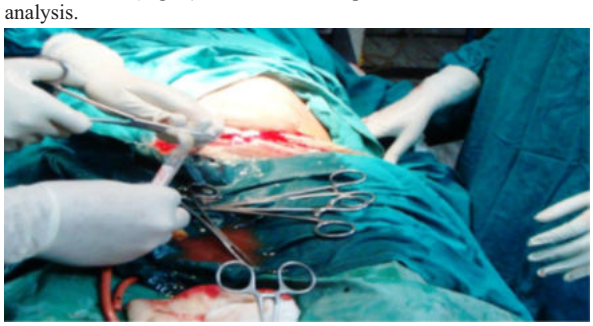

Fig-1]: Collection of Humane Umbilical cord blood during Caesarian Section

Biochemical markers were measured by internationally recommended methods, in BECKMANCOULTER-AU480, Fully Auto-analyzer based on the principle and the parameters will be as follows: Glucose (Glu) (GOD/POD-enzymatic method), Measurement of serum cholesterol by (CHO -Trinder's method) Cholesterol esterase hydrolyses cholesterol esters in the specimen into free cholesterol and fatty acid. In the second reaction, total cholesterol oxidase converts cholesterol to cholest-4-en-3-one and hydrogen peroxide. In presence of peroxidase, hydrogen peroxide oxidatively couples with 4-aminoantipyrine and phenol to produce red quinoneimine dye which has absorbance maximum at 520 nm. The intensity of red color is proportional to the total cholesterol in the sample.

Measurement of HDL cholesterol by Phosphotungstate precipitation method Umbilical Cord blood HDL estimation will be done by Glycerol phosphate oxides method on Beckman AU480 biochemistry Fully automated analyser(19).

Phosphotungstate/Mg2+ precipitates chylomicrons, low density lipoprotein cholesterol and very low-density lipoprotein cholesterol fractions. After centrifugation, high density lipoprotein fraction remains unaffected in supernatant. Total Cholesterol content of HDL fraction is assayed using ready to use reagent supplied with cholesterol kit Measurement of Serum triglyceride by Glycerol phosphate oxides method(GPO-PAP)/ Trinder's method. Glycerol released from hydrolysis of serum triglycerides by lipoprotein lipase of the kit is converted by glycerol kinase to glycerol-3- phosphate, which is oxidized by glycerol phosphate oxidase to dihydroxya cetoneph osphate and H_2O_2. In presence of peroxidase, H_2O_2 oxidizes phenolic chromogen to a red coloured compound and intensity of the colour is measured using an auto analyzer(19).

Estimation of LDL and VLDL
LDL cholesterol was calculated by Friedwald's formula
Serum LDL = Serum total cholesterol - (serum VLDL + Serum HDL)
VLDL Cholesterol in mg % = Serum Triglyceride / 5
The following atherogenic indexes were calculated: total cholesterol / HDL cholesterol, LDL cholesterol / HDL cholesterol.

STATISTICAL ANALYSIS

Data analysed using SPSS
For statistical analysis students unpaired 't' test will be used to compare the both groups and p value <0.05 will be taken as statistically significant.

INCLUSION CRITERIA

- All neonates are inclusion between 31 weeks to 41 weeks.

EXCLUSION CRITERIA

- Congenital anomalies and syndromes
- APGAR score at 5 minutes below 7
- Sick neonates
- Maternal chronic pancreatitis, thyroid disorders, Cushing's disease, primary hypercholesterolemia
- Maternal intake of drugs which affect neonatal lipid levels

RESULT :

Table-I Compression biochemical parameters At Birth for pre-term and Term Neonates.

BIOCHEMICAL PARAMETERS	Pre-term	Term	P. Value
	Mean ± SD	Mean ± SD	
BABY WEIGHT (kg)	1.63±0.22	3.07±0.30	.001
RBS	46.52±12.66	82.44±5.84	.001
Total cholesterol	70.28±0.62	66.04±0.65	0.000
Triglyceride	48.79±0.64	51.16±0.55	0.004
HDL	30.16±0.42	29.16±0.40	0.916
LDL	30.36±0.74	26.65±0.77	0.000
VLDL	9.74±0.12	10.22±0.10	0.004

The mean value of baby weight in preterm neonates was 1.63±0.22 and term neonates were 3.07±0.30.

The mean value of serum blood sugar in preterm neonates was 46.52± 12.66 and term neonate's value was 82.44±5.84. The mean value of serum total cholesterol in term and preterm neonates was found to be 66.04±0.65 and 70.28±0.62 respectively. Significant lower values of serum total cholesterol were observed in term neonates as compared to preterm neonates (P. value 0.000)

The mean value of serum triglycerides in and term neonates was found to be 51.16 ± 0.55 and 48.79 ± 0.63 respectively. Significant lower values of serum triglycerides were observed in term neonates as compared to preterm neonates ($p<0.05$).

The mean value of serum high density lipoprotein cholesterol (HDL) in term and preterm neonates was found to be 29.16± 0.40 and 30.16 ±0.42 respectively. No significant difference was observed in HDL cholesterol vales in term neonates as compared to preterm neonates. The mean value of serum low density lipoprotein cholesterol (LDL) in term and term neonates was found to be 26.65 ± 0.77 and 30.36 ± 0.74 respectively. Significant higher values of serum LDL-cholesterol were observed in term neonates as compared to preterm neonates ($p<0.0001$). The mean value of serum very low density lipoprotein cholesterol (VLDL) in term and term neonates was found to be 10.22 ± 0.10 and 9.74 ± 0.12 respectively. Significant lower values of serum VLDL-cholesterol were observed in term neonates as compared to preterm neonates ($p<0.01$).

DISCUSSION:

The objective nature of cord blood biochemical parameters, reflecting the fetal anaerobic metabolism and eventual development of metabolic disorder, makes them attractive to use as outcome measures indicating the newborn's status.

In India low birth weight is major problem where the prevalence of low birth neonates is high up to 28%. Birth weight of neonates is a good indicator for mother's health and nutritional status, as well as outcome for survival growth long term health and psychosocial development of the neonates. LBW neonates weighing less than 2.5kg face a high risk of dying and are the main contributor with respect to neonates. Infant and under five mortality, Out of those who survive have impaired immune function and have high risk of early onset of adulthood disease.

Umbilical Cord lipid profile is a reflection of lipid metabolism during fetal life and at birth because most fetal lipids are synthesized de-novo through conversion of glucose to various fatty acid containing compounds. Only part of it is derived from placental circulation. Total cholesterol increases after birth; it might be presumed that the total cholesterol levels of preterm neonates are similar to or lower than those observed in term infants. The total cholesterol levels detected in human umbilical cord blood were lower than those found in plasma of adults. This was in agreement with Hellmuth (20). However, our results demonstrated that the cholesterol levels of the premature group were substantially higher than those of the term group, in agreement with a previous report(21).

Out of total 300 subjects 150 pre-term 31 to 36 week and 150 full-term 37 to 41 week neonates were involved in the study. The term neonates had the highest concentration of cord blood cholesterol. The highest amount of cholesterol in cord blood was documented in preterm neonates. In the total study group, highly significant difference existed in the mean of triglycerides levels. In the theory of development of

atherosclerosis, increased plasma levels of cholesterol and triglycerides are considered to be of most important factors. Atherosclerosis begins early in life, and the studies done on cord blood lipid profile had unreliable findings. In this study we also found atherogenic index from given data, which came out to be at risk in both pre-term and term neonates. Normal atherogenic index should be lower than 0.11, it is intermediate between 0.11 to 0.21 and more than 0.21 value is at higher risks.

Findings of the current study are not consistent with a previous study on cord blood cholesterol, which found higher cholesterol in preterm than in term newborns (22,23,24).In another study, preterm infants had a high level of cholesterol concentrations (25). A study reported that preterm neonates have higher TC and TG levels but a statistically significant difference was found only in TC ($p<0.001$) levels(26). Other one study concluded that TG, LDL, HDL were higher in preterm neonates compared to term neonates with the statically significant difference in TC and LDL levels, but HDL had no statistically significant difference. All values were more in preterm compared to a term which was statically significant(27). Other study concluded that in cord blood lipid profile all values were lower in preterm neonates compared to term neonate's, but statistically ,a significant difference was found with TC levels ($p<0.001$) and no statistically significant difference was found with HDL and LDH levels(28). In our study higher cord blood lipid profile levels in preterm neonates could be explained by the face that preterm babies lack both hepatic carbohydrate and subcutaneous adipose stores, with a result that circulation fuel in low and may run out (29). The rise in cord blood lipids levels may reflect the metabolic adaptation to provide adequate energy especially to organs like the brain(30).

CONCLUSION

The findings of the study again reaffirm the link between prenatal factors and cord blood serum glucose and lipid parameters.

The primary prevention of risk of cardiovascular diseases in future may depend on strategies that promote fetal growth. Early diagnosis followed by prudent dietary and drug therapy in this high risk neonates may provide an opportunity for a long range over primary amelioration of risk factors that contribute to development of CVD in adult life. From this study, it is evident that the total cholesterol and LDL cholesterol in near term group was higher than a term; triglyceride and VLDL were higher in term neonates as compared to near term neonates. Fall in HDL was not significantly observed in term neonates as compared to near term neonates. Hence, it was clearly visible a trend to worse lipid profile in Indian near-term infants. It may be interesting to see whether these susceptible neonates are at increased risk of developing cardiovascular diseases in future. The study also hints about the role of adverse maternal conditions in origin of early onset.

Acknowledgement

We sincerely thank Santosh Medical College and Hospital extending all the facilities for conducting the work .I am thankful to all the study subjects for being part of this study and their cooperation. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

REFERENCES

1. World Health Organization. Infant, Newborn [Internet].Geneve: WHO; 2015 [cited 2015 Sep 17]. Available from: http://www.who.int/topics/infant_newborn/en/
2. Rellan Rodríguez S, García de Ribera C, Paz Aragón García M. El reciénnacidoprematuro. ProtocoloDiagnósticoTerapéutico de la AEP: Neonatología. Madrid: Asociación Española de Pediatría; 2008. p. 68–77.
3. Mandy T, Weisman G, Leonard S, Kim M. Short-term complications of the premature infant. UpToDate. 2015.
4. L. Wang, Marvin J. Dorer, David P. Fleming, Michael A. Catlin E. Clinical Outcomes of Near-Term Infants. Pediatrics. 2004;114:372–6.
5. World Health Organization. Born too soon: the global action report on preterm birth [Internet].Geneve: WHO; 2012 [cited 2015 Oct 22]. Available from: http:// www.ncbi.nlm.nih.gov/pubmed/23911366
6. Gluckman E, Broxmeyer HA, Auerbach AD.Haematopoietic reconstruction in a patient withfanconi'sAnaemia by means of Umbilical cord blood from HLA identical sibling. N Eng J Med. 1989;321:1174-1178.
7. Issaragrisil S, Visuthisakchai S, Suvalte V, Tauphaichitr US, Chandanayinggyong, et al. Brief report: Transplantation of cord blood stem cell into a patient with severe thalassaemia. New Eng J Med. 1995;1068-1073.
8. Brustein CG, Setubal DC, Wagner JE. Expanding the role of umbilical cord blood transplantation. Br J Haematol. 2007;137:20-35.
9. Cairo MS, Wagner JE. Placental and/or umbilical cord blood: an alternative source of haematopoietic stem cell for transplantation. Blood. 1997;90:4665-4678.
10. Wagner JE, Kerhan NA, Steinbuch M, Broxymeyer HE, Gluckman E. Allogenic sibling umbilical cord transplantation in children with malignant and non-malignant diseases. Lancet. 1995;346:214-219.
11. World Health Organization (WHO) & United Nations Children's Fund (UNICEF). *Low birthweight: Country, regional and global estimates*. New York: UNICEF and Geneva: WHO; 2004.
12. Dadhich JP, Paul VK. State of India newborns. New Delhi/ Washington: National Neonatology Forum and Saving Newborn Lives, Save the Children (US); 2004.
13. Nicolaides KH, Economides DL, Soothill PW. Blood gases, pH, andlactate in appropriate- and small-for-gestational-age fetuses. Am JObstetGynecol 1989; 161:996–1001.
14. Soothill PW, Nicolaides KH, Rodeck CH, Campbell S. Effect of gestationalage on fetal and intervillous blood gas and acid-base values inhuman pregnancy. Fetal Ther 1986;1:168–75.
15. Kitlinski ML, Ka¨ lle´nK,Marsa´ l K, Olofsson P. Gestational age-dependent reference values for pH in umbilical cord arterial blood at term. Obstet Gynecol 2003;102:338–45.
16. Wiberg N, Ka¨ lle´n K, Olofsson P. Physiological development of a mixedmetabolic and respiratory umbilical cord blood acidemia with advancinggestational age. Early Hum Dev 2006;82:583–9.
17. Hellmuth K.: Specificity of placental opzime for interforametric diagnosis Kline Wchneschr. 1926; 5 : 2006.
18. Diaz M., Leal C., Ramon y. Cajal J: Jiminez MD, Martinez H., Pocovi M., Grande F: Cord blood lipoprotein-cholesterol : relationship birth weight and gestational age of newborns. Metabolism, 1989; 38: 435 – 438.
19. Imamura, S., Hirayama, T., Arai, T., Takao, K., Misaki, H.: An enzymatic method using 1,2-diglyceride for pancreatic lipase test in serum: Clin. Chem.1989;35: 1126.
20. 207.Hellmuth K.: Specificity of placental opzime for interforametric diagnosis Kline Wchneschr. 1926; 5 : 2006.
21 Diaz M., Leal C., Ramon y. Cajal J: Jiminez MD, Martinez H., Pocovi M., Grande F: Cord blood lipoprotein-cholesterol : relationship birth weight and gestational age of newborns. Metabolism, 1989; 38: 435 – 438.
22 Morillas JM, Moltó L, Robles R, Gil A, Sánchez-Pozo A. Lipoproteins in preterm and small-for-gestational-age infants during the first week of life. ActaPaediatr 1992;81:774-8.
23 Nagano N, Okada T, Yonezawa R, Yoshikawa K, Fujita H, Usukura Y, *et al.* Early postnatal changes of lipoprotein subclass profile in late preterm infants. ClinChimActa 2012;413:109-12.
24 24.Donegá S, Oba J, Maranhão RC. Concentration of serum lipids and apolipoprotein B in newborns.Arq Bras Cardiol 2006;86:419-24.
25 Tohmaze RM. Cord blood lipid profile in premature, near-term and term newborn infants. Iran J Neonatol 2014;5:8-10.
26 Dogra J, sengar GS, Mathur HC, Misra SN. Serum lipids in neonatal cord blood in families with diabetes mellitus type-1. Ind pediatr.1988 Mar;25(3):267-71
27 Kumar AJ, Gupta A, Malhotra VK, Agarwal Ps, Thirupuram S, Gaind Be. CORD blood lipid levels in low birth weight newborns. Indpediatr. 1989jun;26(6):571-4
28 Van der Schouw YT, AL MD, Hornstra G, Bulstra-ramakers MT, Huisjes HJ.Fatty acid composition of serum lipids of mothers and their babies after normal and hypertensive pregnancies. Prostaglandins, leukotrienes and essential fatty acid 1991 dec1;44(4):247-52.
29 Kherkeulidze P, Johansson J, Carlson LA.High density lipoprotein size distribution in cord blood.ActaPaediatrica. 1991 Aug;80 (8-9):770-9.
30 Averna MR, Barbagallo CM, Di GP,Labisi M, Pinna G, Marino G,et al Total cholesterol, LDL- cholesterol and apoprotein B in Umbilical cord blood: cross- sectional study. Minerva Pediatr. 1992 Sep;44(9):395-9