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A Study Of Biochemical Profiling In Human Umbilical Cord Blood In Preterm And Term Neonates

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ABSTRACT

Background: The major causes of death both in developed and developing countries are diabetic mellitus, jaundice, cardiovascular disorders and hyperbilirubinemia. Higher concentration of cord blood glucose, urea, total protein and albumin in pre term neonates may increase their future risk of cardiovascular diseases. Early diagnosis and dietary modifications and proper management may rectify the risk factors and prevent future risk of disease. Our study aims to Study the biochemical profiling in human Umbilical cord blood in preterm and term Neonates.
Methods: It is cross sectional observational study conducted for a period of one year from October 2019 to November 2020 in the Departments of Biochemistry and Gynecology of KD Medical College, Hospital and Research Center, Mathura & Santosh Medical College and Hospitals, Ghaziabad.
Results: Among 100 neonates including 50 (50%) term and 50 (50%) preterm, blood sugar, Total bilirubin, direct and indirect bilirubin, Urea, Creatinine, uric acid, Total protein and albumin, were higher in preterm as compared to term babies while Urea level 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, jaundice, cardiovascular disorders and hyperbilirubinemia diseases in their later part of life.
Key words: Newborn, Preterm neonates, Umbilical cord blood study

INTRODUCTION

As per reports, about 130 million infants are born every year globally. Out of these 4 million infants fail to thrive and die in their neonatal period. These deaths predominantly take place in the developing nations. The mortality rate of under-five children has reduced in the past twenty years; however the mortality rate of new born infants still remains a challenge.(1, 2).

Human baby in womb is known to permanently change their physiology and metabolism to adapt to the limited supply of nutrients in utero. These programmed changes can later be the cause of the origin of diseases like coronary artery disease, diabetes mellitus, and hypertension (1). The human umbilical cord blood biochemical markers may be associated with lifelong changes in the metabolic functions of the individual (2). Study of the Biochemical markers of human umbilical cord blood shows that it acts as a mirror and reflects the neonatal status. Fetal distress can be assessed by measurement of lactate in the umbilical cord blood of the fetus (3). The umbilical cord blood leptin and adiponectin act as the predictors of adiposity in neonates. The detection of certain infections can also be done in the human umbilical cord blood samples (4,5). The widely accepted system for the evaluation of the status of a neonate's infant is the Apgar score (6- 8).

The development of the neonate's skeleton requires large amounts of energy, protein, and minerals. Minerals, such as calcium and phosphorus, are actively acquired by the baby from the mother. By the 2nd

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semester of pregnancy, fetal serum Calcium and Phosphorous concentrations are ~20% higher than maternal serum concentrations. Internalization of the bones occurs predominantly during the 3rd semester. If the increased baby demand of minerals is not met, then
Inadequate fetal bone mineralization of the bones occurs.
Unhealthy child lifestyle practices and behaviors are well accepted as contributing factors, but the true origins of these diseases may actually be found in uteri. Primarily human umbilical cord blood screening has been utilized to detect the population at higher risk of developing atherosclerosis, a biochemical and pathological hallmark of coronary heart disease. All exchanges of various essential elements take place through the human placenta. Normally during intra-uterine life glucose is the primary source of energy for the fetus (6). Immediately after birth, with the cessation of maternal blood supply, free fatty acids become an important source of energy during the first few hours of life (7). Umbilical cord blood serum Creatinine is the most widely used biochemical marker of renal function and can be used to estimate the glomerular filtration rate (GFR) (9).
In one of the recent studies in Canadian, the investigators established a reference interval for the umbilical cord blood total alkaline phosphatase (10,11). The people below the poverty line or the rural villagers of the coastal belt are the most vulnerable population to be socioeconomically affected by natural calamities. Hence our study is focused mainly on the health status of term newborns of Mathura. Keeping all of the above biochemical markers lab investigations into consideration, our main objective of this cross-sectional study was to determine the biochemical parameters levels of preterm and term neonates. Umbilical cord blood biochemical parameters like Glucose, Total Protein, Albumin, Urea, Uric acid, Creatinine, Total bilirubin, Direct bilirubin, Indirect bilirubin of the term newborns and preterm newborn were taken into our study. Collection of human umbilical cord blood without any painful procedure provides a convenient way of sampling the fetal blood.
The aim of the study is to estimate the biochemical parameters such as serum blood sugar, total bilirubin, direct & indirect bilirubin, serum urea, Creatinine, total protein, and albumin in Umbilical cord blood in preterm and full-term neonates, determine the reference ranges.

Materials and Methods:
The present study was carried out in the Department of Biochemistry, KD Medical College and Hospital, Mathura in collaboration Santosh Medical College and hospital Ghaziabad UP. India. Samples for the study were procured from Obstratics and Gynaecology department of KD medical College of Mathura. The study was conducted with 100umbilical cord samples of preterm and term babies. Neonates were divided into two groups. Group A- 50 preterm neonates (32 weeks to 36 weeks) and group B- 50 full term neonates (37 weeks to 41weeks). Birth weight was measured by using digital electronic weighing scale.
The participants of the study were randomly selected. The clinical conditions of the selected full term and preterm delivery individuals were carefully monitored throughout all the stages of labor. Human Umbilical Cord blood was collected in plain and fluoride vial, about 5ml of Human Umbilical Cord blood was collected from the placental end of umbilical vein (Fig.1) Serum was deep freezed at -20^0 C till further analysis.

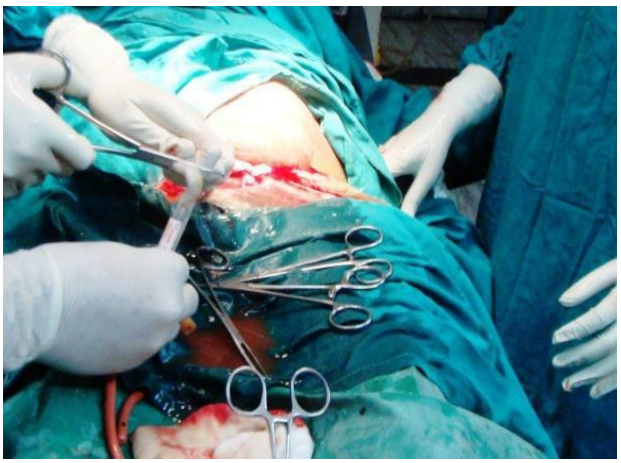


Fig 1: Collection of Humane Umbilical cord blood during Caesarian Section

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Biochemical markers were measured on Fully Automatic-analyzer - Beckmancoulter-AU480. Glucose was estimated by GOD/PAP-enzymatic method, Urea (U) by UV-kinetic method, Creatinine (Cr) by Kinetic Jaffe's method), Uric Acid (UA) by urease enzymatic-colorimetric method, Total bilirubin (TB), Direct bilirubin and Indirect bilirubin by colorimetric method, Total proteins (TP) by Biuret- colorimetric method) and Albumin (Alb) by colorimetric bromocresol green method).

Inclusion criteria

- All neonates between age group 32 weeks to 41 weeks were included.

Exclusion criteria

- Women with pre-existent medical illness/complications including diabetes mellitus, eclampsia, preeclampsia, anemia, thyroid disorders, cardiovascular diseases and HIV, women receiving glucocorticoid therapy for fetal lung maturation, women with family history of cardiovascular diseases; particularly coronary artery disease.

Statistical Analysis

The data were collected analyzed through MS excel 2010. Paired t-test was used to compare the means of pre-term and term neonates where 'p' value <0.05 was taken as statistically significant.

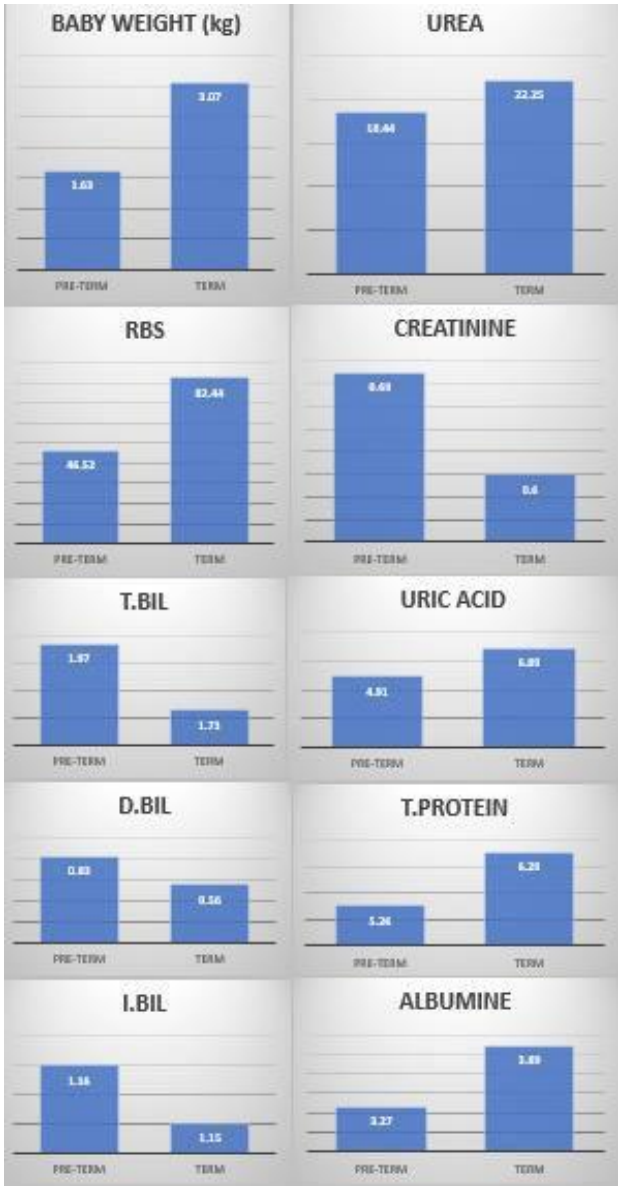
RESULT

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

BIOCHEMICAL PARAMETERS	Pre-term Mean ± SD	Term Mean ± SD	P Value
BABY WEIGHT (kg)	1.63±0.22	3.07±0.30	.001
RBS (mg/dl)	46.52±12.66	82.44±5.84	.001
T.BIL (mg/dl)	1.97±0.97	1.73±0.37	.074
D.BIL(mg/dl)	0.83±0.86	0.56±0.14	.025
I.BIL(mg/dl)	1.16±0.43	1.15±0.32	.920
UREA(mg/dl)	18.44±8.26	22.25±4.97	.004
CREATININE (mg/dl)	0.69±0.94	0.60±0.23	.514
URIC ACID(mg/dl)	4.91±2.04	5.89±8.14	.122
T.PROTEIN (g/dl)	5.26±2.02	6.29±0.72	.001
ALBUMINE(g/dl)	3.27±1.24	3.89±0.38	.001

Baby weight, RBS, Total bilirubin, direct bilirubin, indirect bilirubin, Urea, Creatinine, Uric acid, Total protein and Albumin were higher in preterm neonates as compared to term neonates. Mean baby weight in preterm neonates was 1.63±0.22 and term neonates were 3.07±0.30. Mean of RBS in preterm neonates was 46.52± 12.66 and term neonate's value was 82.44±5.84. Mean of total bilirubin in preterm neonates were 1.97±0.97 and term neonates were 1.73±0.37. Mean value of direct bilirubin in preterm baby was 0.83±0.86 and term baby were 0.56±0.14. Mean of indirect bilirubin in preterm neonates were 1.16±0.43 and term neonates were 1.15±0.32. Mean value of Urea in preterm neonates was 18.44±8.26 and term neonates were 22.25±4.97. Mean of Creatinine in preterm baby were 0.69±0.94 and term neonates mean value were 0.60±0.23. Mean value of Uric acid in preterm neonates were 4.91±2.04 and term neonates mean value were 5.89±8.14.Mean value of total protein in preterm neonates were 5.26±2.02 and term neonates were 6.29±0.72. Mean value of albumin in preterm neonates were 3.27±1.24 and term neonates mean value were 3.89±0.38. All the values of the different parameters in human Umbilical cord blood from both the preterm neonates and term neonates control group were expressed as the mean and standard deviation value (Table -1).

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021



Graph 1: Comparative account of all the parameters of preterm and term Babies

A significant increase in baby Wt., RBS, T. bilirubin, D. bilirubin, I. bilirubin, Urea, Creatinine, uric acid, T. protein and Albumin value was observed in human umbilical cord blood preterm neonates with respected term neonates control group. There was high significant difference in the preterm and term neonates (Table-1).

DISCUSSION

WHO has reported an incidence of around 9-12% for preterm birth, which leads to an estimated birth of 15 million such neonates every year (12). India has an incidence of around 11%, and the figure shares two-thirds of the global burden of preterm births (13). The incidence of preterm birth rates is perceived to be decreasing on one hand due to better antenatal care and increased hospital and institutional delivery rate in India. But on the other hand, owing to the increase in artificially conceived pregnancies, late procreation, and better obstetric interventions, the numbers of term babies is constantly rising.

A well-established supplementation programmed for children of more than nine months of age already exist in many nations, and recommendations to supplement extremely low birth weight (ELBW) babies are also reasonably clear. The decrease observed in gestation weeks and newborn weight in pathological

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newborns from pathological mothers with respect to the control group might be associated with the Intrauterine growth restriction (IUGR) related to these disorders. Significant differences were observed in some biochemical parameters with respect to the maternal age.

Birth weight is a measure of fetal growth that summates body size, body length, baby weight, and subcutaneous fat. This study has shown that neonates who have a reduced birth weight in relation to gestation tend as babies to develop syndrome "X" a combination of hypertension, non-insulin-dependent diabetes mellitus, Jaundice, diabetic Mellitus, cardiovascular diseases, disordered lipids, obesity, and abdominal fatness (14).

This study observed the increase in serum Glucose, Total Protein, Albumin, and Urea values in preterm neonates when compared to the full term neonates. Not many studies have been documented in the preterm neonates and term neonates for fetal metabolites and enzymes present in the umbilical cord blood from mothers with underlying metabolic disorders. Studies have been documented about the normal levels and alterations of metabolites and enzymes, in neonatal human umbilical cord blood from mothers with underlying metabolic/ chronic disorders, infections of the lower genital tract, underlying inflammatory, or immunological conditions, and diseases associated with gestation.

In the study, the mean cord blood glucose level with SD in preterm neonates was found to be 46.52±12.66mg/dl with the term neonates were 82.07±0.30 mg/dl. This mean value was similar to that of umbilical cord blood glucose level (3.9 ± 0.5mmol/L or 70 mg/dL) of cord blood, as observed in one of the studies (15). The study also showed that during cesarean and normal delivery the mode of cord blood glucose level remains unaltered. As per reports, the stress associated with labor or surgery and the administration of anesthetic agents does not affect the glucose levels of the umbilical cord blood. However, conducting the study with a larger sample size would help to scientifically explain the etiology behind the results obtained.

As the protein is the most important nutrient of a developing fetus, hence the total protein evaluation of cord blood will provide the health status of the newborn. Total protein and albumin level in preterm neonates were 5.26±2.02, 3.27±1.24 and term neonate's level was 6.29±8.14, 3.89±0.38. This mean value was similar to that of total protein and albumin level in one of the observational study conducted in Kerala, India, reported the range of 4.4-7.4gm/dl, 1.7-3.4gm/dl respectively (16), which was less than the calculated range of present study, while our mean total protein and albumin value was similar to that of the suggested value (4.1 ± 6.2gm/dl) of preterm babies in another study (17).

No significant difference was observed between the maternal serum & cord blood uric acid levels in full & preterm infants (18). The levels of indirect bilirubin, Creatinine in maternal and cord blood serum showed no or slight differences in one of the investigational study (19). The evaluated mean values of Urea in preterm neonates was 18.44±8.26 and term neonates were 22.25±4.97. Mean of Creatinine in preterm baby were 0.69±0.94 and term neonates mean value was 0.60±0.23. The mean value of Uric acid in preterm neonates was 4.91±2.04 and the term neonates mean value was 5.89±8.14 which was consistent with that of other studies (18).

An increase in the bilirubin level is a common clinical condition requiring evaluation and treatment in neonates and a frequent reason for hospital readmission during the 1st week of life. Jaundice is a common occurrence which requires attention for a few days after birth. Apart from 8%–10% of healthy newborns, most of the healthy newborns develop jaundice in the physiological range that does not require any intevention. The others require interventions such as phototherapy or exchange transfusion, or other treatment modes. Incidence of hyperbilirubinemia in this study was 11.2%, which is in accordance to studies conducted by other authors such as 12.80% in a study by Awasthi and Rehman (20), 12.00% as per a study by Randev and Grover(21), and 11.4% in a study(22), many other studies, where at cord serum albumin levels less than 2.8 g/dl, 58.35%, 82% and 95% of newborns developed significant hyperbilirubinemia in all of the aforementioned studies (23,24,25). At levels greater than 3.3 g/dl, no infants developed jaundice. However, in the study, 12.68% developed hyperbilirubinemia at cord blood serum albumin greater than 3.5 g/dl(23).

In the study, the mean cord blood total bilirubin, direct and indirect bilirubin level with SD in preterm neonates was found to be 1.97±0.97 and term neonates were 1.73±0.37. The mean value of direct bilirubin in the preterm babies was 0.83±0.86 and term babies were 0.56±0.14. The mean of indirect bilirubin in preterm neonates was 1.16±0.43 and term neonates were 1.15±0.32. The large variation (standard

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deviation) in some analytes as observed in (Table-1) in cord blood of term newborn suggesting future larger multicentric studies on these parameters.

CONCLUSION

Findings demonstrate that total baby weight, cord blood glucose, bilirubin, urea, total protein, and albumin were significantly deffered in preterm neonates compared with term infants, showing a trend to worse biochemical preterm neonates. Future studies are needed to determine if this atherogenic profile in the preterm neonate can affect neonate's metabolism, increasing the risk for Jaundice, diabetic Mellitus, and cardiovascular diseases in adult life. Taking the maternal disease into consideration along with early markers of neonatal damage could help prevent future maternal and perinatological complications.

Limitation: Lack of separate gender wise study, sample size small and single center study, no correlation of baby's biochemical profile with mothers biochemical profile.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTIONS

OP drafted the manuscript, compiled information from the literature, and designed the figures and tables. OP and AAC drafted the manuscript and gathered information from the literature. PS supervised and reviewed the manuscript. PK, TK and AS supervised and reviewed the manuscript and designed the figures and tables.

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None

DATA AVAILABILITY

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

Ethical Clearance for the study was obtained from the Institutional Ethics Committee.

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