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Original Article

Paediatrics Section

Correlation between Selected Micronutrient Status in Maternal Blood and Cord Blood of Newborn from a Tertiary Care Hospital in West Bengal, India: A Cross-sectional Study

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ABSTRACT

Introduction: The demand for most micronutrients increases during pregnancy for obvious reasons. Micronutrients like copper and zinc are indispensable co-factors for various enzymes in metabolism. The reduction in the concentration of serum iron and ferritin is a common phenomenon in pregnancy, and early diagnosis is crucial for favourable maternal and foetal outcomes. However, there is a dearth of studies on the metabolism of micronutrients in pregnancy.

Aim: The aim of this cross-sectional study, conducted from July 2018 to February 2019 in the Department of Gynaecology and Obstetrics and the Department of Biochemistry, College of Medicine and Sagore Dutta Hospital, West Bengal, India, was to assess the serum levels of copper, zinc, and iron in maternal serum and foetal cord blood. Additionally, the study aimed to correlate the concentrations of these micronutrients between maternal serum and foetal cord blood.

Materials and Methods: A total of 336 pregnant women of childbearing age, irrespective of gravida, were included in the study. Blood samples were collected from the pregnant women, and cord blood samples were collected from the foetal end in clot vials for the estimation of copper, zinc, and iron levels. Correlation was assessed between the concentration of these micronutrients in maternal serum and cord blood of the newborn. Data normality was determined using the Shapiro-Wilk normality tests, and the significance level was set at p-value ≤0.05.

Results: The study included a total of 336 pregnant women in the age group of 18-33 years, with a mean age of 29.72±4.39 years. In maternal serum, the mean concentration of copper was 122.79±33.67 μg/dL, zinc was 78.47±27.62 μg/dL, and iron was 114.5±45.05 μg/dL. In foetal cord blood, the mean concentration of copper was 48.02±16.37 μg/dL, zinc was 75.82±27.64 μg/dL, and iron was 185.30±52.74 μg/dL. The correlation coefficients between maternal serum and foetal cord blood concentrations were statistically significant for zinc and iron (p-value <0.05). Additionally, the correlation was statistically significant for copper (p-value=0.030). The mean concentration of haemoglobin in maternal serum was 10.9±1.96 g/dL, compared to 14.05±2.13 g/dL in cord blood. The mean maternal serum ferritin was 73.53±56.15 μg/L, and the mean cord blood ferritin was 147.21±61.13 μg/L.

Conclusion: The study demonstrated a positive correlation between the concentrations of iron and zinc in maternal serum and foetal cord blood, while a negative correlation was observed for copper concentration.

Keywords: Copper, Iron, Maternal serum, Pregnancy, Zinc

INTRODUCTION

Micronutrients are inorganic elements and vitamins that are needed in very minute quantities but are essential in the human body [1,2]. These micronutrients, namely iron, copper, and zinc, have an important influence on the health of the pregnant woman and the growing foetus. The demand for micronutrients increases during pregnancy for obvious reasons, and suboptimal levels of any of these could affect the progress and outcome of delivery [3,4]. Copper and zinc are important components of metalloproteins that play a vital role in metabolism. Copper and iron are required for the post-translational modification of collagen and elastin, thus being important for the structural integrity of these proteins [2,3]. Minerals such as zinc and manganese have also been demonstrated to play a role in antioxidant mechanisms. This is important because oxidative reactions are more frequent in pregnancy and may contribute to preeclampsia [5,6]. Although iron deficiency is known to be the most common cause of anemia during pregnancy in India, simple iron supplementation often fails to correct anaemia [7,8]. This may be due to the fact that copper-containing ceruloplasmin plays an important role in iron metabolism [9]. Some studies have demonstrated an improvement in maternal haemoglobin levels with iron supplementation along with zinc [10-13]. Similarly, zinc is also necessary for foetal and neural development [14,15]. There is a lack of studies on the metabolism of micronutrients during pregnancy, mainly due to its inherent complexity. As micronutrients have a profound influence on pregnancy outcomes, including intergenerational ones, the present study was conducted to estimate the concentration of copper, zinc, and iron in maternal serum and foetal cord blood. Additionally, we aimed to investigate whether any correlation exists between maternal serum and foetal cord blood levels of copper, zinc, and iron.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Gynaecology and Obstetrics, in association with the Department of Biochemistry, College of Medicine and Sagore Dutta Hospital, Kolkata, West Bengal, India, over a period of eight months, from July 2018 to February 2019. Ethical clearance was obtained from the Institutional Ethical Committee (IEC) (Registration No. ECR/1210/Inst/WB/2019).

Inclusion criteria: Pregnant women of childbearing age group, irrespective of gravida, were included in the study. Only full-term apparently healthy neonates were included. The subjects were selected from those admitted to the maternity wards of the hospital for delivery.

Exclusion criteria: Pregnant women with a history of smoking, hypertension (either chronic or pregnancy-induced), convulsion, gestational diabetes or known diabetes, or with any obstetrical abnormalities were excluded from the study. Newborn babies weighing less than 2.5 kg, gestational age less than 36 weeks, and an APGAR score of less than seven were also excluded.

Sample size: Statistics from previous years showed that the average number of deliveries per month was around 220 in the hospital, which comes to an average of seven per day. The samples were collected two days per week, resulting in 56 per month. Therefore, the sample size was calculated to be 336 (i.e., 56×6) subjects, including mothers and their respective babies over a period of six months.

Data collection: Blood samples were collected from the pregnant women (after obtaining their written informed consent) in a clotted vial for the estimation of copper, zinc, and iron levels. Similarly, cord blood samples were collected from the foetal end in clot vials for the estimation of copper, zinc, and iron levels. The estimation of copper, zinc, and iron was performed using reagents procured from government resources in the Departmental Clinical Laboratory. The serum copper was estimated by a colorimetric method and measured at 580 nm in a semiautomated analyser. The normal reference range of copper in females is 88-155 µg/dL, and in newborns, it is 12-67 µg/dL. The serum iron was estimated by the Ferrozine method and measured at 578 nm in a semiautomated analyser. The normal reference ranges of iron in females is 35-145 µg/dL, and in newborns, it is 150-220 µg/dL. The serum zinc was estimated by a colorimetric method and measured at 570 nm in a semiautomated analyser. The normal reference range of zinc in neonates is 64-118 µg/dL, and in adults, it is 80-120 µg/dL [16-19].

STATISTICAL ANALYSIS

The data regarding the laboratory parameters thus obtained were compiled in a Microsoft Excel worksheet and double-checked for errors. The data were then statistically analysed using the Statistical Package for the Social Sciences (SPSS) Statistics 20.0 software. The data were tested for normality using the Kolmogorov-Smirnov test. The t-test was used to statistically analyse the data for copper and zinc, while the Mann Whitney U-test was used for iron. The level of significance was considered to be <0.05.

RESULTS

A total of 336 subjects were enrolled in the study. The mean age of the pregnant mothers was 29.72±3.32 years, with a range of 18 to 33 years. The average birth weight of the newborns was 2.57±0.73 kg, and the mean gestational age was 37.2±0.25 weeks. Out of the 336 neonates, 169 were males, and the remaining were females.

In maternal serum, the mean concentration of copper was 122.79±33.67 µg/dL, zinc was 78.47±27.62 µg/dL, and iron was 114.5±45.05 µg/dL. Copper and zinc followed a parametric distribution, while iron followed a non-parametric distribution. In cord blood serum, the mean values for copper were 48.02±16.37 µg/dL, zinc was 75.82±27.64 µg/dL, and iron was 185.30±52.74 µg/dL. The mean values of haemoglobin, ferritin, and iron were higher in foetal cord blood compared to maternal serum [Table/Fig-1].

The maternal concentration of iron and zinc positively correlated with the foetal cord blood concentrations, while the copper concentrations in maternal and foetal cord blood were negatively correlated [Table/Fig-2].

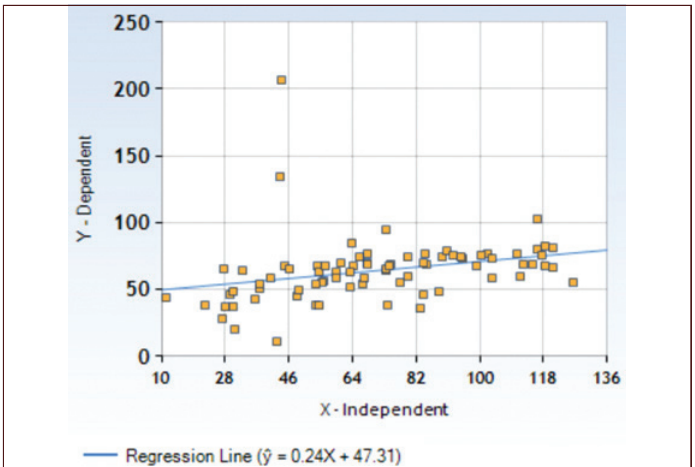
[Table/Fig-3] depicts the positive correlation between the maternal serum zinc concentration and foetal cord blood zinc concentration. [Table/Fig-4] illustrates the negative correlation between the maternal serum copper concentration and foetal cord blood copper concentration. [Table/Fig-5,6] show the correlation between maternal serum iron and foetal cord iron, and maternal serum ferritin and foetal cord ferritin, respectively.

Variables	Maternal serum	95% CI	Cord blood	95% CI	p-value
Copper (µg/dL)	122.79±33.67	116.63-128.34	48.02±16.37	45.05-51.03	0.00001
Zinc (µg/dL)	78.47±27.62	73.42-83.51	75.82±27.64	70.76-80.87	0.0006
Iron (µg/dL)	114.5±45.05	106.18-122.82	185.30±52.74	175.66-194.94	0.00152
Haemoglobin (g/dL)	10.9±1.96	10.67-11.13	14.05±2.13	13.8-14.3	0.00005
Serum ferritin (µg/dL)	73.53±56.15	66.94-80.11	147.21±61.13	140.23-154.36	0.00001

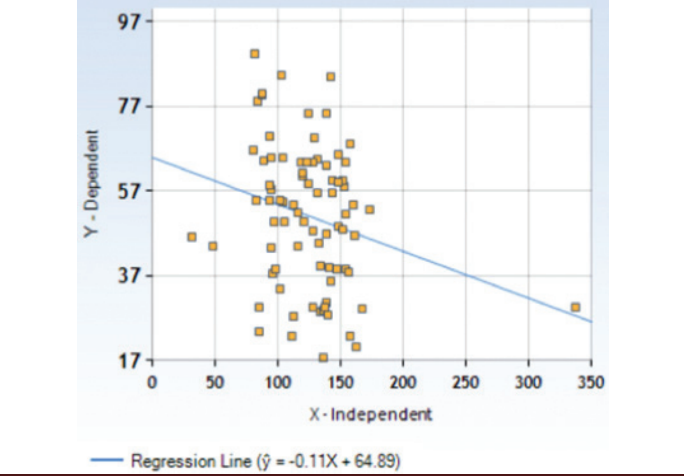
[Table/Fig-1]: Comparison of the mean concentration of the micronutrients, (copper, zinc and iron) in maternal serum and foetal cord blood.
t-test was used to statistically analyse the data for copper and zinc and Mann-Whitney U-test for iron

Parameter	Correlation	p-value
Copper	-0.011	0.030
Zinc	+0.46	0.012
Iron	+0.626	0.006
Ferritin	-0.134	0.002
Haemoglobin	+0.203	0.001

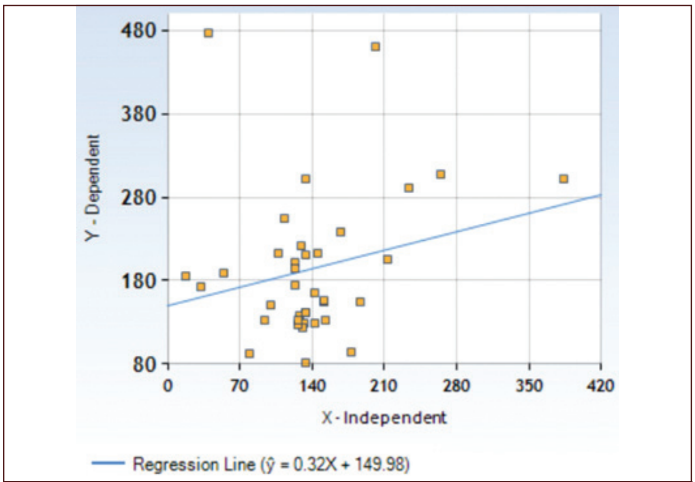
[Table/Fig-2]: Showing the correlation coefficient between maternal serum and foetal cord blood.
Pearson's correlation, p-value, significant if <0.05



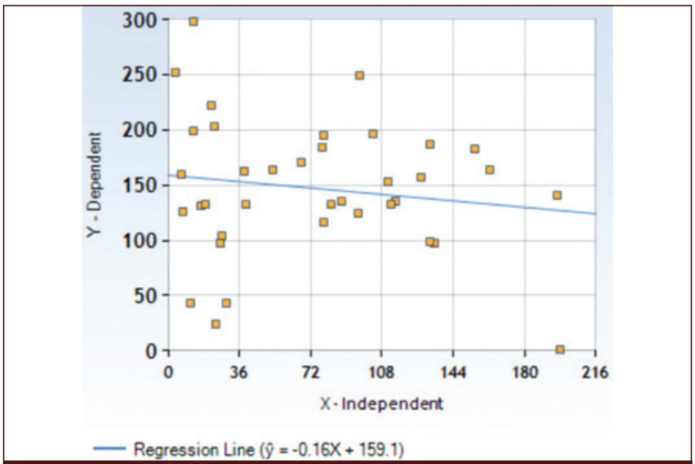
[Table/Fig-3]: Showing the correlation between the maternal serum zinc concentration and foetal cord blood zinc concentration.
(X-axis shows the maternal serum zinc concentration, Y-axis shows foetal cord blood zinc concentration)



[Table/Fig-4]: Showing the correlation between the maternal serum copper concentration and foetal cord blood copper concentration.
(X-axis- independent variable maternal serum copper concentration, Y-axis dependent variable-foetal cord blood copper concentration)



[Table/Fig-5]: Showing the correlation between the maternal serum iron concentration and foetal cord blood iron concentration.
(X-axis-independent variable-maternal serum iron concentration, Y-axis-dependent variable- foetal cord blood iron concentration)



[Table/Fig-6]: Showing the correlation between the maternal serum ferritin concentration and foetal cord blood ferritin concentration.
(X-axis-independent variable-maternal serum-ferritin concentration, Y-axis-dependent variable- foetal cord blood ferritin concentration)

DISCUSSION

The present study aimed to identify the correlation among the levels of selected micronutrients, namely copper, iron, and zinc, in maternal serum and foetal cord blood.

Firstly, the distribution of copper in both maternal serum and foetal cord blood was found to be parametric. In this study, the correlation coefficient of copper between maternal serum and foetal cord blood was found to be negative (-0.011, p-value <0.05). This can be explained by the fact that the mean serum copper concentration in maternal serum increases during pregnancy. This increase is attributed to an increase in ceruloplasmin synthesis, induced by oestrogen during pregnancy, along with an increased binding affinity of ceruloplasmin with copper. As a result, only a small amount of copper passes through the placenta and reaches the foetus. The serum levels of copper may also be influenced by the mobilisation of copper from maternal tissues to the foetus [20,21].

A study conducted by Jariwala M et al., found that the cord blood concentration of copper was only 28% of the maternal serum concentration of copper [22]. However, a positive correlation was found between copper concentration in maternal serum and foetal cord blood in an Egyptian study [23].

The distribution of zinc in maternal serum and foetal cord blood was also found to be parametric. The correlation coefficient of zinc was found to be 0.46 (p-value <0.05, significant), indicating a positive correlation. A similar significant positive correlation was found between zinc levels in neonates and their mothers in a study conducted by Abdellatif M et al., [23]. Usually, there is a passive transplacental transfer of zinc from mother to foetus. The zinc binding capacity decreases during pregnancy, which may facilitate the efficient transfer of zinc to the foetus. Similar findings have been observed in a few other studies conducted in Jordan, although a negative correlation was also observed in another study [24,25]. On the contrary, another study reported significantly higher cord blood levels of zinc and significantly lower cord blood levels of copper compared to maternal levels [23].

A significant finding in this study was the positive correlation coefficient (+0.626, p-value <0.05) between iron levels in maternal serum and foetal cord blood. This suggests that iron concentration in maternal serum directly affects the iron levels in cord blood. Furthermore, mothers with sufficient iron stores tend to have babies with adequate iron levels in their cord blood. These findings align with previous studies [26,27]. Upadhyay C et al., also reported a strong positive correlation between iron levels in mothers and cord blood [28].

Additionally, the levels of ferritin and haemoglobin in newborns can be compared to those in maternal serum. The distribution of ferritin and haemoglobin in both maternal serum and foetal cord blood was found to be symmetrical. The mean values of ferritin and haemoglobin in maternal serum were 73.53±56.15 μg/dL and 10.9±1.96 g/dL, respectively, while in foetal cord blood, they were 147.21±61.13 μg/dL and 14.05±2.13 g/dL, respectively. In these parameters, cord blood exhibited higher concentrations than maternal serum. This can be explained by the significant transfer of iron stores from mothers with sufficient iron levels to their foetuses. The transplacental transfer of iron is also influenced by hepcidin, a protein involved in regulating placental iron uptake. Additionally, there is maximal stimulation of erythropoiesis towards the end of the gestational period, which may explain the high ferritin index observed in other studies [29,30].

Limitation(s)

In the present study, no information was collected regarding the socioeconomic status and dietary habits of the pregnant mothers. Secondly, since this was a hospital-based project, the results of the present study cannot be generalised. Thirdly, due to the inclusion of only full-term healthy babies, statistical analysis regarding the newborn variables was not possible.

CONCLUSION(S)

In the above study, the concentration of iron and zinc in foetal cord blood was similar to that in the mother, but the concentration of ferritin and haemoglobin was higher in foetal cord blood. Furthermore, a negative correlation was observed between the concentration of copper in maternal serum and that in foetal serum. Thus, it can be concluded that the micronutrient status of the newborn is largely influenced by that of the pregnant mother. Larger, well-designed studies are needed to establish proper reference intervals for micronutrients, which would enable the development of appropriate methods and dosages for supplementing these micronutrients during pregnancy, ultimately leading to healthier outcomes.

REFERENCES

[1] Irwinda R, Wibowo N, Putri AS. The concentration of micronutrients and heavy metals in maternal serum, placenta, and cord blood: A cross-sectional study in preterm birth. J Pregnancy. 2019;2019:5062365. 7 pages.
[2] Sandström B. Micronutrient Interactions: Effects on absorption and bioavailability. Br J Nutr. 2001;85(Suppl. 2):S181-85.
[3] Lewicka I, Kocyłowski R, Grzesiak M, Gaj Z, Oszukowski P, Suliburska J. The role of trace elements during pregnancy. Ginekol Pol. 2017;88(9):509-14.
[4] Pathak P, Kapil U, Kapoor SK, Saxena R, Kumar A, Gupta N, et al. Prevalence of multiple micronutrient deficiencies amongst pregnant women in a rural area of Haryana. Indian J Pediatr. 2004;71(11):1007-14.
[5] Bakacak M, Kılınç M, Serin S. Changes in copper, zinc, and malondialdehyde levels and superoxide dismutase activities in pre-eclamptic pregnancies. Med Sci Monit. 2015;21:2414-20.
[6] Tabrizi FM, Pakdel FG. Serum level of some minerals during three trimesters of pregnancy in Iranian women and their newborns: A longitudinal study. Indian J Clin Biochem. 2014;29(2):174-80.
[7] Tandon R, Jain A, Malhotra P. Management of iron deficiency anemia in pregnancy in India. Indian J Hematol Blood Transfus. 2018;34(2):204-15.
[8] Sharma DC, Kiran R, Ramnath V, Khushlani K, Singh PP. Correction of anemia and iron deficiency in vegetarians by administration of ascorbic acid . Indian J Physiol Pharmacol. 1995;39(4):403-06.
[9] Gaware V, Kotade K, Dhamak K, Somawanshi S. Ceruloplasmin its role and significance: A review. Int J of Biomed Res [Internet]. 2010;1(4):153-62.
[10] Kolsteren P, Rahman S, Hilberbrand K, Diniz A. Treatment for iron deficiency anaemia with a combined supplementation of iron, vitamin A and zinc in women of Dinajpur, Bangladesh. Eur J Clin Nutr. 1999;53:102-06.
[11] Saaka M. Combined iron and zinc supplementation improves haematologic status of pregnant women in Upper West Region of Ghana. Ghana Med J. 2012;46(4):225-33.
[12] Siregar EDP, Amir A, Irawati N. Correlation between zinc and folic acid intake with hemoglobin levels in pregnancy. Science Midwifery. 2022;10(5):3767-75.
[13] Hanson Z, Kaur S, Lee S, Akhtari M. P1529: Hemoglobin response to zinc supplementation in patients with zinc deficiency and chronic anemia. Hemasphere. 2022;6:1410-11.
[14] Terrin G, Berni Canani R, Di Chiara M, Pietravalle A, Aleandri V, Conte F, et al. Zinc in early life: A key element in the fetus and preterm neonate. Nutrients. 2015;7(12):10427-46.
[15] Bermúdez L, García-Vicent C, López J, Torró MI, Lurbe E. Assessment of ten trace elements in umbilical cord blood and maternal blood: Association with birth weight. J Transl Med. 2015;13:291.
[16] Abe A, Yamashita, S, Noma A. Sensitive, direct colorimetric assay for copper in serum. Clin Chem. 1989;35(4):552-54.
[17] Burtis CA, Ashwood ER, Burns DE. Tietze Textbook of Clinical Chemistry and Molecular Diagnostics: 5th ed: India.: Elsevier; 2012.
[18] Makino T. A sensitive, direct colorimetric assay of serum zinc using nitro PAPS and microwell plates. Clin Chem Acta. 1991;197(3):209-20.
[19] Siedel J. Improved ferrozine based reagent for the determination of serum iron (transferrin iron) without deproteinization. Clin Chem. 1984;30:975.
[20] Özden TA, Gökçay G, Cantez MS. Copper, zinc and iron levels in infants and their mothers during the first year of life: A prospective study. BMC Pediatr. 2015;15:157.
[21] Ugwuja EI, Nnabu RC, Ezeonu PO, Uro-Chukwu H. The effect of parity on maternal body mass index, plasma mineral element status and new-born anthropometrics. Afr Health Sci. 2015;15(3):986-92.
[22] Jariwala M, Suvarna S, Kiran Kumar G, Amin A, Udas AC. Study of the concentration of trace elements fe, zn, cu, se and their correlation in maternal serum, cord serum and colostrums. Indian J Clin Biochem. 2014;29(2):181-88.
[23] Abdellatif M, Elhawary IM, Mahmoud MM, Youness ER, Abuelhamd WA. Cord levels of zinc and copper in relation to maternal serum levels in different gestational ages. Egypt Pediatric Association Gaz. 2021;69:11.
[24] Awadallah SM, Abu-Elteen KH, Elkarmi AZ, Qaraein SH, Salem NM, Mubarak MS. Maternal and cord blood serum levels of zinc, copper, and iron in healthy pregnant Jordanian women. J Trace Elem Exp Med. 2004;17:01-08.
[25] Iqbal AS, Shahidullah M, Islam MN, Akhter S, Banu S. Serum zinc and copper levels in the maternal blood and cord blood of neonates. Indian J Pediatr. 2001;68:523-26.
[26] Kohli UA, Rajput M, Venkatesan S. Association of maternal hemoglobin and iron stores with neonatal hemoglobin and iron stores. Med J Armed Forces India. 2021;77(2):158-64.
[27] Siddappa AM, Rao R, Long JD, Widness JA, Georgieff MK. The assessment of newborn iron stores at birth: A review of the literature and standards for ferritin concentrations. Neonatology. 2007;92:73-82.
[28] Upadhyaya C, Mishra S, Ajmera P, Sharma P. Serum iron, copper and zinc status in maternal and cord blood. Indian J Clin Biochem. 2004;19(2):48-52.
[29] Bothwell TH. Iron requirements in pregnancy and strategies to meet them. Am J Clin Nutr. 2000;72:S257-64.
[30] Lorenz L, Peter A, Poets CF, Franz AR. A review of cord blood concentrations of iron status parameters to define reference ranges for preterm infants. Neonatology. 2013;104(3):194-202.

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