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Comparative study of trace elements and serum ceruloplasmin level in normal and pre-eclamptic pregnancies with their cord blood

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Abstracts

The aim of the present study is to assess the comparison of trace elements and serum ceruloplasmin level in normal and pre-eclamptic pregnancies with their cord blood. Pregnancy is associated with increased demand of all the micronutrients like Iron, Copper, Zinc, Vit B12, Folic acid and Ascorbic acid. The pregnant women were admitted in maternity ward, Department of Obstetric and Gynecology, Command Hospital, Pune. The study group comprised of 61 pregnant women and their newborns. Venous blood (5 ml.) was collected from mother at the time of delivery and cord blood (10 ml.) was taken from maternal end of umbilical cord. Of 61 pregnant women, 14 were pre-eclamptic and 47 were normal pregnant women. In normal pregnancy, the copper & ceruloplasmin concentration were statistically significantly increased ($p<0.01$) in maternal blood as compared to cord blood. Serum iron and zinc concentration were observed significantly raised ($p<0.01$) in cord blood compared to maternal blood. Similar results were found in pre-eclamptic pregnancies. The significant difference ($p<0.001$) was observed in all biochemical parameters between maternal and cord blood pre-eclamptic pregnancies. On comparison of the normal and pre-eclamptic pregnancy, the serum iron significantly increased ($p<0.01$) in normal pregnancy than pre-eclamptic, but no statistically significant variations were observed in serum zinc, copper and ceruloplasmin concentration. Our study infers that iron is the most important micronutrient and it should be supplemented as a daily requirement in pregnant women. Ceruloplasmin can be used as a diagnostic measurement in pregnancy period.

Keywords: Pregnancy, Pre-eclampsia, Cord Blood, Trace Elements, Ceruloplasmin

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Introduction

Pregnancy is associated with increased demand of all the micronutrients like Iron, Copper, Zinc, Vitamin B12, Folic acid and Ascorbic acid [1]. The deficiency of these nutrients could affect pregnancy, delivery and outcome of pregnancy. Vitamins and minerals are collectively referred to as micronutrients and have important influence on the health of pregnant women and growing fetus [2]. The four trace elements namely Zinc, Manganese, Copper and Chromium are necessary during pregnancy and these elements should be supplemented as a daily requirement in pregnant women [3, 4]. Zinc is an essential for the growth and development of human life and has an active role in body function. During pregnancy, zinc is also used to assist the fetus to develop the brain and also to be an aid to the mother in the I^{ST} and II^{nd} stage of labor. Copper, another important trace element, joins to many Cu-dependent enzymes such as lysyl oxidase (extracellular matrix protein cross-linking), cytochrome *c* oxidase (energy production), tyrosinase, dopamine-β-hydroxylase, peptidylglycine alpha-amidating monooxygenase, and monoamine oxidase (pigment and neurotransmitter production and metabolism), ceruloplasmin (ferroxidase activity), and copper–zinc superoxide dismutase (CuZn-SOD; SOD1), known as oxidant defense enzymes. Manganese is a mineral that helps to form bone and cartilage. It is also a component of enzymes that play a role in the formation of carbohydrates, amino acids, and cholesterol. As part of a powerful antioxidant called manganese superoxide dismutase, it helps to protect cells from damage. Chromium is a mineral that helps the body break down and store fats, carbohydrates, and protein. It also works with the hormone insulin to maintain normal levels of

glucose (sugar) in the body. Hypertension is unique to pregnancy and it is a clinical syndrome that affects both mother and fetus. There is evidence that pre-eclampsia develops as a sequence of alterations in the vasculature supplying blood to the placenta. These alterations in placental circulation probably occur in early second trimester, whereas the maternal manifestations of the disease are not apparent until late in pregnancy, most often near term. Pre-eclampsia, a pregnancy specific disorder is a leading cause of maternal mortality and increases perinatal mortality. The clinical diagnosis is based on the new onset of hypertension and appearance of proteinuria, oedema during pregnancy after 20 weeks of gestation. It is more common in nalliparous women, the incidence in such women ranging from 2-10% in different population [5, 6]. Zinc is transferred across the placenta to the fetus against a concentration gradient and taken up there after by the fetus. Pregnancy associated with significant physiological changes, which increases the demand for iron. Iron is most important trace element and it also an essential component of hemoglobin synthesis. Iron is needed for additional erythrocyte production during pregnancy. It is estimated approximately 750-800 mg of elemental iron is required for entire pregnancy [7]. Serum ceruloplasmin is an α-2, copper transporting globulin synthesized in liver microsomes and possesses feroxidase activity. It acts as an antioxidant in serum by oxidizing ferrous iron which could otherwise act as a catalyst in generating toxic free radicals [8]. The present study was done to assess the comparison of trace elements and serum ceruloplasmin level in normal and pre-eclamptic pregnancies with their cord blood.

Material and Methods

The study was conducted in Department of Biochemistry, Armed Forces Medical College in association with Department of Obstetric and Gynecology, Command Hospital, Pune. The pregnant women were admitted in maternity ward, Department of Obstetric and Gynecology, Command Hospital, Pune. The study group was comprised of 61 pregnant women during labor ranging in age from 19-35 years and their newborns. In which, 14 cases were pre-eclamptic (having hypertension, proteinuria and oedema) while 47 were normal pregnant women. Women with obstetrical condition like multiple pregnancy, gestational diabetes and history of cesarean, breech delivery were excluded. Venous blood (5 ml.) was collected from mother at the time of delivery and cord blood (10 ml.) was taken from maternal end of umbilical cord to coinside precisely with newborns venous blood levels. The samples were transferred to labeled sterile vials and allowed to clot at room temperature. Blood was centrifuged at 3000 rpm for 5 minutes. The supernatant was used to quantify the copper and iron (Crest Biosystem, Goa) by semi autoanalyzer (Microlab 300, Merck, Vital Scientific, N.V., Dieren, Netherlands). Zinc was estimated by atomic absorption spectrometry (AAS) method [9]. Serum ceruloplasmin was estimated by kinetic method [10] on Shimadzu CL-750 spectrophotometer.

Statistical Analysis

Data was reported as mean ± standard deviation (SD). The data was compared using ANOVA "t"-test. The confidence limit was kept at 95%, hence a "p" value <0.05 and "p" value <0.001 was considered to be statistically significant.

Results

The results were observed as follows. Of 61 pregnant women, 14 were pre-eclamptic and 47 were normal pregnant women. In normal pregnancy, the copper & ceruloplasmin concentration were statistically significantly increased ($p<0.01$) in maternal blood as compared to cord blood. Serum iron and zinc concentration were observed significantly raised ($p<0.01$) in cord blood compared to maternal blood. Similar results were found in pre-eclamptic pregnancies. The significant difference ($p<0.001$) was observed in all biochemical parameters between maternal and cord blood pre-eclamptic pregnancies. On comparison of the normal and pre-eclamptic pregnancy, the serum iron significantly increased ($p<0.01$) in normal pregnancy than pre-eclamptic, but no statistically significant variations were observed in serum zinc, copper and ceruloplasmin concentration (Table 1).

Table 1: *Comparison of trace elements and serum ceruloplasmin level in pregnancies with their cord blood*

S. No.	Parameter	Normal pregnancies	Pre-eclamptic pregnancies	Normal pregnancies	Pre-eclamptic pregnancies
		Maternal blood	Maternal blood	Cord blood	Cord blood
1.	Copper (mg/dl)	1.44 ± 0.2*	1.58 ± 0.2***	0.26 ± 0.1	0.81± 0.1
2.	Zinc (µg/dl)	57.5 ± 21.6	49.2 ± 17.8***	90.8 ± 28.4**	79.9 ± 24.7
3.	Iron (µg/dl)	120.4 ± 25.2$^{\$}$	96.3 ± 25.2***	153.4 ± 40.3**	118.6 ± 44.6
4.	Ceruloplasmin (IU/L)	1736 ± 295*	1728 ± 176***	335 ± 107	376 ± 77

Normal pregnancies (n=47), Pre-eclamptic pregnancies (n=14)
Value was mean ± SD;
$^{\$}p$ <0.01 normal pregnancies as compared to pre-eclamptic pregnancies
**p <0.01 normal pregnancies maternal blood as compared to normal pregnancies cord blood*
***p <0.01 normal pregnancies cord blood as compared to normal pregnancies maternal blood.*
****p <0.001 pre-eclamptic pregnancies maternal blood as compared to pre-eclamptic pregnancies cord blood*

Discussion

Pregnancy is a period of rapid growth and cell differentiation for both the mother and fetus. Consequently, it is a period both are vulnerable to changes in dietary supply, especially of those micronutrients that are marginal under normal circumstances. In developed countries this vulnerability applies mainly to micronutrients. Iron deficiency is a common disorder, especially in pregnancy [11]. Pre-eclampsia is the most common medical complication of pregnancy associated with increased maternal and infant mortality and morbidity. The exact etiology is not known, although several evidences indicate that various elements might play an important role in pre-eclampsia [12].

In the present study we observed that the serum copper and ceruloplasmin levels were higher in maternal blood than cord blood in normal pregnancies. The copper difference was found statistically significant while the ceruloplasmin was observed highly statistically significant between maternal and cord blood. The maternal blood ceruloplasmin was observed about five times greater than cord blood. This is due to non-transportation of ceruloplasmin across the placenta; hence its circulation in the cord blood must be, entirely of fetal origin.

In the present study, pre-eclamptic pregnancies the copper and ceruloplasmin concentration was observed to the similar significant difference between maternal and cord blood as normal pregnancies. On comparison between normal and pre-eclamptic pregnancies the serum copper and ceruloplasmin concentration was decreased in pre-eclemptic pregnancies than normal pregnancies. Parveen S *et al* (2002) [13] reported that the copper remains in cord blood plasma at much lower conc. than in the mother, suggesting that prematurity may place the newborn infant at a greater risk than the term infant to copper deficiency. This situation, together with a reduced synthesis in the fetus of the transport protein ceruloplasmin, creates another potential challenger in the nutritional support of the premature infants.

The serum zinc and iron conc. were significantly higher in cord blood than maternal blood in normal pregnancies. The increased fetal iron demand or maternal iron insufficiency is related to both an increase in the expression of placental transferrin receptor on the syncytiotrophoblast and an increase in the expression of the ferritin receptor in the placental microvilli membrane. Expression of the endosomal membrane iron transporter, divalent metal ion transporter (DMT-1), has also been shown to be involved in the transfer of iron from the syncytiotrophoblastic endosome into the cytoplasm. Moreover, placental iron regulatory protein 1 activity has been directly related to transferrin receptor messenger RNA concentrations in human placenta, and expression of this protein has been found to be related to the iron content of the placenta [14]. Zn is passively transferred from mother to fetus across the placenta and there is also decreased Zn binding capacity of maternal blood during pregnancy which facilitates efficient transfer of Zn from mother to fetus resulting in an increase level of Zn in cord blood. Zn is essential for proper growth of fetus and the fall in Zn during pregnancy could also be a physiological response to expanded maternal blood volume [15]. Islam M *et al* (1994) [16] reported that the increased zinc in cord blood suggested that may be due to efficient transfer of zinc from mother to fetus irrespective of maternal status and high proteosynthetic activity in fetus. The decreased zinc in maternal blood is attributed by some workers to physiological adjustment in response to expanded maternal blood volume. The placental transfer of zinc, as inferred from maternal and fetal concentrations of zinc, is similar in normal pregnancies, pregnancies with intrauterine growth retardation, and pre-eclamptic pregnancies is transferred across the placenta to the fetus against a concentration gradient and is taken up there after by the fetus.

On comparison between normal and pre-eclamptic pregnancies, the serum zinc was observed in significantly decreased in pre-eclamptic pregnancies. Kumrus *et al* (2003) [17] reported that the assessment of trace elements in normal and pre-eclamptic pregnancies. They observed that the serum zinc and copper ($p< 0.001$) levels significantly lower in pre-eclamptic pregnancies as compared to normal pregnancies.

Conclusion

Iron deficiency is a common disorder, especially in pregnancy. Our study infers that iron is the most important micronutrient and it should be supplemented as a daily requirement in pregnant women. Ceruloplasmin is higher in normal pregnancies in comparison to pr-eclamptic pregnancies hence it can be used as a diagnostic measurement in pregnancy period.

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