Assessment of Serum Copper, Ceruloplasmin, Copper:Ceruloplasmin ratio in Pregnant women in and around of Warangal

Pullaiah Akinepalli [1], Narender Gaddam [2]

[1,2]**Assistant Professor, Department of Biochemistry, Kakatiya Medical College, Warangal,Telangana,India.**

Address for correspondence: Dr. Pullaiah Akinepalli, Assistant Professor,Department of Biochemistry, Kakatiya Medical College, Warangal, Telangana, India.

E-mail: pullaiahakine@gmail.com

ABSTRACT

Background: Copper is an essential micronutrient and has an important role in foetal development. Disorders of Copper and Ceruloplasmin levels has been associated with pathological pregnancies.The determination of Copper:Ceruloplasmin ratio has been proposed as one of the better indicator of Copper status in pregnancy.

Objectives: The present study was undertaken to assess the Copper status in healthy pregnant women of in and around warangal comparing with the age matched non-pregnant women without history of usage of oral contraceptives.

Materials & Methods: The venous samples from twenty healthy pregnant women aged 20-40yrs in the third trimester as study group and from twenty healthy non-pregnant women as control group was taken to compare the levels of Serum Copper, Ceruloplasmin and Copper:Ceruloplasmin ratio between groups. Estimation of serum copper was done by End point colorimetric method, Ceruloplasmin by Immunoturbidometric assay on Auto analyzer and Copper:Ceruloplasmin ratio is calculated by formula.

Results: A statistically significant increase($p<0.05$) in serum copper levels of pregnant women (41.64µmol/L ± 6.62) was noticed when compared with non-pregnant women (21.46 µmol/L ± 3.59). Serum ceruloplasmin levels of pregnant women (0.43 gm/L ± 0.07) was statistically significant increase compared with controls (0.21 gm/L ± 0.02) ($p<0.05$) and a decrease in Copper:Ceruloplasmin ratio of pregnant women (12.87 µmol/gm ± 1.51) when compared to control group (13.22 µmol/gm ± 1.6) was observed, not statistically significant.

Conclusion: Serum levels of Copper and Ceruloplasmin were significantly increased in pregnant women and Copper:Ceruloplasmin ratio decreased but not significant statistically.

Keywords: Copper, Ceruloplasmin, Copper: Ceruloplasmin ratio, Pregnancy

INTRODUCTION

In India, pregnancy is a precious state in the women's life. Pregnancy is a state of altered but a normal physiological process[1]. While most of the pregnancies result in the birth of a healthy baby occasionally some pregnancies goes wrong from the beginning[2]. Pregnancy is associated with increased demand of all micronutrients like Iron, Copper, Zinc and have an important influence on the health of pregnant women and the growing foetus. The deficiency of these nutrients could affect pregnancy, delivery, increase of gestation age and outcome of pregnancy[3]. Nutritional deficiencies are common during pregnancy and trace elements have been documented to play an important role in determining the foetal outcome. It has been reported that more than 50% of human conception fail to implant and of them implanted approximately 30% fail to reach the term due to copper deficiency[4].

Copper found in trace amount in all tissues in the body and an essential nutrient that plays a role in the production of the myelin, collagen and melanin. It also helps to make a component of connective tissue by binding with ascorbic acid, an essential cofactor for many enzymes. Copper, majority transported bound to ceruloplasmin, the rest is bound to albumin, transcuprein and copper aminoacid complex. Copper is important for normal foetal development[5]. Serum copper level increases during early pregnancy and continues upto third trimester. Serum copper in pregnancy can be used as an indicator of the condition of pregnancy and foeto-placental unit and could be introduced into the protocol of routine prenatal diagnostics. The placental transport system changes during the later stages of the development resulting in the transport of higher copper values towards the end of gestation than that of earlier pregnancy[6]. Low levels of serum copper in pregnancy could be predictor of some pathological pregnancies (habitual abortion, missed labour, spontaneous abortion and premature rupture of membranes[6]. Conditions not directly related to copper nutrition such as pregnancy, infections and inflammation which increase serum copper concentration even during copper deprivation may be expected to conceal change in copper status.

Ceruloplasmin is a weak, late reacting acute phase protein carries about 70% of total copper in human plasma and exhibits copper dependent oxidase activity. Ceruloplasmin oxidase was higher in normal pregnancies in comparision to other groups with pregnancy complications. Ceruloplasmin levels are increased significantly by oestrogen as in case of pregnancy and in oral contraception[1]. Pregnancy accelerates the rise of ceruloplasmin protein synthesis and release with an increase of serum copper. Physiological changes during pregnancy increase serum copper concentration due to increase of ceruloplasmin as a result of elevated levels of oestrogen and move across the placenta by passive transfer[4]. Factors that increase the hepatic synthesis of ceruloplasmin such as acute phase response or the oral contraceptive pill will increase plasma copper independently of dietary copper.

Early intervention and appropriate diagnosis by estimation of serum copper and ceruloplasmin can substantially reduce morbidity and mortality in pregnancy associated with hepatic derangements[1]. Plasma copper and ceruloplasmin assays are convenient and widely used to confirm severe copper deficiency. However they are not sensitive indicators in marginal copper depletion[7]. Women showed~ 2.5 times higher inter individual variability of copper and ceruloplasmin than men, a difference that disappeared for copper:ceruloplasmin ratio[8]. The Copper:Ceruloplasmin ratio showed the smallest biological variability and higher index of individuality.

Determination of free copper which is physiologically active fraction met with some difficulties and the determination of Copper:Ceruloplasmin ratio has been proposed as one of the better indicator of copper status in pregnancy[9]. Assessment of free copper in serum can produce biologically implausible negative results in a significant number of patients, the use of copper:ceruloplasmin ratio has been proposed to overcome such problems. It has been suggested that interpretation of copper value can be properly assessed only by an adjusted copper:ceruloplasmin ratio. In the present study we have undertaken to assess the copper status in pregnant women and determine the copper:ceruloplasmin ratio in pregnant women of in and around Warangal.

MATERIALS AND METHODS

Case control study and a total of 40 venous samples are collected among which twenty healthy pregnant women of in and around warangal aged between 20-40yrs in the third trimester, who attended antenatal clinic having without any history of microbial and metabolic diseases are included in the study group to compare with twenty healthy non-pregnant women of in and around warangal as control group. All the samples are centrifuged and analyzed for levels of serum copper and ceruloplasmin to compare between the healthy pregnant and non pregnant women groups. Copper and ceruloplasmin levels were determined by using End point colorimetric and an Immunoturbidometric assay respectively. Copper:Ceruloplasmin ratio was calculated by the formula[10].

Students t-test is used for statistical analysis.

RESULTS

A total of 40 samples of women among which 20 were healthy normal pregnant women and 20 healthy non-pregnant women were analyzed, the assay data results were expressed as Mean ± SD and represented in Table 1. A statistical significant(p-value<0.05) increase in serum copper levels of pregnant women (41.64 µmol/L ± 6.62) was noticed when compared with the non-pregnant women control group (21.46 µmol/L ± 3.59). Serum ceruloplasmin levels in the study group (0.43 gm/L ± 0.07) showed statistically significant (p-value<0.05) increase when compared with control group (0.21 gm/L ± 0.02). Copper:ceruloplasmin ratio of pregnant women (12.87µmol/gm ± 1.51) showed a decrease when compared with controls (13.22 µmol/gm ± 1.6) but was not statistically significant. Comparison between the groups was performed by students t-test and p-values < 0.05 was taken as statistically significant.

Table 1: Mean ± SD of Serum Copper, Ceruloplasmin, Cu:Cp ratio in the groups.

S.No.	Parameter	Mean ± SD		p-value	Significance
		Cases	controls		
1	Serum Copper. µmol/L	41.64 ± 6.62	21.46 ± 3.59	< 0.00001	Significant
2	Serum Ceruloplasmin gm/L	0.43 ± 0.07	0.21 ± 0.02	< 0.00001	Significant
3	Cu: Cp ratio. µmol/gm	12.87 ± 1.51	13.22 ± 1.6	>0.05	Not significant

DISCUSSION

In the present study significantly higher serum copper and ceruloplasmin levels were observed in pregnant women than non-pregnant women. This finding was in aggrement with those of some other studies[1, 4, 11,12, 13, 14]. It has been suggested that high serum copper concentration during pregnancy might be due to increase binding affinity with ceruloplasmin, increase ceruloplasmin production and passive transfer across the placenta. In addition increased copper may be due to oestrogen induced ceruloplasmin synthesis during pregnancy. Amongst various factors affecting copper level, elevated level of oestrogen during pregnancy also increase the synthesis of ceruloplasmin by making copper available through mobilization from maternal tissues especially liver. The increase in serum copper during pregnancy is mainly in a bound form due to increase in the carrier protein ceruloplasmin in response to stimulation by maternal oestrogen. Moreover there is also increased copper retention during pregnancy.

Since copper:ceruloplasmin ratio varies from region to region, we therefore in the present study determined Copper:Ceruloplasmin ratio in normal pregnant women of in and around Warangal. It has been observed in the present study that the copper:ceruloplasmin ratio in pregnant women was decreased when compared with the non-pregnant women. Similar findings was observed in Louro M O et al study[14], suggested that although pregnancy accelerates the rate of ceruloplasmin protein synthesis and release with an increase of serum copper, the decrease in specific oxidase activity of circulating ceruloplasmin would be an indicator of the degree of depletion of the mothers copper deposits in order to deal with foetus needs. Aceruloplasmin increases in blood serum during copper depletion, this will contribute to the total ceruloplasmin assay. Most of the accumulation of copper in the foetal liver occurs in last three months of pregnancy. Whereas in the study of DP Oparinde et al[9] Copper:ceruloplasmin ratio during first, second and third trimester are significantly higher than control non-pregnant women. Average copper:ceruloplasmin ratio in total pregnant population was significantly higher than in controls. Copper:Ceruloplasmin ratio is highest during first trimester and gradually decreases as pregnancy advances, this decrease may imply a decrease in available free copper to the fetus[9]. Therefore a molecule of ceruloplasmin containing less than 0.064 imol/g of copper may suggest excess product ion ceruloplasmin in relation to available copper which has been associated with pathologic pregnancies especially Pre-eclampsia and eclampsia.

CONCLUSION

Levels of serum copper and ceruloplasmin in pregnant women of in and around Warangal was significantly increased with a decrease in copper:ceruloplasmin ratio but was not statistically significant. The decrease in copper:ceruloplasmin ratio in third trimester of pregnant women was due to the increased transfer of copper to the fetus during last trimester and increased production of aceruloplasmin due to copper depletion which cause increased ceruloplasmin assay. Copper:Ceruloplasmin ratio as a better indicator for copper status in pregnant women of in and around Warangal needs more evaluation.

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