SERUM COPPER AND CAERULOPLASMIN LEVELS IN PREGNANT LACTATING AND NON-PREGNANT NIGERIAN WOMEN

By

ONWUAMEZE I.C. [1] M. SC, PH D, **OKEREKE S.N.** M. SC. FIMLT **AND UGONABO M.C.** MB B. CH, M SC, FWACP

Department of Chemical Pathology, University of Nigeria, Enugu Campus

SUMMARY

Objective To determine the serum levels of copper and caeruloplasmin in pregnant and lactating women from South Eastern Nigeria.

Methods Serum copper and Caeruloplasmin levels from 60 pregnant women at various stages of pregnancy and sixty (60) nursing mothers in their immediate postnatal period, all aged between 20 and 45 years were determined.

For control, a total of 60 healthy non-pregnant women matched for age were used for the study.

Results A comparison of the results obtained from the subjects with that from the control group showed that the mean serum copper levels in the 2nd and 3rd trimester groups were significantly higher than the non-pregnant and control groups. Interestingly, the mean values obtained from the post-natal group, though lower than those for the 3rd trimester group, were still higher than the values for the controls. For example, mean serum copper in umol/L for 2nd trimester (n=60) is 20.3 ± 5.9 ($p< 0.05$); 3rd trimester (n = 60) is 26.4 ± 5.6; post-natal women (n = 60) is 25.4 ± 4.9 ($p < 0.05$); and controls (n = 60) is 19.3 ± 5.8.

Similarly, mean serum caeruloplasmin levels in all the pregnant groups as well as in the post-natal group were significantly higher than in the control group. Mean serum caeruloplasmin levels (g/L) in the 1st trimester is 0.73 ± 0.16; in the 2nd trimester 0.98 ± 0.18 ($p < 0.05$); in 3rd trimester 1.04 ± 0.26 ($p < 0.01$); in the post-natal group 0.56 ± 0.16; and in the controls 0.41 ± 0.15.

Conclusion Serum copper and caeruloplasmin is elevated in all stages of pregnancy and in lactating women, the increase being highest in the third trimester of pregnancy.

***Key Words**: Copper, Caeruloplasmin, Pregnancy*

INTRODUCTION

Copper is an important trace element and is a component of many metalloenzyme systems such as cytochrome oxidase, superoxide dismutase (SOD), caeruloplasmin uricase and tyrosinase. Caeruloplasmin is a copper-containing alpha-globulin formally, though erroneously, thought to be a transport protein for copper in plasma. Once synthesized, it neither gains nor loses copper unless metabolized. It catalyses rapidly the oxidation of Fe(II) to Fe(III) and this ferroxidase activity is essential for transformation of Fe(II) at the cell surface before it can be bound to transferrin[1]. This, perhaps, explains the genesis of anaemia due to low plasma caeruloplasmin. Increased absorption of copper from the gut leads to increased synthesis of caeruloplasmin. Therefore, synthesis of caeruloplasmin provides a first line reaction to potential copper toxicity. It also plays a role as an anti-oxidant in acute phase reaction.

Serum copper level is elevated in acute and chronic leukaemia, liver cirrhosis, various forms of anaemia, lymphomas, thyroid disorders, homocystinuria and acute rheumatic fever. Low serum levels of copper occur in neutropenia, hypochromic anaemia, osteoporosis and reduced skin pigmentation. A variety of abnormal conditions have been linked to loss of cupo-enzyme activity; these include ataxia, failure of pigmentation, connective tissue defects and abnormal catecholamine conversions.

The elevation in serum copper level during pregnancy [2,3,4] has been attributed to increased oestrogen secretion. Increased serum copper levels have also been reported in women on oestrogen containing oral contraceptives[5].

Correspondence Author:
***Onwuameze I.C.**, Dept. of Chemical Pathology, University of Nigeria, Enugu Campus*
Accepted for publication on 17th September 2001

Serum levels of caeruloplasmin are elevated in certain malignant conditions of the stomach, bronchus and lungs[6], biliary cirrhosis, and in pregnancy[4]. It is, however, decreased in hepatolenticular degeneration (Wilson's disease).

There are no known reports on the serum levels of both copper and caeruloplasmin in pregnant Nigerian women. However, a paucity of reports exists on the serum copper and caeruloplasmin levels in pregnant Nigerian women.

Although the changes in serum copper levels during pregnancy are believed to be influenced by oestrogens, it is likely that changes in caeruloplasmin may be attributable to protein diet. High levels of copper and alpha$_2$-globulin fraction will result in increased levels of caeruloplasmin and vice versa. Since dietary habits as well as type of diet change from one geographical area to another, this study was embarked upon to determine the serum levels of these parameters in pregnant women from south Eastern Nigeria.

MATERIALS AND METHOD

Selection of Subjects

A total of 120 women aged between 20 and 45 years who were attending ante-natal/post-natal clinics at the University of Nigeria Teaching Hospital (UNTH), Enugu, South Eastern Nigeria were selected for the study. These comprised 60 pregnant women in their 1st, 2nd, 3rd trimesters and in their immediate post-natal (4 to 6 weeks post partum) period.

Sixty (60) age matched non-pregnant women drawn from students and staff of the hospital were used for the control.

Subjects with eclampsia, hypertension, hepatic, renal or pulmonary disease as well as those with malignant diseases of the stomach, lungs and lymphatic system were excluded from the study. Also women on oestrogen-containing oral contraceptives, aplastic anaemia, pernicious anaemia, megaloblastic anaemia, iron deficiency anaemia and sickle cell anaemia were excluded.

Preparation of subjects/collection of samples

Following informed consent, 10ml of venous blood were collected between 10.00am and 2.00pm, into sterile plain vacutainer tubes and this was allowed to clot for 2 to 3 hours at room temperature. The separated sera were stored in a deep-freezer at -20°C until required for assay. All assays were performed in batches and within a fortnight of specimen collection.

Serum copper was determined by the highly sensitive colorimetric method of Makin and Itoh[8]. Serum caeruloplasmin determinations were performed by means of radial immunodiffusion technique, using M-Partigen kit obtained from Hoechst Co Ltd. The plates were incubated for 48 hours at 25°C, after 5ul of specimen, standard and controls were placed in respective wells. The diameters of the precipitin rings were measured using a special measuring viewer. The concentrations of caeruloplasmin were calculated from a standard curve.

Twenty (20) replicate analyses of pooled blood bank sera were used to determine the precision of the assay.

Statistical Analysis

The data were analyzed and the significance of the mean values determined by Student paired t-test.

RESULTS

Table 1 shows the mean values with the standard deviation and ranges of serum copper and caeruloplasmin in the pregnant and non-pregnant (control) groups. Both the serum copper and caeruloplasmin concentrations were elevated in the pregnant group when compared to the non-pregnant group ($p < 0.05$). The increase in the third trimester is significant for both parameters.

Table 1
Serum Copper and Caeruloplasmin Levels in Pregnant, Lactating and Non-Lactating Nigerian Women

Group of Women	Copper (umol/L)		Caeruloplasmin (g/l)	
	Mean	Range	Mean	Range
Non – Pregnant Women (Controls)	29.3 ± 5.8	13.3 – 24.8	0.41 ± 0.15	0.20 – 0.70
Pregnant Women 1st Trimester (5-14 weeks)	17.6 ± 3.9	14.8 – 22.4	0.73 ±0.16	0.40 – 1.10

Pregnant Women 2nd Trimester (15-28 weeks)	20.3 ±5.9	14.8 – 26.5	0.98 ± 0.18	0.60 – 1.35
Pregnant Women 3rd Trimester (29 – 40 weeks)	26.4 ± 5.6	18.8 – 29.6	1.04 ± 0.18	0.25 – 0.80
Post – Natal Women 4 – 6 weeks post-partum	25.4 ± 4.9	19.8 – 29.6	0.56 ± 0.16	0.25 – 0.90

DISCUSSION

Plasma copper consists of a non-dialyzable fraction (95%) attached to caeruloplasmin and a dialyzable fraction (5%) loosely-bound to albumin and histidine. Copper is believed to be transported in the dialyzable form from the gut to the liver; it is then incorporated into caeruloplasmin apoprotein which is released into the blood stream[9]. Since nearly all plasma copper is present as caeruloplasmin, levels of both copper and caeruloplasmin almost always change proportionately.

The result of this study shows that serum copper and caeruloplasmin levels are significantly higher in the pregnant state than in the controls. The values which were decreased during the early post-natal period were slightly higher than in the non-pregnant controls.

The highest rise in serum copper which was observed in the 3rd trimester of pregnancy is quite in agreement with the work of Fenuku[3], who worked on pregnant women in Accra, Ghana. The continuous rise observed in serum copper and caeruloplasmin as pregnancy progresses seems to confirm the work of Burrows and Pekala[4]. The highest level which was recorded in the 3rd trimester is an expected physiologic response, since it is during this period of gestation that the bulk of blood required by the growing foetus is elaborated.

The changes in serum copper and caeruloplasmin during pregnancy is due to hormonal influences. The rise in serum copper is attributed to increased oestrogen secretion[3]. Women on oestrogen-containing oral contraceptives have also been shown to have raised serum copper and caeruloplasmin[7]. Caeruloplasmin, a late acute phase reactant, is the principal copper-containing plasma protein. It is an alpha-glycoprotein, a ferroxidase that catalyses the oxidation of iron Fe (II) to Fe (III) state, prior to its binding by plasma transferring. Another possible role for caeruloplasmin is as an anti-oxidant. Spontaneous oxidation of many organic substances in contact with molecular oxygen is a constant threat to life but this is prevented by the presence of anti-oxidants in plasma and tissues. This is perhaps the role of caeruloplasmin in acute phase reaction.

CONCLUSION

This study reveals that, as in other population groups and despite varying diets, the serum levels of copper and caeruloplasmin are elevated in pregnant and lactating South-Eastern Nigerian women when compared with their non-pregnant controls.

ACKNOWLEDGEMENT

We are indebted to Dr. PC Nweke for allowing us do this study on his patients. We are also thankful to Mr. Kenechukwu Okafor for his secretarial assistance.

REFERENCES

1. Tietz, NW (Ed) Fundermentals of Clinical Chemistry 3rd ed. Philadelphia WB Sunders Co 1987.

2. Fenuku, RIA Serum copper and iron in pregnancy and prolonged lactation in Accra. Ghana Medical Journal 1978; 16: 212 – 215.

3. Olatunbosun, DA, Adedevoh BK, and Adeniyi FA. Serum copper in normal pregnancy in Nigeria. Brit J Obstet and Gynaecol 1974; 81: 475 – 478.

4. Burrows S and Pekala B. Serum copper and caeruloplasmin in pregnancy. Amer

J Obstet and Gynecol 1971; 109: 907 – 909.

5. Olatunbosu DA, Adeniyi FA and Adedevoh BK. The effect of oral contraceptives on serum copper levels in Nigerian women. Brit J Obstet and Gynaecol 1973; 80: 937 – 939.

6. Scanni A, Licciardolla L and Travato M. Serum copper and caeruloplasmin levels in patients with neoplasm localized in the stomach, large intaetine or lungs. Tumori 1977; 63: 175 – 180.

7. Deering TB, Dickson ER, Fleming CR, Geall MG, McCall JT and Baggenstross AH. Effct of D-penicillamine on copper-retention in patients with primary biliary cirrhosis. Gastroenterology 1977; 72: 1208 – 1212.

8. Makino T and Itoh JI. Ahighly sensitive colorimetric determination of serum copper using 4-N-trimethylaminophenyl porphine. Clin. Chim Acta 1982; 111: 1 – 8.

9. Gutteridge JMC and Stocks J. Caeruloplasmin: Physiological and Pathological perspectives. CRC Crit. Rev. Clin. Lab. Sci. 1981; 14: 259 -329.