

SERUM COPPER AND CERULOPLASMIN LEVELS IN NORMAL AND ABNORMAL PREGNANCY

by

R. R. MELINKERI

and

P. S. VASANTGADKAR

SUMMARY

It is concluded from this study that determination of serum copper and ceruloplasmin could serve as an additional index for early detection of pregnancy but has got very limited use as prognostic aid in Pathological Pregnancy.

Introduction

The biological importance of trace elements, especially iron, copper, magnesium, zinc and iodine is studied in health and disease now a days with increasing interest due to the improved technology, i.e. introduction of atomic absorption spectrophotometer and newer chemical methods.

A definite co-relation is established between serum copper levels and urinary excretion of estriol in pregnant women. Since estimation of estriol in urine during pregnancy is an accepted method for valuating fetoplacental function, it was considered of interest to study the changes in copper status in normal and abnormal pregnancy and therefore, to assess whether the determination of these parameters could serve as an additional test for early detection of pregnancy and fetal well being in cases of pre-eclampsia and threatened abortion.

Material and Methods

The present study was conducted on 144 subjects. They were grouped in the following way.

TABLE I

Group	Type of cases	No. of cases
I	Normal healthy non-pregnant women	26
II	Normal pregnant women (I trimester)	52
III	Normal pregnant women (III trimester)	24
IV	Cases of pre-eclampsia	21
V	Cases of threatened abortion	21

Copper was estimated by the method of Eden and Green (1970) and Ceruloplasmin was measured by Ravin's (1961) method.

Patients having blood pressure 140/90 mmHg with trace or (+) albumin (conc.

0.26 to 0.5 gm/L) and slight or no oedema were labelled as mild pre-eclamptic.

Blood samples were collected from obstetric and gynaec O.P.D. and wards of Sassoon General Hospital, Pune. To avoid the diurnal variation, blood samples were collected in the morning between 10 a.m. to 11 a.m. Serum was separated and preserved at 4°C to 10°C.

Results

Fifty-two cases of normal pregnant women from 6 to 10 weeks were studied and results were tabulated in Table II.

Friedman (1969) reported serum copper value as 114-118 microgram% while Schenkar (1969) reported it as 129 ± 12.7 microgram%. Ravin (1961) found the

value of ceruloplasmin as 32.3 ± 4 . Our values were well in agreement with those reported by the above workers.

From the results stated in Table II, the levels showed a continuous increase with increase in weeks of gestation when compared with normal healthy non-pregnant women. The increase was statistically significant.

Serum copper and ceruloplasmin levels in threatened abortion were studied in 21 cases and the results were divided into Table III (a) and Table III (b). The blood sample was taken on the same day of admission for estimation of serum copper and ceruloplasmin. Of these 21 patients, 13 aborted and their results are tabulated in Table III (a). In the remaining 8 patients the bleeding

TABLE II
Serum Copper and Ceruloplasmin Levels in Early Pregnancy

Weeks of gestation	Serum ceruloplasmin in mg% (Mean value)	Serum copper in microgram% (Mean value)	Value of P	Significance
6 weeks (N = 18)	56 ± 10.8	165 ± 15.88	0.005	Highly significant
8 weeks (N = 20)	65 ± 10.3	189 ± 7.05	0.005	Highly significant
10 weeks (N = 14)	83 ± 12.9	204 ± 10.53	0.005	Highly significant
Normal non-pregnant women	36.75 ± 7	129 ± 19.7		

TABLE III (a)
Serum Copper and Ceruloplasmin Levels in Patients who Aborted

Weeks of gestation	Serum ceruloplasmin in mg% (Mean value)	Serum copper in microgram% (Mean value)	Value of P	Significance
6 (N = 4)	28.87 ± 7	133.3 ± 10	.005	Highly significant
8 (N = 5)	53.37 ± 9	165 ± 12.2	.005	Highly significant
10 (N = 4)	76.12 ± 7	186 ± 7	.005	Highly significant

stopped and pregnancy continued; their results are tabulated in Table III (b).

TABLE III (b)
Serum Copper and Ceruloplasmin Levels in Those who Continued the Pregnancy

Weeks of gestation	Serum ceruloplasmin in mg% (Mean value)	Serum copper in micro-gram% (Mean value)
6 (N = 1)	48	156
8 (N = 4)	58	182
10 (N = 3)	85	195

The serum copper and ceruloplasmin levels showed a statistically significant decrease ($P < 0.005$) when compared with the normal pregnant women of same gestation Group I.

There was no decrease in serum copper and ceruloplasmin levels when compared with normal pregnant women of same gestation. The values were within the normal range. Serum copper and ceruloplasmin levels of—pre-eclamptic patients were compared with pregnant women of third-trimester. From this group, 18 cases were of mild toxæmia and 3 were of severe toxæmia. Their results are tabulated in Table IV.

TABLE IV
Serum Copper and Ceruloplasmin Levels in Normal and Pre-eclamptic Patients

Subject	Serum ceruloplasmin in mg% (Mean value)	Serum copper in mg% (Mean value)
Normal pregnant women of III trimester (N = 24)	99.7 ± 18	315 ± 17
Pre-eclampsia (N = 21)	106 ± 20	322 ± 27

The values in toxæmia were essentially similar to those in normal pregnant women. Only in the 3 cases of severe toxæmia the values were raised.

Discussion

In normal Pregnancy as early as from sixth week of gestation, the levels of copper and ceruloplasmin start rising (Tompsett, 1969; Sarata, 1935).

The increasing levels of estrogens are responsible for the increased levels of copper and ceruloplasmin to transport iron and copper for the developing fetus (Evans, 1973). Ceruloplasmin functions as ferroxidase II enzyme in iron metabolism and therefore required in the developing fetus.

Estrogens act by regulating ceruloplasmin synthesis at the transcriptional level. They stimulate the production of MRNA coding for the protein ceruloplasmin (Gutteridge and Stocks, 1981). Actinomycin D and Cyclohexamide which are the inhibitors of protein synthesis, decrease the synthesis of ceruloplasmin.

In cases of threatened abortion, where the cause is placental insufficiency, the levels are decreased (Heijkenakjol, 1962). For the proper functioning of placenta, the enzymes which are needed are rich in copper.

Submucous myoma, uterine malformation, cervical insufficiency are the other causes where inspite of the higher copper

levels pregnancy terminated (Freidman, 1969).

In toxæmia according to the degree of severity, liver and brain are damaged by

generalised vasoconstriction due to high blood pressure and copper is released from these damaged organs which may account for the hypercupremia observed in toxæmia. In the present study, the values were not statistically increase. One reason could be that 90% cases were of mild toxæmia, where there may not be much damage to the liver. Piskazeck (1960) had reported the significantly increased levels of serum copper and ceruloplasmin only in severe toxæmia where there is extensive liver damage.

Acknowledgement

We are thankful to the Department of Gynaecology and Obstetrics, B.J. Medical College, Pune for allowing us to collect the blood samples from the Out Patient

Department and antenatal ward of Sassoon General Hospital.

References

1. Eden, A. and Green, H. H.: *Biochem. J.* 34: 1202, 1970.
2. Evans, G. W.: *Physiological Reviews*, 63: 536, 1973.
3. Friedman, S.: *Obstet. Gynec.* 33: 189, 1969.
4. Cutteridge, J. and Stocks, J.: *Clin. Lab. Sc.* 14: 1, 1981.
5. Heijkenakjold, F.: *Acta Obstet. Gynec. Scand.* 41: 41, 1962.
6. Piskazeck, K.: *Gynaecologia* 49: 113, 1960.
7. Ravin, H. A.: *J. Lab. Clin. Med.* 58: 161, 1961.
8. Sarata, U.: *Japan J.M. Sc II Biochem* 1: 3, 1935.
9. Tompsett, S. L.: *Brit. J. Exp. Path.* 16: 1955, 1967.