

SERUM COPPER LEVELS IN NORMAL AND ABNORMAL PREGNANCIES

By

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Introduction

The role of copper in biological processes has not yet been clearly elucidated. Of the various cations, serum copper levels in women fluctuate the most, increasing significantly during pregnancy and during oestrogen administration.

Serum copper levels in normal non-pregnant women as reported by Gubler *et al.*, (1952), De Jorge *et al.*, (1965), Friedman *et al.*, (1969) and Schenker *et al.*, (1969) range between 105-130 ug per cent. Krebs (1931) showed that serum copper rises considerably during pregnancy and this was confirmed by other workers. Borglin and Heijkenskiold (1967) have reported a linear increase of serum copper from the third to the ninth month. Dokumov (1968) has shown that serum copper rises throughout the pregnancy with a steep rise at the beginning of the second trimester.

O'Leary *et al.*, (1966) and Schenker *et al.*, (1969) have reported an increase in serum copper levels in pre-eclamptic toxæmia cases. Friedman *et al.*, (1969), on the other hand, have reported a decrease.

The present investigation has been undertaken to study the changes of serum copper level during normal and abnormal

pregnancies with a view to evaluate its role as an index of placental function.

Material and Methods

The study consisted of the following groups:

1. Normal non-pregnant—25 cases.
2. Normal pregnant, in different trimesters of pregnancy, during labour, 3 to 7 days postpartum and 4 to 6 weeks postpartum—50 cases.
3. Maternal and cord blood—15 cases.
4. Threatened abortion—25 cases.
5. Pre-eclamptic toxæmia and eclampsia—20 cases.

Serum copper was estimated by the method of Gubler *et al.*, (1952). Copper was extracted from serum by treatment with 2H. HCL. Proteins were precipitated with 20 per cent trichloroacetic acid. Interference of serum iron with the colour reagent, sodium diethyl dithiocarbamate, was prevented by use of sodium pyrophosphate. Optical density was read on a photo-electric colorimeter at a wavelength of 450 nm.

Results

Table I gives the serum copper values in normal non-pregnant women and normal pregnant women. A follow up study in the three trimesters, during labour, and 3-4 days postpartum is represented graphically in Fig. 1. There is a gradual increase in serum copper throughout pregnancy, with a sharp rise between 10th to 16th week of gestation. A peak level

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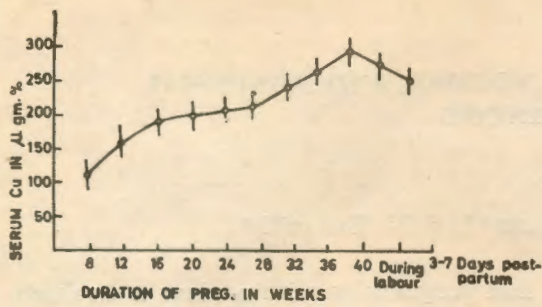


Fig 1

Mean serum copper levels in different weeks of pregnancy

is reached at term. With onset of labour there is a slow decline, but the levels remain higher than the non-pregnant levels even at 4-6 weeks postpartum.

Figure 2 graphically represents the relation of serum copper level of foetal cord blood with that of maternal blood during labour. Serum copper level from foetal cord blood is considerably lower than that of maternal blood.

Data on threatened abortion cases are given in Table II. There is no significant difference in serum copper between those who aborted and those who continued pregnancy upto 13 weeks of gestation. However, a significant difference of about 30-40 ug per cent has been observed between the two groups from 16-21 weeks of gestation.

Table III and Figure 3 represent the data in mild and severe pre-eclamptic

TABLE I

Serum Copper in Non-pregnant Controls and in Normal Pregnancy

No. of patients	Duration of pregnancy in weeks	Serum copper levels in microgram per cent		
		Average	Mean	S.D.
25	Non-pregnant	104.7	104.7	11.2
20	8-12	146.9	146.9	12.25
7	16-20	189.2	201.8	10.4
12	21-24	201.9		
1	25-28	214.3		
5	29-32	240.0		
8	33-36	244.6	247.9	8.15
7	37-40	259.7		

TABLE II

Serum Copper in Threatened Abortion

Duration of pregnancy in weeks	Serum copper levels in microgram per cent					
	Pregnancy continued			Pregnancy ending in abortion		
	Average	Mean	S.D.	Average	Mean	S.D.
8-9	133.95	164.83	25.55	128.6	141.38	8.25
10-11	139.30			139.30		
13-14	158.58			147.33		
16-17	171.44			141.67		
20-21	192.87			150.01		
22-23	192.87	—	—			

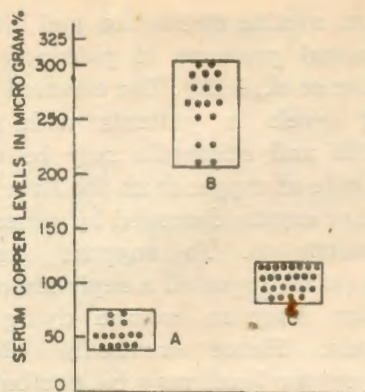


Fig. 2

Relation of serum copper level of foetal cord blood with that of maternal blood during labour and normal nonpregnant women.

- A. Serum copper level in foetal cord blood.
- B. Serum copper level in maternal blood.
- C. Serum copper level in normal nonpregnant women.

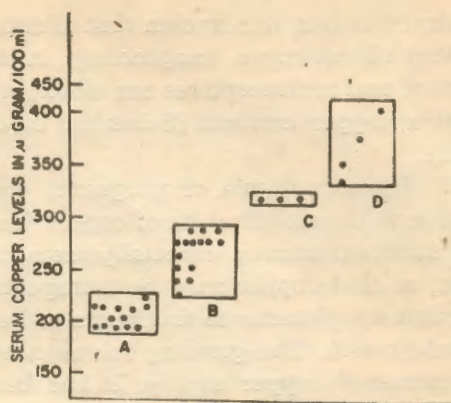


Fig. 3

Serum copper levels in mild pre-eclamptic toxemia, normal pregnancy, severe toxemia and eclampsia. Cases in same period of gestation (32-40 weeks).

- A. Mild pre-eclamptic toxemia.
- B. Normal pregnancy.
- C. Severe pre-eclamptic toxemia.
- D. Eclampsia.

toxaemia and eclampsia. It is evident that serum copper levels in mild pre-eclamptic toxemia decrease, whereas those in severe pre-eclamptic toxemia and eclampsia increase.

Discussion

The exact mechanism responsible for increase in serum copper levels in pregnancy is not clearly understood. There are two main possibilities for the hypercupraemia of pregnancy.

1. The endogenous oestrogen which rises during normal pregnancy, may be associated with a rise of ceruloplasmin, an enzyme to which the copper is tightly bound. During normal pregnancy there is a considerable increase of serum levels of enzyme such as ceruloplasmin, histaminase, mono- and diamino-oxidase, as these enzymes are produced and stored in the placenta. In the present study the abrupt rise between the 10th to 16th week of gestation lends weight to this

TABLE III

Serum Copper in Mild and Severe Pre-eclamptic Toxaemia and Eclampsia

No. of patients	Type of patients	Period of gestation in weeks	Serum copper level in ug. %	
			Mean	S.D.
20	Normal pregnancy	36-40	271.9	12.2
13	Mild P.E.T.	36-40	213.45	13.9
3	Severe P.E.T.	36-40	321.15	—
4	Eclampsia	36-40	372.5	31.5

theory. Further, it is known that administration of oestrogen exogenously in the form of oral contraceptives can elevate the plasma copper content (Schenker *et al.*, 1971).

2. Hypercupremia of pregnancy may be due to the mobilization of copper from the maternal tissues, especially from the liver, so that copper may be transported through the placenta to the foetus to help foetal growth. The growing foetus needs an increased copper supply. It has been shown that foetal organs, especially liver and spleen, contain more copper as compared with those of the adult.

Effkeman and Rottger (1950) have attributed the increase of serum copper during pregnancy to a resistance reaction of the maternal organism against the continuously invading metabolic products from the foetus into the maternal circulation.

The lower serum copper levels of foetal cord blood is due to the fact that the copper does not easily diffuse across the placenta but accumulates in the layers of the placenta and from there it is transferred to the foetus by an active process of diffusion according to the needs of the foetus.

Serial estimation of serum copper may aid in evaluating any placental insufficiency. An early diagnosis of impending abortion on the basis of a single serum copper determination may not be possible, as serum copper depends on the time which has elapsed since foetal and placental death. However, a low serum copper level in cases of threatened abortion is a poor prognostic sign, though a normal or high level does not necessarily indicate a successful pregnancy.

In mild toxæmia the serum copper levels are lower than those in normal pregnancy in the same period of gestation. This is probably due to vasoconstriction,

deficient uterine circulation and low oxygen partial pressure in placental blood (Sandier *et al.*, 1962). The elevated serum copper levels in patients with severe toxæmia and eclampsia may be due to the release of copper from the liver, brain and other organs damaged by generalised vasoconstriction. To support this fact Razuli (1963) reported a depletion of copper from liver in women dying from eclampsia. Hence markedly elevated serum copper level may be attributed to hepatic damage and may be taken as a sign of impending eclampsia in cases of pre-eclamptic toxæmia.

Summary

1. Serum copper level increased progressively throughout the pregnancy. There was a sharper rise between the 10th to the 16th week of gestation, followed by a steady rise in the second and the third trimesters. With onset of labour, the level dropped sharply. Thereafter, it remained slightly higher till 4 to 6 weeks postpartum.

2. Copper level of the foetal cord blood was 5.5 times lower than that of maternal blood during labour.

3. In threatened abortion there was no significant difference in serum copper levels between those who aborted and those who continued pregnancy upto 13 to 14th weeks.

4. In pre-eclamptic toxæmia, the serum copper level was found to be lower than that of normal pregnant women in same period of gestation. But in cases of severe toxæmia and eclampsia the serum copper level was significantly higher.

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