

ESTIMATION OF SERUM COPPER LEVEL IN PROGNOSIS OF THREATENED ABORTION

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SUMMARY

The data presented demonstrates that determination of serum copper in patients of threatened abortion can be used as a relatively reliable index of placental function and outcome of pregnancy with advantages over more complicated hormone estimation and biological tests and extremely expensive immunologic tests. Although it is difficult to diagnose an impending abortion by a single estimation because serum copper level depends on time elapsed since foetal and placental death. However, a low level is a negative prognostic sign, though a normal or high value does not necessarily indicate a successful outcome of pregnancy.

Introduction

The role of trace elements, particularly copper and zinc, has been studied by various workers in human reproduction. The rise in serum copper level during pregnancy was first described by Krebs (1928). This increase has been attributed to excessive production of hormones particularly oestrogen by the placenta. This assumption has been strengthened by observation that administration of oestrogen to non-pregnant women produces an increase in serum copper level (Russ and Raymunt, 1956). It has been seen that RBC copper remains constant throughout pregnancy. The rise in serum copper is primarily due to increase in ceruloplasmin, a alpha-2 macroglobulin.

Estimation of urinary oestradiol and oestriol is the most reliable method for evaluation of foetal and placental well being in high-risk pregnancies. However, it suffers from the drawback of costlier, complicated and sophisticated methodology for its determination. The serum copper and oestradiol levels run parallel to each other so far foetal well being is considered. Hence it was considered of interest to study serum copper level as an index of prognosis in threatened abortion with advantages that its estimation is easy, not expensive, results are reproducible and do not require collection for 24 hours.

Material and Methods

The present clinico-biochemical study was conducted in Umaid Hospital, attached to Dr. S.N. Medical College, Jodhpur. The study included 30 cases each of threatened abortion and normal preg-

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nancy both in first trimester and 10 non-pregnant healthy menstruating women between the ages of 20-30 years with Hb between 8-10 gm%. All patients with medical disorders and infection were excluded. Routine investigations were done for each patient.

In cases of threatened abortion who did not abort, second sample was taken 15 days after the first sample and serum copper again determined.

Procedure: About 5 ml of blood was withdrawn from the antecubital vein and allowed to clot. To 1.5 ml of clear serum 1.5 ml of 25% trichloroacetic acid was added to remove the protein. The specimen was mixed immediately and after 15 minutes, centrifuged at the rate of 2000 r.p.m. for 5 minutes. Then supernatant clear fluid was transferred to copper free polyethylene tubes with cork and serum copper determined by atomic absorption spectrophotometer by the method of Piper and Higgins, modified, 1967.

Atomic absorption spectrophotometry is undoubtedly the method of choice for the determination of copper in biological fluids, tissues and food. It offers the required sensitivity, specificity, reliability, speed and ease of measurement and does not require any preliminary operation. The only disadvantage with this is relatively high cost of apparatus.

Observations

Control group: Serum copper level in non-pregnant cases was 94-140 ug% with mean of 112 ug%. An increase in serum copper level was seen as pregnancy advanced. At 6 weeks mean serum copper level was 146.66 ug% which is statistically significantly ($p < 0.01$) higher than the non-pregnant level. At 8, 10 and 12 weeks mean serum copper level was 168.44, 186.00 and 200.28 ug% respectively which is again statistically significantly higher ($p < 0.001$) than the non-pregnant level (Table I).

TABLE I

Relation of Serum Copper Level (ug%) to non-pregnant, Normal Pregnancy (First Trimester) and Threatened Abortion (First Trimester) Cases

	Number of cases	Serum copper ug%			P value
		Range	Mean	\pm S.D.	
Non-pregnant	10	94-140	112.00	13.35	
Pregnant					
6 weeks	NP 6 TA 4	124-178 112-140	146.66 127.00	17.72) 10.05)	Not significant
8 weeks	NP 9 TA 7	148-196 130-170	168.44 152.57	15.96) 7.88)	< .05
10 weeks	NP 8 TA 10	160-210 150-190	186.00 166.00	15.03) 9.53)	< .001
12 weeks	NP 7 TA 9	170-234 168-198	200.28 183.11	19.84) 10.15)	< .001

NP = Normal pregnancy.

TA = Threatened abortion.

Study group: (i) Mean serum copper level was lower in threatened abortion cases than in normal pregnancy of same period of gestation, with a statistically significant difference of $p < 0.05$ at 8 weeks and $p < 0.001$ at 10 and 12 weeks of gestation, but at 6 weeks there was no statistically significant difference between the two (Table I).

(ii) Mean serum copper level in threatened abortion cases who continued pregnancy inspite of vaginal bleeding and pain in abdomen was 158.00, 173.25, 186.00 ug%, while in those who aborted it was 145.33, 161.00 and 173.33 ug% at 8, 10 and

12 weeks respectively showing no statistically significant difference between the two (Table II).

(iii) Mean serum copper level in threatened abortion cases who continued pregnancy uninterrupted showed an increase in level 15 days after the first sample indicating an improvement in placental function and oestrogen production ($p < 0.01$ at 8, 10 and 12 weeks of gestation). In our study cases of 6 weeks of gestation aborted while 4, 4 and 6 cases of 8, 10 and 12 weeks of pregnancy respectively continued the pregnancy (Table III).

TABLE II
Relation of Mean Serum Copper Level (ug%) to Threatened Abortion with Favourable and Unfavourable Outcome

Pregnancy duration in weeks		Number of cases	Range	Mean	\pm S.D.	P value
8	F	4	150-170	158.00	7.35)	Not significant
	UF	3	130-158	145.33	11.58)	
10	F	4	160-190	173.25	10.80)	Not significant
	UF	6	150-170	161.00	6.60)	
12	F	6	170-198	186.00	10.32)	Not significant
	UF	3	168-184	173.33	6.79)	

F = Favourable.
UF = Unfavourable.

TABLE III
Relation of Mean Serum Copper Level (ug%) Initially and After 15 Days to Cases of Threatened Abortion who Continued Pregnancy

Period of gestation (in weeks)	No. of cases	Serum copper (ug%)				P value between I and II
		Initial		After 15 days		
		I	II	I	II	
		Mean	\pm S.D.	Mean	\pm S.D.	
8	4	158.00	7.35	172.50	6.84	<0.01
10	4	173.25	10.80	190.00	8.83	<0.01
12	6	186.00	10.32	196.66	12.19	<0.01

Discussion

The mean serum copper level in non-pregnant women according to our study group is similar to those of west (Neuweiler, 1943; Lahey *et al*, 1953; and Johnson, 1961; Kapoor, 1977; Prema, 1980).

Our study in normal pregnant group revealed a marked rise in serum copper level even as early as 6 weeks ($p < 0.01$) and a statistically significantly higher level ($p < 0.001$) at 8, 10 and 12 weeks of gestation. Our results are comparable to Kapoor (1977) and Mirchandani and Verma (1980). Bhan (1975) showed a sharp rise at 10-16 weeks of gestation. Stoyan and Dokumov (1968) found a rapid rise in serum copper level by the end of first trimester and a progressive and gradual rise thereafter reaching peak at 10th lunar month.

Mean serum copper level in threatened abortion of our study group was significantly lower than the normal pregnancy of same period of gestation but there is no statistically significant difference in the value of threatened abortion cases with favourable and unfavourable outcome.

Heijkenskjold and Hedenstedt (1962) observed that mean serum copper level was lower in cases who ultimately aborted than who did not, while Borglin Heikenskjold (1967) found no significant difference in the value between the two. Friedman and Bahary (1969) studied serum copper level and found a mean level of 270 and 115 ug% in cases of threatened abortion with favourable and unfavourable outcome respectively at second month while a value of 276 and 161 ug% at third month respectively, indicating serum copper level

may be used as a relatively reliable index for prognosis of threatened abortion. Bhan (1975) found no significant difference in first trimester cases, while a 30-40% of difference was observed between 16-21 weeks of gestation. Mirchandani and Verma (1980) have reported lower value for threatened abortion cases than those of normal pregnancy of same duration. Prema (1980) obtained no such difference in serum copper level, their mean for normal pregnancy being 135 ug%, for threatened abortion cases which aborted 126 ug% and for cases which did not abort 132 ug%.

In our study group, those cases of threatened abortion who continued pregnancy inspite of vaginal bleeding or pain in abdomen showed a significant rise ($p < 0.01$) in serum copper level after 15 days indicating an improvement in placental function and oestrogen production. Similar results were obtained by Mirchandani and Verma (1980).

References

1. Bhan, S. K., Eduljee, S. Y. and Bhatt, I. N.: J. Obstet. Gynaec. India, 25: 451, 1975.
2. Borglin, N. E. and Heijkenskjold, F.: Acta Obstet. Gynec. Scand. 46: 119, 1967.
3. Friedman, S., Bahary, C., Eckerlind, B. and Gans, B.: J. Obstet. Gynec. 33: 189, 1969.
4. Heijkenskjold, F. and Hedenstedt, S.: Acta Obstet. Gynec. Scand. 41: 41, 1962.
5. Johnson, N. C.: Proc. Soc. Exp. Biol. Med. 108: 518, 1961.
6. Kapoor, M., Kishore, N. and Gupta, K.: J. Obstet. Gynaec. India, 27: 367, 1977.
7. Krebs, H. A.: Klin. Wchnschr. 7: 584, 1928.

8. Lahey, M. E., Gubler, C. J., Cartwright, G. E. and Wintrobe, M. M.: J. Clin. Invest. 32: 322 & 329, 1953.

9. Mirchandani, J. J. and Verma, A.: J. Obstet. Gynaec. India, 30: 924, 1980.

10. Neuweiler, W.: Helvet Med. Acta. 5: 619, 1943.

11. Piper, K. G. and Higgins, G. (1967) from

Clinical Chemistry, Principles and Technique, 2nd Edition, 1974.

12. Prema, K.: J. Obstet. Gynaec. India, 31: 554, 1980.

13. Russ, E. and Raymunt, J.: Proc. Soc. Exp. Biol. Med. 92: 465, 1956.

14. Stoyan, I. and Dokumov, S.: Am. J. Obstet. Gynec. 101: 217, 1968.