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Original Research Article

Correlation of microelements like plasma copper and zinc concentrations with female infertility

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ABSTRACT

Background: The aim of present study was to determine the role of trace elements copper and zinc and impairment of infertility.

Methods: The study was a randomized, comparative, clinical trial where study group included 74 patients with primary or secondary infertility and control group included 20 patients who were fertile females of reproductive age group having no gynaecological or systemic disease. Venous blood samples were taken and plasma copper and zinc concentrations were measured.

Results: In the normal fertile non-pregnant healthy female's plasma copper ranged from 98.78 - 169.2 mcg% (mean 124.72 mcg%). In patients of unexplained infertility plasma copper was found to be low. It ranged from 63.0 - 145.14 mcg% (mean 95.5 mcg%) difference being statistically significant, ($P < 0.001$). The difference in plasma zinc concentration in both group was not statically significant ($P > 0.05$).

Conclusions: Our results show that copper deficiency might have a role to play in the etiogenesis of otherwise unexplained infertility. We can also conclude that zinc deficiency may not play a significant role in female infertility.

Keywords: Copper, Infertility, Zinc

INTRODUCTION

Motherhood is bliss. Many unfortunate women who are deprived of this eternal pleasure feel a lacuna in their life. Dr. Jhaveri wrote in his editorial address in the proceedings of the 16th all India Obstet and Gynae Congress (1972), 'Everything in life and, love is a problem; solution is a child'.

The problem of infertility as to its aetiology and management is still a dilemma for the gynaecologist. To start with cause of infertility was thought to be either blocked tubes or failure of ovulation. Recently it is found that trace elements are also essential for life activities and they are closely related to female infertility abortion and fetal growth. They are calcium, cadmium cobalt, chromium, copper, iron, magnesium, manganese,

molybdenum, nickel, lead, rubidium, selenium, vanadium and zinc. In this study, we have undertaken correlation of Plasma copper and zinc concentration with infertility.

Rucker et al postulated that low plasma Copper in the infertile women operates by impairing the structure and function of the supporting collagen in graafian follicle.¹ Lindbloom and Hamberger found that Copper stimulated both longitudinal and vascular smooth muscles similar to PGF2 α and they postulated that low plasma Copper in infertile women operates by direct inhibition of ovum transport through fallopian tubes.²

Jerome suggested that a defect in DNA synthesis is responsible for infertility in zinc deficiency.³ The present study was therefore undertaken with the aim to study the

relation between plasma levels of Copper and Zinc and unexplained human infertility.

Aims and objectives

Detection of levels of plasma copper and zinc in primary and secondary infertility and unexplained female infertility.

METHODS

The patients were selected from the outpatient and inpatient department of Obst and Gynae, Muzaffarnagar Medical College, Muzaffarnagar. All the patients for the study were in the reproductive age group (18-39 years). Study group included the married female of primary or secondary infertility. Control group comprised of married fertile females of reproductive age group. None of the infertile or control subjects were receiving any medication or suffering from any infection during the study.

In all the cases, detailed history was taken regarding the age, age at marriage, duration of infertility, type of infertility, history regarding contraception, details of menstrual history and obstetric history with regard to the number of full term deliveries, still births, type of labour, puerperium and history of MTP or D and C or pelvic inflammatory disease.

A thorough clinical and systemic examination to rule out any systemic disease and per speculum and prevaginal examination was carried out in all patient to exclude pelvic pathology.

Table 2: Comparison of plasma, copper and zinc concentration in control, explained and unexplained infertility.

Group	Total no. of patient	Plasma Cu concentration			Plasma Zn concentration		
		Range	Mean	SD	Range	Mean	SD
Control	20	98.78-169.2	124.72	20.74	90.0-126	107.29	10.54
Explained	48	82.57-217.71	123.98	32.29	85.0-126	106.7	11.81
Unexplained infertility	26	63.0-145.14	95.5	20.48	69.91-133.33	102.74	16.30

The difference in plasma Zinc concentration in three groups was not statistically significant ($P>0.05$).

DISCUSSION

The problem of infertility still baffles the gynaecologists as this is one of the common cases encountered in practice. The causative factor is yet to be found in case of unexplained infertility which would help in deciding the line of management in these patients.

Copper is essential to human life and health. It plays a key physiological role as the prosthetic element of more than a dozen specific copper protein and has a significant role to play in haem and collagen production and

infertility investigations were done in these women in form of follicular study, tubal patency tests and seminal analysis of their partners were done to exclude male factor. Venous blood samples were taken from the infertile women and from 20 fertile non-pregnant women of closely similar age, weight, height and plasma Copper and Zinc concentrations were measured.

RESULTS

Incidence of unexplained infertility (i.e. those cases where complete investigations show no reason for their infertility was 26(35.14%) out of which 12 were primary infertility and 14 were secondary infertility.

Table 1: Unexplained infertility in study group.

Infertility	Total patient		Primary infertility		Secondary infertility	
	No.	%	No.	%	No.	%
Unexplained	26	35.14	12	27.27	14	46.6
Explained	48	64.86	32	72.27	16	53.38
Total	74		44		30	

In the normal fertile non-pregnant healthy female's plasma Copper ranged from 98.78-169.2 mcg% (mean 124.72 mcg%; SD 20.74). In patients of unexplained infertility plasma copper was found to be low. It ranged from 63.0 to 145.14 mcg% (mean 95.5 mcg% SD 20.42). The difference in serum copper value is highly significant as $P<0.001$.

function. The role of copper in human reproduction has not been much investigated. This study was therefore done to find relation between plasma levels of copper and zinc and unexplained infertility.

In the present study incidence of unexplained infertility (that is those cases where complete investigations show no reason for their infertility) was 26 cases (35.14%) and was higher in cases of secondary infertility (46.67%) as compared to primary infertility (27.27%).

M H Soltan and DM Jenkin also found mean plasma copper to be lower (17.3; SE 0.43 mmol/liter) in the 48 infertility women than in 35 control subjects (22.44; SE 0.82).⁴

These results suggest that hypocupraemia may be a factor in the aetiology of infertility in these women. Plasma Copper is a sensitive index of tissue copper status and hypocupraemia and hyperceruloplasminaemia are the earliest detectable manifestation of copper deficiency.⁵ Blood copper concentration is influenced by the level of dietary copper and by the ratio of copper to other components of diet probably molybdenum inorganic sulphate, zinc and iron.

The mechanism by which copper deficiency may be involved in infertility has not yet been explained. Rucker et al postulated that low plasma tissue copper operates by impairing the structure and function of the supporting collagen in the graafian follicle Lindbloom and Hamberger found that copper stimulated both longitudinal and circular smooth muscles in a manner similar to prostaglandin F_{2α}.^{1,2} They postulated that low plasma copper in infertile women operates by direct inhibition of fallopian tube hindering ovum transport.

The absence of significant difference in plasma zinc concentration between fertile and infertile women in our study does not support the hypothesis of A-L-Saraf et al and Jerome Nriagu that zinc deficiency causes female infertility.^{3,6} Saad A Husain concluded that the increase in copper zinc ratio may have an important aetiological role in the pathogenicity of unexplained infertility which is contradictory to our study.⁷

However, our finding is in accordance with those of MH Salton and DM Jenkin who found no significant difference in plasma zinc concentration between infertile women and control subjects.⁸

CONCLUSION

Plasma copper concentration was found to be significantly lower in cases of unexplained infertility as compared to subjects of control group and those of explained infertility. This denotes that copper deficiency might have a role to play in the etiogenesis of otherwise unexplained infertility.

The difference in mean plasma zinc concentration was statistically insignificant. Hence, we can conclude that zinc deficiency may not play a significant role in female infertility.

The association of dietary factors with human infertility remains unclear. Some researchers have reported improved female infertility by consuming some micronutrients. Their deficiency leads to oxidative stress and unexplained infertility.

We need further studies to investigate the interventional strategy of micronutrients supplementation (Group B vitamin, Vitamin C and D, selenium iron and magnesium) in oxidative status of infertile women.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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