

## Estimation of serum zinc and copper levels patients with schizophrenia: a preliminary study

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### Introduction

Trace elements are essential for normal metabolism. Their dysregulation adversely affects biological processes and may play a role in the pathogenesis of various diseases including schizophrenia. The role of micronutrients in schizophrenia has been investigated in a limited number of studies; the results are inconclusive.

### Aims

To examine the serum levels of zinc and copper in patients with schizophrenia in comparison to healthy controls and also assess these levels in the acute and chronic stage of the illness.

### Methods

The study population comprised of 150 cases and 150 age-matched controls. Their serum zinc and copper levels were measured by an Atomic Absorption Spectrophotometer. Among the cases, the stage of illness was assessed using the Positive and Negative Syndrome Scale (PANSS) score.

### Results

The zinc and copper levels were higher significantly in patients with schizophrenia than in the control group.

### Conclusions

The evaluation of zinc and copper levels in patients with schizophrenia warrants further study.

SL J Psychiatry 2013; 5(1): 14-17

## Introduction

A complex balance of trace elements is vital for the maintenance of physical and mental health, as they are required for numerous metabolic and physiological processes in the human body (1, 2). In the peripheral and central nervous systems they play important functional roles and are also components in nervous tissue (3-8). Imbalances in the optimum levels of these elements may adversely affect biological processes and are associated with many psychiatric diseases including schizophrenia (9-11).

Schizophrenia is among the most debilitating of psychiatric disorders with devastating effects on both its victims and their families. Furthermore, it extracts an enormous economic cost from society (12).

The hypothesis that excess copper (Cu) levels in tissues can lead to schizophrenia has neither been compellingly demonstrated nor convincingly refuted. However, plasma Cu concentrations were shown to be elevated in patients with schizophrenia and a study of trace metals in scalp hair samples of patients with schizophrenia has shown an increase in Cu concentrations (13-17).

The present study is an attempt to examine serum levels of Zinc (Zn) and Cu in patients with schizophrenia and to ascertain whether the levels of these trace elements could be correlated to the severity and duration of schizophrenia.

## Methods

In this case control study, 150 women and men with schizophrenia (ages ranging from 17-56 years of age with a mean age of  $35.96 \pm 9.77$  years) attending the out-patients' department of a tertiary care centre

served as cases, and 150 age and sex matched healthy individuals served as controls. The diagnosis of schizophrenia was confirmed by a senior consultant psychiatrist, with clinical evaluation and using ICD-10 criteria. On the basis of duration and symptoms of illness and PANSS score (18, 19) each patients with schizophrenia was further categorised as, in the acute (n=79, 68 male and 11 female) or chronic (n=71, 32 male and 39 female) stage of the illness.

Subjects with a history of drug abuse, chronic systemic diseases such as diabetes mellitus, hypertension, severe head injury or seizure, and inflammatory diseases and those who were taking certain drugs (anticonvulsants, contraceptives, glucocorticoids) known to affect trace element metabolism were excluded from the study after obtaining a detailed history and conducting routine laboratory investigations.

Informed consent was obtained from all subjects of the study for which ethical approval was obtained from the Rajasthan University of Health Sciences in Jaipur, India.

Venous blood (7ml) was collected using aseptic techniques from the antecubital vein of all subjects in the study into a metal free vial. Samples were left standing at room temperature for 20 minutes. Subsequently the serum was separated by centrifuging at 3000 rpm for 15 minutes, and preserved at -20°C until assayed.

The Zn and Cu levels in the serum of each group were measured with the help of an Atomic Absorption Spectrophotometer (AAS 4141A). The specifications of the instruments used for the analysis are summarised in Table 1.

**Table 1. Atomic Absorption Spectrophotometer specifications used in Cu and Zn analysis**

Specifications	Zn	Cu
Wavelength	213.9 nm	324.7 nm
Slit Setting	1.0 nm	0.5 nm
Flame Type	Air-Acetylene Flame (Lean Blue)	Air-Acetylene Flame (Lean Blue)

## Results

The Zn and Cu levels were compared in cases and controls as well as among cases with acute and chronic disease, as indicated by their Positive and Negative Syndrome Scale (PANSS) scores. The statistical difference between groups were determined by the student's 't' test;  $p < 0.05$  was considered significant. The results are summarised in Tables 2 and 3.

The Zn levels in cases were significantly higher than in controls ( $p < .0001$ ). Similarly, the Cu levels in cases were also significantly higher than in controls ( $p < .0001$ ).

The Zn levels in those with acute illness were lower than those with chronic illness but the difference was not statistically significant ( $p > 0.001$ ).

However, the Cu levels in those with acute illness were higher than those with chronic illness but the difference was not statistically significant ( $p > 0.001$ ).

## Discussion

Schizophrenia is a severe and debilitating disorder which affects general health, level of functioning, autonomy, subjective wellbeing, and life satisfaction of those who suffer from it (20). It is established that deficiency as well as excess in either Zn or Cu can produce a variety of biochemical and physiological changes (21). In addition, these two essential trace elements are neuroactive substances that are synaptically released during neuronal activity. They have been implicated in neuropathological diseases such as schizophrenia and depression (22).

The findings of previous studies on the role of trace elements in patients with schizophrenia have been equivocal. Some authors did not find a significant deviation from normal in concentrations of serum Cu; others found a decrease in hair Cu concentrations in female patients with chronic schizophrenia (23, 24).

Cu is critical for energy production in cells. It is also utilised in nerve conduction, in connective tissue, the cardiovascular system and the immune system. Cu stimulates production of the neurotransmitters epinephrine, norepinephrine and dopamine. It is also required for monoamine oxidase, an enzyme related to serotonin production. Excess of dopamine due to stimulation of its production and inhibition of serotonin production may cause psychosis and symptoms of schizophrenia (25).

The objective of this study was to measure serum Zn and Cu levels in patients with schizophrenia and to compare it with normal healthy controls. The serum trace element levels in patients with acute and chronic schizophrenia were also compared.

In this study, serum Zn was found to be significantly higher ( $p < .0001$ ) in patients with schizophrenia than the corresponding levels in the healthy control group. However no patient in either group had higher than normal Zn levels. Arinola et al found significantly higher values of Zn in patients with schizophrenia who were on antipsychotic medication than in controls (26). Yanik et al also found that Zn levels in patients with schizophrenia were higher than in controls; however the difference was not statistically significant (15). Olabanji et al also found increased levels of serum Zn in patients with schizophrenia compared to controls (27). Craven et al found no significant differences in Zn levels in blood, urine, hair, or gastric aspirate in unmedicated patients with schizophrenia compared to controls (28).

Zn is utilised in the functioning of more than 200 enzymes, some of them related to DNA and RNA synthesis and Zn is also a factor in the functioning of the immune system. Zn also plays an important role in axonal and synaptic transmission and is necessary for nucleic acid metabolism and brain tubulin growth and phosphorylation (29). Since Zn is a necessary element for the normal functioning of superoxide dismutase

**Table 2. Serum Zn and Cu levels in case and control groups**

Trace element	Mean $\mu\text{g/dl}$ (SD)	Significance
<b>Zn</b>		
Case (n=150)	95.35(5.21)	$p < 0.0001$
Control (n=150)	92.14(3.35)	
<b>Cu</b>		
Case (n=150)	149.75(8.07)	$p < 0.0001$
Control (n=150)	114.72 (10.80)	

**Table 2. Serum Zn and Cu levels in acute and chronic schizophrenia**

Trace element	Mean $\mu\text{g/dl}$ (SD)	Significance
<b>Zn</b>		
Acute (n=79)	95.14 (3.27)	$p = 0.41$
Chronic (n=71)	95.59 (3.44)	
<b>Cu</b>		
Acute (n=79)	149.87 (8.21)	$p = 0.84$
Chronic (n=71)	149.60 (7.96)	

and thymidylate synthase enzymes, raised Zn levels in patients with schizophrenia lead to increased antioxidative capacity and reduced oxidative stress. In this study, serum Cu levels were significantly higher in patients with schizophrenia compared to the control group. This is consistent with other studies reporting high Cu levels in patients with schizophrenia (14, 16, 21). Wolf et al demonstrated that both serum Cu and ceruloplasmin were elevated in patients with schizophrenia (30). These findings suggest abnormalities in Cu metabolism may play a role in schizophrenia by exacerbating or perpetuating dopaminergic dysregulation (12).

In this study, Zn and Cu levels were not significantly related to the stage of disease (acute or chronic) or duration of illness.

## Conclusion

The results of this study are consistent with previous research which suggests that there is an alteration of Zn and Cu metabolism in schizophrenia. However their role in its causation requires more scrutiny through randomised double blind studies and long term follow up. This study also suggests that the duration of disease does not significantly alter the level of the trace elements. However it is unknown at this stage whether these trace elements contribute to the mental illness or whether the body attempts to store more of these in response to the illness. The role of micronutrients in the pathogenesis and course of Schizophrenia warrants further study.

## Declaration of interest

None declared

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