

# Evaluation of Serum Ca, Mg, Cu, Fe, Zn and Mn in Conversion Disorder Patients

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**ABSTRACT:** The aim of the study was to determine the concentration of serum Ca, Mg, Cu, Fe, Zn and Mn in Bangladeshi conversion disorder patients compared to control subjects and to correlate the changes, if any, with different socio-demographic factors and nutritional status. Forty five conversion disorder patients were randomly recruited. Forty five healthy control subjects were also recruited by matching the socio-demographic status to that of the patients. Blood samples were analyzed to determine the concentration of serum Ca, Mg, Cu, Fe, Zn and Mn using atomic absorption spectroscopy. Except for Mg, the concentrations of the other elements (Cu, Fe, Zn, Ca, and Mn) decreased in patients compared to control, but the changes were not statistically significant ( $p > 0.05$ ). Serum Mg level increased insignificantly in patients ( $p > 0.05$ ). No significant relationship was found between the socio-demographic variables and serum Ca, Mg, Cu, Zn and Mn levels, except for serum Fe, where a significant negative correlation was found between serum Fe level and BMI ( $r = -0.428$ ;  $p = 0.023$ ).

**Key words:** Conversion disorder patients, serum elements, socio-economic status

## INTRODUCTION

Conversion disorder involves the loss or alterations in sensory or voluntary motor function by unexplained pathophysiological mechanisms.<sup>1</sup> Usual symptoms are similar to neurological dysfunctions e.g. paralysis, tremors, gait disturbances and pseudo-seizures.<sup>1</sup> In DSM-IV, it is categorised as a somatoform disorder, along with somatisation disorder, hypochondriasis, body dysmorphic disorder and pain disorder.<sup>2</sup> Confusingly, in ICD-10, conversion disorder falls under the category of dissociative (conversion) disorders alongside dissociative amnesia and fugue states.<sup>3</sup> Conversion disorder may present at any age but is rare in children

younger than 10 years or in the elderly.<sup>4</sup> Studies suggest a peak onset in the mid-to-late 30s.<sup>4-6</sup> 'Hysteria' (Conversion disorder) was originally understood to be a condition exclusively affecting women, though it has increasingly been recognised in men.<sup>5</sup> In recent studies, women continue to predominate, with between 2 and 6 female patients for every male.<sup>5-6</sup> Other studies suggest that the symptoms are most common in young women<sup>1</sup>, rare in children under 8 years old, more common in rural areas, among uneducated people, and in the lower socio economic classes.<sup>7</sup>

Ca, Mg, Cu, Fe, Zn and Mn are required for numerous metabolic and physiological processes in the human body.<sup>8</sup> Therefore imbalances in the optimum levels of these elements may adversely affect biological processes, and are associated with

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Dhaka Univ. J. Pharm. Sci. 9(2): 119-124, 2010 (December)

many diseases.<sup>8</sup> Zinc and its metalloenzymes are involved in a variety of regulatory functions in the body including immune development, catalytic functions, and maturation of reproductive system.<sup>9</sup> Copper and iron are crucial for physiological functions, antioxidant defence, and immune development.<sup>8</sup> Copper acts as an antioxidant by being a part of two crucial antioxidants of the body, Cu-Zn superoxide dismutase and monoamino oxidase.<sup>10</sup> Calcium plays a crucial role in skeletal mineralization, blood coagulation, neuromuscular conduction, maintenance of normal tone, and excitability of skeletal and cardiac muscle.<sup>11</sup> Along with its function as cofactor, Mg is involved in cellular energy production, glycogen breakdown, protein synthesis, and cell growth.<sup>12</sup> The nervous system is the major target of the toxic effect of Mn and its compounds.<sup>13</sup>

Calcium (Ca), magnesium (Mg), zinc (Zn), copper (Cu), iron (Fe) and manganese (Mn), etc. have been studied in many diseases, including autoimmune, neurological, drug addiction, and psychiatric disorders e.g. as schizophrenia, panic disorder.<sup>14-16</sup> Excessive copper and zinc levels may cause brain dysfunction.<sup>17</sup> Copper level is generally higher in depressed patients than in normal individual.<sup>18</sup> It has been observed that plasma Cu concentrations were significantly higher ( $p < 0.01$ ) and Mn and Fe concentrations were lower ( $p < 0.05$ ) in schizophrenic patients than in controls.<sup>19</sup> Low serum iron has been reported in a variety of neuropsychiatric motor disorders.<sup>19</sup>

These observations suggest that alterations in Ca, Mg Zn, Cu, Fe and Mn may play a role in the pathogenesis of conversion disorder. As no work has been reported regarding Ca, Mg, Zn, Cu, Fe and Mn levels in Bangladeshi conversion disorder patients, the serum levels of these elements were determined in our study. The correlation between these elements in conversion disorder patients with different socio-demographic factors was also investigated.

## MATERIALS AND METHODS

**Subjects and study design.** Forty five conversion disorder patients (12 males & 33 females), age ranging from 17 to 41 years, were randomly recruited from the Department of Psychiatry, Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital, Dhaka, Bangladesh. Two specialist psychiatrists, who were trained in the use of Diagnostic and Statistical Manual of Psychiatry Disorders (DSM-IV, Text revision, Fourth Edition) conducted the diagnosis and interviewed the patients with conversion disorder. The control group included 45 healthy individuals matched by age, sex, BMI, marital status, education, area of residence, smoking habit, and socio-economic status to the patient group, with no previous history of any psychiatric disorders or any medical history that can affect the immune system.

All patients were evaluated clinically (history and clinical examination). Laboratory investigations including 1) Complete blood count: to exclude patients with anaemia, leucopenia, leucocytosis, eosinophilia or any other abnormal figures in blood count, 2) Thyroid function tests: to exclude patients with high or low serum T3 and T4 levels, 3) Renal function tests (serum creatinine and creatinine clearance): to exclude patients with renal impairment, 4) Liver function tests: to exclude patients with liver insufficiency, especially those with high liver enzymes or those with diminished albumin levels or high globulin levels, 5) Urine and stool analysis : to exclude urinary tract infection or parasitic infestations, were carried out. Exclusion criteria were patients with previous diseases that can affect immunity, e.g. rheumatic fever, rheumatoid arthritis, liver diseases, renal diseases, etc.; patients under medication for mania. Patients who were mentally retarded and suffered from comorbid psychiatric disorders, those with substance disorder were also excluded from the study.

The study subjects were briefed about the purpose of the study and written consent was taken from each of them. Each of the subjects filled up a questionnaire form which contains personal information, socio-economic data, history of illness etc. The forms of the patients who had no formal education were filled out with the help of an investigator. Ethical approval was obtained from the Ethical Review Committee of Bangabandhu Sheikh Mujib Medical University Hospital (BSMMU), Dhaka, Bangladesh. The study was conducted during the period of February 2008 to January 2009.

**Blood sample collection.** Ten ml venous blood was collected from each of the conversion disorder patients during the attack of conversion disorder symptoms and control subjects. Blood samples were allowed to clot for half an hour. Samples were then centrifuged for 15 minutes at 5000 rpm. Clear supernatant was collected from the tube and stored in pre-cleaned metal-free tubes at  $-80^{\circ}$  C until further analysis.<sup>17</sup>

**Analysis of elements.** Flame atomic absorption spectrometry (Spectra AA 220) was used to determine serum Ca, Mg, Zn, Cu, Fe and Mn levels in both conversion disorder patients and control subjects. To ensure assay accuracy all the standard solutions were run for every 10-test samples. Wavelengths used were 213.9 nm, 327.4 nm, 248.3 nm, 422.7 nm, 279.806 nm, and 279.5 for determining Zn, Cu, Fe, Ca, Mg, and Mn respectively.<sup>14-16</sup> Concentrations of all the elements were calculated by using calibration curve with the help of a software package (Spectra AA).

**Statistical analysis.** All the data were analyzed by using the SPSS software package (Version 15.0, SPSS Inc., Illinois, USA). Values were expressed as percentage, mean, and standard deviation. To assess distribution pattern for case and control, one sample *kolmogorov-smirnov* test was done. Comparison of the socio-demographic data between conversion disorder patients and control group was performed by *Chi-square* test. To determine the contribution of different socio-demographic factors and BMI on the concentration levels of Ca, Mg Zn, Cu, Fe and Mn,

independent sample student's *t*-test, Pearson's correlation analysis, multiple regression analysis and Analysis of variance (ANOVA) were carried out. In all calculations, 2-tailed comparisons were carried out and  $p < 0.05$  was considered statistically significant.

## RESULTS AND DISCUSSION

Socio-economic data of conversion disorder patients ( $n = 45$ ) and control subjects ( $n = 45$ ) are presented in Table 1. Socio-economic data of the conversion disorder patients in the present study shows that most of the patients were female (73.33%). Similar results were obtained in different studies where a higher frequency of conversion disorder was found in women than in men<sup>1,4-5</sup>, other studies have found no difference between the sexes.<sup>7</sup> Most of the patients in our study were young (mean age, 22.06 years), had a poor monthly income of ( $9375 \pm 3074.08$  BDT), came from rural areas (68.89%), and had secondary level of education (55.55%). Similar results were found in a study where they found that conversion disorder is more common in rural areas, among uneducated people, and in the lower socio economic classes.<sup>7</sup> The mean (SD) BMI of the conversion disorder patients and control subjects were 22.06 (8.33) years and 21.05 (3.39)  $\text{Kg/m}^2$ , respectively. The biophysical characteristics of conversion patients and control subjects are shown in Table 2.

From statistical analyses, it was observed that serum zinc, copper, iron, calcium, and manganese concentration of conversion disorder patients decreased in comparison with controls, but was not statistically significant ( $p > 0.05$ ). But in case of magnesium, an insignificant increase ( $p > 0.05$ ) in serum concentration of patients was observed than the control subjects (Table 3). Pearson's correlation analysis revealed no significant relationship between the socio-demographic variables and serum Ca, Mg Zn, Cu, Fe and Mn levels at 5% level of significance, except for serum Fe level, where a significant negative correlation was found between serum Fe level and BMI ( $p = 0.023$ ) (Table 4). For regression

analysis and ANOVA, we considered the serum Zn, Cu, Fe, Ca, Mg, and Mn concentrations as dependant variable and socio-demographic factors e.g. age, BMI, income, occupation, education, residence, and

smoking habit as independent variables. No significant relationship between these variables was observed at 5% level of significance ( $p > 0.05$ ).

**Table 1. Socio-demographic data of conversion disorder patients (n = 45) and control subjects (n = 45).**

Parameter	Patients (n=45)			Control (n=45)		
	n	%	Mean (SD)	n	%	Mean (SD)
<b>Education</b>						
Illiterate	3	6.67		4	8.89	
Can read only	3	6.67		2	4.44	
Secondary	25	55.55		28	62.22	
Higher secondary	9	20		7	15.56	
Graduate & above	5	11.11		4	8.89	
<b>Occupation</b>						
Service	5	11.11		10	22.22	
Business	9	20		10	22.22	
Student	0	0		5	11.11	
Housewife	12	26.67		8	17.78	
Others	19	42.22		12	26.67	
<b>Monthly income in BDT<sup>‡</sup></b>						
0-5000	3	6.67	9375	1	2.22	17267
5001-20000	36	80	(3074.08)	38	84.45	(1830.95)
20001-30000	5	11.11		5	11.11	
>30000	1	2.22		1	2.22	
<b>Age in years</b>						
17-20	8	17.78	22.06	4	8.89	23.93
21-25	31	68.89	(8.33)	32	71.11	(8.06)
26-35	4	8.89		8	17.78	
36-41	2	4.44		1	2.22	
<b>Gender</b>						
Male	12	26.67		13	28.89	
Female	33	73.33		32	71.11	
<b>Marital status</b>						
Married	17	37.78		15	33.33	
Unmarried	25	55.55		30	66.67	
Divorced	3	6.67		0	0	
<b>Area of residence</b>						
Rural	31	68.89		35	77.78	
Urban	6	13.33		5	11.11	
Semi-Urban	8	17.78		5	11.11	
<b>Smoking Habit</b>						
Non smoker	39	86.67		37	82.22	
Smoker	6	13.33		8	17.78	

<sup>‡</sup>BDT=Bangladeshi Taka

**Table 2. Biophysical characteristics of conversion disorder patients (n = 45) and control (n = 45).**

Parameter	Patients (n = 45)			Control (n = 45)		
	n	%	Mean (SD)	n	%	Mean (SD)
<b>Height (m)</b>						
1.31-1.50	8	50	1.56	0	0	1.64
1.51-1.70	8	50	(0.10)	11	73.33	(0.087)
1.71-1.90	0	0		4	26.67	
<b>Weight (Kg)</b>						
35-50	7	43.75	52.06	3	20	56.53
51-66	17	106.25	(12.38)	10	66.67	(8.25)
67-82	2	12.5		2	13.33	
<b>BMI (Kg/m<sup>2</sup>)</b>						
15.1-18.0	7	43.75	21.05	14	93.33	20.86
18.1-25.0	7	43.75	(3.39)	11	73.33	(1.86)
25.1-30.0	2	12.5		0	0	

Normal human BMI ranges from 18.5–25 (Food and Agriculture Organization, 1994)

**Table 3. Mean serum Zn, Cu, Fe, Ca, Mg, and Mn level of conversion disorder patients (n = 45) and control subjects (n = 45).**

Trace elements	Mean $\pm$ SD serum concentration (mg/L)			
	Patients	Control subjects	Reference value <sup>#</sup>	p-value
Zn	1.17 $\pm$ 0.77	1.56 $\pm$ 2.30	0.85	0.487
Cu	1.13 $\pm$ 0.51	1.21 $\pm$ 0.36	1.02	0.622
Fe	0.73 $\pm$ 0.24	0.85 $\pm$ 0.28	1.173	0.242
Ca	98.85 $\pm$ 11.93	100 $\pm$ 13.23	80.18	0.812
Mg	23.58 $\pm$ 2.70	22.83 $\pm$ 2.68	19.93	0.472
Mn	0.10 $\pm$ 0.02	0.11 $\pm$ 0.02	0.15	0.932

Independent Sample *t*-test (2-tailed):  $p < 0.05$

<sup>#</sup>Reference values are from Handbook on Metals in Clinical and Analytical Chemistry.<sup>22</sup>

**Table 4. Correlation of serum Zn, Cu, Fe, Ca, Mg, and Mn with BMI, income and age of conversion disorder patients.**

Parameter	Zn	Cu	Fe	Ca	Mg	Mn
Age (Year)	$r = 0.053$ $p = 0.829$	$r = 0.051$ $p = 0.834$	$r = -0.230$ $p = 0.239$	$r = 0.060$ $p = 0.761$	$r = 0.160$ $p = 0.416$	$r = 0.217$ $p = 0.267$
Income (BDT/month)	$r = -0.270$ $p = 0.263$	$r = 0.159$ $p = 0.516$	$r = 0.368$ $p = 0.054$	$r = 0.053$ $p = 0.789$	$r = -0.126$ $p = 0.523$	$r = 0.096$ $p = 0.627$
BMI (Kg/m <sup>2</sup> )	$r = -0.172$ $p = 0.481$	$r = -0.253$ $p = 0.297$	$r = -0.428$ $p = 0.023^*$	$r = 0.022$ $p = 0.910$	$r = 0.268$ $p = 0.168$	$r = 0.355$ $p = 0.064$

Pearson's Correlation Analysis (2-tailed): \*Significance,  $p < 0.05$ .

Yet no study has been reported regarding the alterations of serum Ca, Mg Zn, Cu, Fe and Mn in conversion disorder patients compared to control subjects. However, serum levels of these elements have been investigated in different neuropsychiatric disorders to correlate the alterations in Ca, Mg Zn, Cu, Fe and Mn elemental levels with the pathogenesis and/or progression of the disease. The serum concentration of Zn decreased significantly ( $p = 0.001$ ) in panic disorder patients, but the differences of the concentration of Mn, Ca, Cu, and Mg between patient and control group were not significant ( $p = 0.522$ ,  $p = 0.065$ ,  $p = 0.800$ , and  $p = 0.712$ , respectively).<sup>16</sup> Maes and colleagues<sup>20</sup> found serum zinc levels were significantly lower in depressed patients as compared to healthy matched controls. In a group of 30 patients with mood disorders, 7/30 had a clear zinc deficiency.<sup>21</sup> Plasma Mn and Fe concentrations were found to be lower in schizophrenic patients than in controls.<sup>19</sup> In a variety of neuropsychiatric motor disorders, low Fe level was found. The serum concentration of Mn and Cu increased significantly ( $p = 0.00$ ,  $p = 0.022$  respectively) in somatization disorder patients while the concentration of Zn ( $p = 0.954$ ) remained unchanged.<sup>14</sup> In our study, no significant Ca, Mg Zn, Cu, Fe and Mn alteration was found in the serum of

conversion disorder patients compared to healthy control subjects.

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