Serum Immunoglobulin Profiles of Conversion Disorder Patients

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Abstract

Objective: The aim of the study was to determine the serum immunoglobulin profiles of conversion disorder patients and to compare those parameters with control subjects.

Method: Forty conversion disorder patients were recruited randomly from the Department of Psychiatry, Bangabandhu Sheikh Mujib Medical University Hospital, Dhaka, Bangladesh for this study. The control group included 34 healthy individuals matched by age and sex to the patient group. Serum immunoglobulin concentrations were determined by turbidimetry method using immunoglobulin kits.

Result: The serum concentrations of IgG, IgA and IgM of conversion disorder patients were 22.32 ± 5.9 g/L, 4.83 ± 1.43 g/L and 3.45 ± 1.24 g/L, while these were 20.02 ± 2.04 g/L, 3.65 ± 1.03 g/L and 2.70 ± 0.63 g/L in control subjects respectively. The concentration of IgA and IgM were increased significantly (P < 0.05), but the change of IgG was not significant (P > 0.05). Socioeconomic data revealed that most of the patients were young female and unmarried. The mean BMI of patients (21.27 ± 3.56) were not significantly different (P > 0.05) from the control subjects (20.9 ± 1.78). Moreover statistical analysis revealed that there were no significant correlation between immunoglobulin concentrations and socioeconomic factors and nutritional status.

Conclusion: These findings may suggest a possible immune dysfunction as all the immunoglobulins were increased in conversion disorder patients. But study with larger number of population is required for further evaluation of the relationship between the immune response and disease state to confirm these findings (German J Psychiatry 2008; 11: 141-145).

Keywords: Conversion disorder, immunoglobulin, socioeconomic status

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Introduction

Conversion disorder can be defined as the apparent dysfunction of sensory and motor systems consistent with psychological conflicts and psychosocial stressors (Lazare, 1981). It is considered as a kind of somatoform disorder in DSM-IV which includes somatization disorder and conversion disorder in the same group of illness (American Psychiatric Association, 1994). In ICD-10, conversion disorders are classified as dissociative disorder and named as dissociative motor disorders, dissociative convulsions, dissociative anesthesia and sensory loss and mixed dissociative disorders (WHO, 1992). Spitzer et al. in 1999 reported that dissociative symptoms are more frequent in patients with conversion disorder, whereas general psychopathology is as common as that in other psychiatric conditions (Spitzer et al., 1999).
Conversion disorder is a specific form of somatization in which the patient presents with symptoms and signs that are confined to the voluntary central nervous system (American Psychiatric Association, 2000). “Conversion” or “conversion reaction” refers to the process whereby intrapsychic distress is converted into physical neurologic symptoms (Hurwitz, 1989). Neurologic presentations may, however, involve any aspect of the central nervous system over which voluntary control is exercised. Thus, patients may present with a psychogenic dementia as well as loss of speech and language or a disturbance of any of the special senses (Hurwitz, 1989; Mcevoy and Wells, 1979). This reflects the fact that the neurologic presentation is ideogenic and derives from patient beliefs about how neurologic symptoms should present. The patient applies this belief consciously to govern behavior, resulting in bizarre, atypical, and non-organic findings on neurologic examination.

In contemporary medical practice, with the availability of sophisticated neuroimaging techniques such as magnetic resonance imaging, missed or ganic illness may account for 4% to 15% of individuals initially given a diagnosis of conversion disorder (Binzer and Kullgren, 1998; Kent et al., 1995; Mace and Trimble, 1996; Moene et al., 2000). To avoid error, all patients must be thoroughly medically investigated. However, relatively few studies evaluated outcome and long-term prognosis in children and adolescents (Nemzer, 1996).

Recent recognition of immune system dysfunction in psychiatric patients, particularly those with depression or schizophrenia, has led to some interesting hypotheses for the pathogenesis of these disorders, including infectious and autoimmunity aetiologies (reviewed by DeLisi & Wyatt, 1984). Alternatively, dysfunction of the immune system may be secondary to the primary disease process (i.e. altered neuro transmitter activity), to long-term pharmacological treatment, or a result of an unrecognized concurrent, but unrelated medical disorder (Hall et al, 1980; Zarrabi et al, 1979). Repairing the central nervous system is facilitated by both cellular and humoral components of the immune system. Transfer of macrophages or T cells that activated against CNS antigens promote axon re-growth and protect axons from further damage (Warrington et al, 2001).

Various indices of the immune system have been quantified and have been found to be suppressed also in depressed individuals (Kronfol et al, 1983). The association of impaired cellular and humoral immune response with depression remains controversial (Evans et al, 1974), though it is reported that depression and anxiety alter immunoglobulin levels (Frasure et al., 2000). In schizophrenic patients, rise of serum concentration of IgA, IgM and IgG has been reported (Tiwari et al., 1989, Karim et al., 2005). A significantly higher incidence of antibodies with affinity for dopamine was found in the group of psychotic patients compared with the neuro- logical control group (Bergquist et al., 1993). Stress condition activates the inflammatory response system and severe stress is connected with suicide incidence. It was found that the concentrations of immunoglobulins (IgA, IgM and IgG) were reduced and complement (C3 and C4) were increased in patients who are admitted to hospital for self-injurious behaviour (Moe et al., 2003). A small subgroup of patients, who included six with major depression, one with chronic schizophrenia, and one with a personality disorder, were found to have low IgM concentrations (De-Lisi et al., 1984). An increase of immunoglobulin level was also found in manic patients than the control subjects (Baker et al., 2005). In another study, serum concentration of IgA was significantly decreased in somatization disorder while other IgG and IgM level did not change significantly (Hossain et al., 2007).

A few investigators reported immunological involvement in some psychiatric disorders such as schizophrenia, somatization disorder, mania, depression, anxiety etc (Bergquist et al., 1993, Hossain et al., 2007; Taylor, 2000; Tiwari et al., 1989). But no study regarding immunoglobulin level in conversion disorder patients has yet been reported. Hence, the present study was focused on immunoglobulins level in conversion disorder and to evaluate its correlation with socioeconomic factors and nutritional status.

Material and Methods

Study Subjects

Forty conversion disorder patients comprising 8 males and 32 females, age ranging from 10 to 40 years with mean BMI of 21.27(± 3.56) kg/m², were randomly recruited from the Department of Psychiatry, Bangabandhu Sheikh Mujib Medical University Hospital, Dhaka, Bangladesh. Two specialist psychiatrist, 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 34 healthy individuals matched by age, sex and socioeconomic status to the patient group, with no previous history of any psychiatric disorders or any medical disease that can affect the immune system.

All patients were evaluated clinically (history and clinical examination), searching for signs of immunological changes, e.g. recurrent viral infection and searching for any diseases that can affect immunity, e.g. sore throat, bronchitis, liver diseases, thyroid enlargement etc. Laboratory investigations:

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 increased T3 and T4 serum levels or to exclude patients with low serum T3 and T4 levels, 3) Renal function tests (blood urea and serum creatinine) to exclude patients with renal impairment, 4) Liver function tests: to exclude patients with liver affection, 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 or those who stopped treatment for a period less than 6 months; patients who received any other medication such as oral contraceptives, non-steroidal anti-
inflammatory drugs, corticosteroids, anticonvulsants, and antidepressants, or had ECT during the preceding 6 months. 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, family history 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).

**Blood collection**

Five milliliter of venous blood sample was collected from the antecubital vein of each of the conversion disorder patients and healthy volunteers in a metal-free sterile tube, between 8 to 9 am after an overnight fasting. Samples with signs of hemolysis were discarded. The blood was then allowed to clot at room temperature for 30 minutes and centrifuged for 15 minutes at 3000 rpm to extract the serum. The serum was aliquoted into eppendorf tubes and stored at −80°C for analysis of immunoglobulins. Blood collection and serum separation were carried out in a dust-free environment.

**Immunoglobulin Profiling**

The serum immunoglobulin (IgG, IgA, and IgM) levels in both patients and controls were determined by turbidimetry method using an immunoglobulin kit (Quantia, India). In this method, anti-human antibodies were mixed with samples containing IgG, IgA, and IgM that formed insoluble antigen-antibody complexes. These complexes caused an absorbance change depending upon the immunoglobulin concentration that was quantified by a calibrator.

Calibrator standards of different immunoglobulins were prepared by diluting the reference standards with normal saline to get the desired concentration ranges (40–800 mg/dL for IgG, 6–144 mg/dL for IgA and 4–80 mg/dL for IgM). Separate microtitre plate was used for each of the immunoglobulins.

Five microliter of all the calibrator standards were pipetted into marked wells of each of the microtitre plate. Similarly the 5µL of diluted serum (1:10 with normal saline) samples were also pipetted into respective wells of all three plates. Then 500 µL of Quantia immunoglobulin activation buffer was added and incubated for 5 minutes. Absorbance (A1) was taken, 50 µL of each of three anti-human immunoglobulins (Anti IgG, Anti IgA and Anti IgM) were added to the wells of their respective microtitre plates. The plates were incubated for 5 minutes (as specified in the kit procedure) to react the antihuman immunoglobulin with the test serum and calibrator protein. After proper mixing, absorbance (A2) was taken at 550 nm for IgG and IgA and at 405 nm for IgM. Difference between the two absorbances (ΔA = A2 - A1) was used for calculation. The concentration of immunoglobulins was calculated against the calibration curves of each individual immunoglobulin.

**Statistical Analysis**

The SPSS software package (Version 11.5, SPSS Inc., Chicago, Illinois, USA) was used to analyze the data. Descriptive statistics were used for all variables. Comparison of immunoglobulin levels of patients and controls were performed by cross-table variables and independent sample t-test. Regression analysis was performed to find relation between socio-demographic factors and disease. All comparisons were 2-tailed, and P values of < 0.05 were considered as significant.

**Results**

The socioeconomic information of the conversion disorder patients and control subjects were evaluated statistically. It was found that the majority of conversion disorder patients were female (80%) with various professions having average monthly income of US$ 134.26 ± 42.39 and average age of 21.75 ± 8.95 yrs. The mean age of control group was 23.35 ± 7.73 yrs. There was no statistical difference between the

<table>
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<th>Immunoglobulin (g/L)</th>
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<th>Controls (n = 34)</th>
<th>P-value</th>
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<td>Range</td>
<td>N</td>
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<td>IgG</td>
<td>&lt; 15</td>
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<td>15–20</td>
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<td>IgA</td>
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groups in this regard \((t = 0.578, P = 0.567)\). Around 65% of patients were below the age of 20 years and primarily students (60%). This status indicates that there might be an early onset of the disease. Since the persons in this age range usually go through a lot of stressful conditions (social, psychological and physical), the present data supports the stress related pathogenesis of conversion disorder. It was also found that majority of the patients were unmarried (65%) and education level is up to secondary (50%). The mean BMI of patients \((21.27 \pm 3.56 \text{ Kg/m}^2)\) was not significantly \((P > 0.05)\) different from that of the control subjects \((20.09 \pm 1.78 \text{ Kg/m}^2)\). Further logistic regression was also fitted by considering disease as dependent variable and other sociodemographic factors as independent variables. No significant effects of these factors were observed on disease \((P>0.05)\).

Serum concentrations of immunoglobulins are presented in Table 1. Serum concentrations of IgG, IgA, and IgM of conversion disorder patients were found to be \(22.32 \pm 5.90\ g/L, 4.83 \pm 1.43\ g/L, \) and \(3.47 \pm 1.24\ g/L, \) respectively, and \(20.02 \pm 2.04\ g/L, 3.47 \pm 1.03\ g/L, \) and \(2.70 \pm 0.63\ g/L, \) respectively, in control subjects. From independent sample t-test, it has been revealed that IgA and IgM concentrations were increased significantly \((P<0.05)\) in conversion disorder patients compared to controlled subjects, while no significant change was found for IgG level \((P>0.05)\).

## Discussion

Conversion disorder is a challenging psychiatric disorder that requires long-term commitment on the psychiatrist’s part and uses the full spectrum of psychiatric skills. One important role of the treating psychiatrist is to ensure that any new physical symptom receives appropriate medical investigation from the rest of the medical profession. Early recognition of a conversion disorder will limit unnecessary tests and medications.

In this study 80% of the patients were found to be female which supports the previous findings (Chqand et al., 2001; Kaplan and Sadock, 1995; Ladwig et al., 2000). It has been also reported that conversion disorder are more frequent in lower socioeconomic groups which is similar to our study (Kaplan and Sadock, 1995).

In this study, it was found that IgA and IgM level were increased significantly where as no significant change was observed for IgG level in patient group. These findings are different from other studies in various psychiatric disorders like manic, depression and somatization disorder, where immunoglobulin level decreased significantly whereas no significant change was observed in the present study (Balaita et al., 1992; Hossain et al., 2007; Marazziti et al., 1992, Mubarak et al., 1999). But the present result is similar with the report of some other investigators who noted a rise of serum concnetartions of IgG, IgA and IgM in schizophrenic and manic patients (Baker et al., 2005; Karim et al., 2005; Tiwari et al., 1989). As somatization and conversion disorder are very similar hence the reason of this type of immunoglobulin profiling in conversion disorder patients for diagnosis could be a greater focus for researchers. These findings could direct our attention towards considering compromised immunity as a part of healthcare of this group of patients.

## References


