Serum Immunoglobulin Profile in Somatization Disorder Patients

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Abstract

Objective: The aim of the study was to determine the serum concentrations of immunoglobulins of somatization disorder patients and to find out the relationship between immunoglobulin level with their nutritional status and socioeconomic factors.

Method: The study was conducted among 46 somatization disorder patients and 45 healthy volunteers. Each patient was selected from four different hospitals by random sampling. Serum immunoglobulin concentrations were determined by turbidimetry method using immunoglobulin kit.

Result: It was found that IgG, IgM and IgA concentrations of somatization disorder patients were 24.14±4.44 (g/L), 2.05±1.12 (g/L) and 2.11±0.75 (g/L), while these were 26.34±4.94 (g/L), 2.36±1.25 (g/L) and 2.76±0.86 (g/L) in control subjects respectively. The concentration of IgA decreased significantly (P=0.02) in somatization disorder patients while the concentration of IgG (P=0.218) and IgM (P=0.443) were found to be unchanged. Socioeconomic data reveals that most of the patients were poor, middle- aged and unmarried. Mean BMI of the patients (20.26±3.04) was significantly (p<0.001) lower than that of the control subjects (23.56±2.03). Correlative analysis suggested that only the IgA value had a significant inverse correlation with the BMI (r = -0.553, p = 0.006), which was further justified from the regression analysis (R^2 = 43%; t = −3.948; p = 0.001) and one-way ANOVA test (F = 9.245; p = 0.006).

Conclusion: IgA level was found to be decreased significantly that may have a prognostic significance for the detection of somatization disorder. Further studies are warranted with large number of population to confirm these findings. (German J Psychiatry 2007; 10: 13-17).

Keywords: Somatization disorder; immunoglobulin; serum

Introduction

Somatization disorder is one of the most frequent psychiatric illnesses. It represents a group of disorders characterized by physical symptoms suggesting a medical disorder (Adler et al., 1989). It represents a psychiatric condition because the physical symptoms present in the disorder cannot be fully explained by a medical disorder, or mental disorder (Fink et al., 1999). Symptoms of somatization provide a challenge to the physicians to differentiate it from other mental illness. Frequent concomitants of somati-

zation are major depressive disorders, anxiety disorders, and personality disorders. Several recent studies found that 61 to 72 percent patients with somatization disorder also have co-occurring personality disorders (Turkson and Asamoah, 1999). In many studies, it was shown that patients with neurological disease had higher rate of being attacked by somatization disorder (Hansen et al., 2005). Neuropsychological testing demonstrates an equal bifrontal impairment of cerebral hemispheres and nondominant hemispheric dysfunction in patients with somatization disorder (Wexler et al., 1980). Preliminary evidence indicates that patients with somatization disorder may have an abnormality in cortical functioning (Rief et al., 1998).

Somatization disorder usually begins in middle to late adolescence, but may start as late as the third decade of life (Mullick, 2002). No research data are yet available as to how long a modal episode of illness continues. Clinical wisdom indicates that a typical episode continues for 6 to 9 months, with quiescent periods lasting from 9 months to a year. It is unlikely that patients with somatization disorder can go for more than a year without developing a new symptom and seeking some type of health care (Simon et al., 1999).

The Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition (DSM-IV) provides some specific sign and symptoms for diagnosing somatization disorder (American Psychiatric Association, 1994) which has been explained below.

A. A history of many physical complaints beginning before age 30 years that occur over a period of several years and result in treatment being sought or significant impairment in social, occupational, or other important areas of functioning.

B. Each of the following criteria must have been met, with individual symptoms occurring at any time during the course of the disturbance:

(1)   *Four pain symptoms:* a history of pain related to at least four different sites or functions (e.g., head, abdomen, back, joints, extremities, chest, rectum, during menstruation, during sexual intercourse, or during urination)

(2)   *Two gastrointestinal symptoms:* a history of at least two gastrointestinal symptoms other than pain (e.g., nausea, bloating, vomiting other than during pregnancy, diarrhea, or intolerance of several different foods)

(3)   *One sexual symptom:* a history of at least one sexual or reproductive symptom other than pain (e.g., sexual indifference, erectile or ejaculatory dysfunction, irregular menses, excessive menstrual bleeding, vomiting throughout pregnancy)

(4)   *One pseudoneurological symptom:* a history of at least one symptom or deficit suggesting a neurological condition not limited to pain (conversion symptoms such as impaired coordination or balance, paralysis or localized weakness, difficulty swallowing or lump in throat, aphonia, urinary retention, hallucinations, loss of touch or pain sensation, double vision, blindness, deafness, seizures; dissociative symptoms such as amnesia; or loss of consciousness other than fainting)

This rarely treated psychotic disorder inflicts primarily teenagers and young adults, leading them to severe psychological, social, and vocational disability during the potentially most creative and productive years of their life (Egger et al., 1999). Not much work has been done to find out the possible etiology of somatization disorder, which is considered to be very important for the treatment of this disease.

Immunology has been the subject of research in finding the relationship with psychiatric disorders and enormous works have been done in this respect. 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). In some neurological diseases IgA is locally synthesized in cerebrospinal fluid (Leary et al., 2000). A significantly higher incidence of antibodies with affinity for dopamine was found in the group of psychotic patients compared with the neurological control group (Bergquist et al., 1993). Several factors including autoimmune factors have been suggested in the etiopathology of schizophrenia (Taylor, 2000). It is further reported that positive emotions produce a significant increase in IgA level and negative emotions are associated with a decrease in the IgA level (Frasure et al., 2000). Inhibition of natural killer cell activity and a decrease number of lymphocytes, markers of depressed immune function, are also associated with negative emotions (Frasure et al., 2000). 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 (DeLisi et al., 1984). Repairing the central nervous system (CNS) 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). In view of these investigations, this study has attempted to investigate the serum immunoglobulins levels of somatization disorder patients, and to find out the relationship between immunoglobulins with their nutritional status and socioeconomic factors.

Materials and Methods

Subjects

Forty-six somatization disorder patients comprising 24 males and 22 females of mean age 29.39±7.8 years were randomly recruited from Dhaka Medical College Hospital, Bangladesh Medical College Hospital, BSMMU and National Mental Institute. The patients were diagnosed by a psychiatrist using DSM-IV. A specialist who was trained in the use of Diagnostic and Statistical Manual of Psychiatric Disorders

(Fourth Edition) conducted the diagnosis and interviewed the patients with somatization disorder. Forty-five healthy volunteers comprising 25 males and 20 females of mean age 28.46±8.8 years were recruited purposively as control. The study subjects were briefed about the purpose of the study and written consent was obtained from each of them. All subjects had to go through clinical examination to find out existence of other diseases such as viral infections, liver disease etc. that might alter immunoglobulin level. Patho-logical test such as complete blood count, thyroid function test, renal impairment test and liver function test were also performed for each subject. Subjects were also under gone a routine physical check up including their organ activity, weight, nutritional condition, blood pressure, chest X-ray and ECG. Patients with previous diseases that affect immu-nity were excluded from the study. Patients who were men-tally retarded and suffered from co-morbid psychiatric dis-orders, those with substance disorder were also excluded from the study. Socio-demographic data were collected in a questionnaire form. That contains several information, socio-economic data, history of illness and family history etc. Ethical approval was obtained from Bangladesh Medical Research Council (BMRC).

Blood analysis

Five ml venous blood specimen was collected from each of the patients and controls. The blood sample was allowed to clot at room temperature for 60 minutes, and then centrifu-ged at 3000 rpm for 15 minutes to collect the serum. The serum was aliquoted in eppendorf tubes and stored at –80°C until analysis of immunoglobulins.

Immunoglobulin profiling

The serum immunoglobulin (IgG, IgA and IgM) level in both patients and controls were determined by turbidimetry method using immunoglobulin kit (Chronolab, Switzerland). 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.

The serum was diluted with saline (1:4), and 10 μl of the diluted serum was pipetted into microtitre plate. Separate microtitre plate was used for each of the immunoglobulins (IgG, IgM and IgA). Five μl, 10 μl, 25 μl, 50 μl and 75 μl calibrator protein were also pipetted into marked wells of each of the microtitre plate for calibration. Then 230 μl of tris-buffer was added to each serum-containing well of the three plates. The tris-buffer was added to calibrator contain-ing wells to make total volume 240 μl. The plate content was mixed well with the help of a vortex mixer. Then diluted respective anti-human IgG, IgM and IgA (1:1 diluted with saline) were added to the wells of respective microtitre plates. Then the plates were incubated for 2 minutes (as specified in the kit procedure) to react the anti-human im-munoglobulin with the test serum and calibrator protein. After proper mixing, absorbances were taken at 550 nm for IgG and IgA and at 405 nm for IgM.

Table 1. Socioeconomic and nutritional status of somatization disorder patients and controls

Parameter	Patients n (%)	Mean±SD	Control n (%)	Mean±SD
Education				
Secondary(vi-x class)	14 (30.43)		12(26.67)	
Higher secondary	20 (43.48)		19 (42.22)	
Graduate and above	12 (26.09)		14 (31.11)	
Occupation				
Service	13 (28.26)		10 (22.22)	
Small business	12 (26.09)		10 (22.22)	
Student	12 (26.09)		14 (31.11)	
Housewife	9 (19.57)		11 (24.44)	
Monthly income in US $				
0-60	26 (56.52)		33 (73.33)	
61-120	16 (34.78)	69.78±48.55	9 (20.00)	54.33±45.09
121-180	4 (8.70)		3 (6.67)	
Age in years				
18-30	26 (56.52)		27 (60.00)	
31-35	6 (13.04)	29.39±7.8	6 (13.33)	28.46±8.8
36-45	14(30.43)		12 (26.67)	
Marital status				
Married	19 (41.30)		20 (44.44)	
Unmarried	27 (58.70)		25 (55.56)	
BMI (Kg/m^2)*				
15.5-18.4(CED)	12 (26.09)		0(0.0)	
18.5-25.0(Normal)	32 (69.57)	20.26±3.04	39(86.67)	23.56±2.03
>25.0 (Obese)	2 (4.35)		6(13.67)	

*p =0.001

Statistical Analysis

SPSS software package (Version 11.5, SPSS Inc. Chicago, USA) was used to analyze the data. Descriptive statistics were used for all variables. Comparison of immunoglobulins of somatization disorder patients and controls were performed by cross-table variables and independent sample t-test. Correlative analysis was performed to find correlation of BMI and socioeconomic factors on the serum immunoglobulin concentrations of the patients. Multiple Regression Analysis and one–way ANOVA were also performed to determine the extent of contribution of socioeconomic factor and BMI to affect the level of immuoglobulins.

Results

Table 1 shows the socio-economic information of the somatization disorder patients and control subjects. It was shown that the majority of study subjects were literate (patients 69%, control 73%) with various professions. Average age of patients and control groups were 29.39±7.8 years and 28.46±8.8 years respectively. The mean BMI of patients (20.26±3.04) was significantly ($p<0.001$) lower than the control subjects (23.56±2.03).

Serum immunoglobulins levels are presented in the table 2. IgG, IgM and IgA concentrations of somatization disorder patients were 24.14±4.44 (g/L), 2.05±1.12 (g/L) and 2.11±0.75 (g/L), while these were 26.34±4.94 (g/L), 2.36±1.25 (g/L) and 2.76±0.86 (g/L) in control subjects respectively. Concentration of IgA in somatization disorder patients decreased significantly ($p=0.02$) while the change of concentrations of IgG and IgM was not significant ($p=0.218$, 0.443).

Correlative analysis suggested that only the IgA value had a significant inverse correlation with the BMI ($r = −0.553$, $p = 0.006$). There was no correlation between other parameter

Table 2. Serum immunoglobulin concentrations of somatization disorder patients and controls

Immuno-globulins (g/L)	Patients n (%)	Mean +SD	Control n (%)	Mean +SD
IgG[a]				
15.5-19.5	12 (26.09)		3 (6.67)	
19.51-26.0	22 (47.83)	24.14±	18 (40)	26.34
26.01-38.5	12 (26.09)	4.44	24 (53.33)	±4.94
IgM[b]				
0.48-1.5	12 (26.09)		9 (20.00)	
1.51-2.5	16 (34.78)	2.05±	24 (53.33)	2.36
2.51-5.0	18 (39.13)	1.12	12 (26.67)	±1.25
IgA[c]				
0.5-2.5	34 (73.91)		21 (46.67)	
2.51-3.5	8 (17.39)	2.11±	12 (26.67)	2.76
3.51-4.0	4 (8.7)	0.75	12 (26.67)	±0.86

Significance $p<0.05$, [a]: $t = 1.23$, $p=0.218$, [b]: $t = 0.76$, $p=0.443$, [c]: $t = -2.36$ $p=0.02$

Table 3. Correlation of serum immunoglobulins with BMI, income and age of somatization disorder patients

Parameter	IgG	IgM	IgA
BMI (kg/m²)	r = - 0.031 p = 0.887	r = 0.125 p = 0.569	r = - 0.553 p = 0.006
Income (US$ in month)	r = - 0.031 p = 0.890	r = - 0.003 p = 0.99	r = - 0.031 p = 0.889
Age (year)	r = 0.039 p = 0.859	r = 0.270 p = 0.212	r = - 0.326 p = 0.130

(Table 3). A regression analysis was also performed using IgA level of patients' as dependent variable and BMI and income as independent variable. From multiple linear regression analysis it was found that IgA level had changed significantly with BMI ($R^2 = 0.438$; $t = −3.948$; $p = 0.001$) (Table 4). Finally ANOVA test was done with the same parameter that showed a significant relation between BMI and IgA level of the patients ($F = 9.245$; $p = 0.006$).

Table 4. Regression analysis using Immunoglobulin A (IgA) of somatization disorder patients as dependent variable and BMI as independent variable.

Parameter	t	p
BMI (kg/m²)	-3.948	0.001*

*$F = 9.245$; $p = 0.006$

Discussion

Somatization disorder is a rarely treated psychiatric disorder that inflicts mostly teenage and young adults. Although there is some evident of communication impairment of brain cells in left hemisphere because of decreased neurotransmitters release (Wexler et al, 1980), etiology of this disorder has yet to be known. A few investigators reported immunological involvement in some psychiatric disorders such as schizophrenia, mania, depression, anxiety etc (Tiwari et al, 1989; Bergquist et al, 1993; Taylor, 2000). We report here the changes in serum immunoglobulins levels in somatization disorder patients, and its correlation with nutritional status and socioeconomic factors.

Results showed somatization disorder was prevalent in poor, young and unmarried people, which is in good match with the findings of Mullick (2002) and Bates et al, (1995). It was further found that BMI value was reduced significantly in somatization disorder patients.

Analysis of serum immunoglobulins indicated that only the IgA level is significantly decreased in somatization disorder patients compared to that of the controls ($p = 0.02$). The level of IgG and IgM did not change significantly. The decreased concentration of IgA might be because of the impairment of some other immune parameter that might be influenced by the presence of major psychiatric disorder (Marazziti et al, 1992). Balaita et al, (1992) also found decreased serum immunoglobulins levels in maniac and depressed patients. However, this result is contradictory to the report of Tiwari et al, (1989) who noted a rise of serum concentrtions of IgA, IgM and IgG in schizophrenic patients.

Correlative analysis resulted in a significant inverse correlation of IgA level with the BMI. This may be predicted for our patients, who were not being suffering from any infections. In general, IgA level is increased to give a fight against infection, and normal BMI is an indicator of individual free from infections. This finding further justified from the regression analysis (R^2 = 43%; t = −3. 948; p = 0.001) and one-way ANOVA test.

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