# Immunoglobulin levels in panic disorder patients

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**Abstract**: The study was conducted to evaluate the serum immunoglobulin levels in patients suffering from panic disorder and to assess the relationship between the changes of immunoglobulin levels and the socioeconomic parameters, as well as nutritional status. 54 panic patients were randomly selected from the Department of Psychiatry, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College Hospital, Bangladesh. Fifty two, age and gender matched healthy volunteers (42 males and 10 females, mean age of 30 ± 6 yrs) were also enrolled in this study. Immunoglobulin levels were measured by turbidimetry method using immunoglobulin kits. It was found that the mean serum immunoglobulin concentrations of IgG, IgM and IgA of panic disorder patients were 0.999±0.26 (g/L), 0.1±0.028 (g/L) and 0.194±0.066 (g/L) respectively whereas the values were 1.24± 0.39 ( g/L ), 0.096±0.022 ( g/L) , 0.194±0.053 (g/L) in healthy volunteers. IgG level in panic disorder patient was found significantly ($p$ <0.05) lower than that of the controls but the change in concentration of IgM and IgA were not significant ($p$=0.497, $p$=0.962). Socioeconomic data reveals that most of the patients were from lower income group and educated. BMI (Mean±SD) of the patients (22.62 ± 3.74 kg/m$^2$) and controls (23.74 ± 2.71 kg/m$^2$) were well within the normal range. From correlative analysis it has been found that income has significant effect ($p$=0 .047) on the change of the serum IgG level in panic disorder patient and it was also been justified by the regression analysis ($p$=0.049). This finding may play a key role in the diagnosis and treatment of the panic disorder patients. Further studies have been suggested with a large number of populations to confirm these findings.

**Keywords**: Panic disorder, immunoglobulin, serum.

## INTRODUCTION

Panic disorder is a rare psychiatric illness described by unexpected and repeated episodes of intense fear accompanied by different physical symptoms like chest pain, heart palpitation, shortness of breath, dizziness or abdominal distress. It is a chronic condition typically associated with significant distress and disability (Pollack and Marzol, 2000). Though the symptoms of this disorder can be fully illustrated by medical disorders, it can be happened from overwhelming feelings of anxiety. The symptoms tend to occur suddenly, without any warning and often for no apparent reasons.

DSM IV (The Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition ) shows some definite sign and symptoms for panic disorder which consists of palpitations, accelerated heart rate, sweating, trembling, sensations of shortness of breath, feeling of choking, nausea or abdominal distress, chest pain, depersonalization, fear of losing control or going crazy, and fear of dying. Panic disorder is a distinct period of intense fear or discomfort, in which four (or more) of the above symptoms may arise abruptly and reached a peak within 10 minutes. Panic disorder with agoraphobia typically involves clusters of situations that include being outside the home alone; being in a crowd or standing in a line; and traveling in a bus, train or automobile. Panic Disorder with or without agoraphobia includes unanticipated panic attack and at least one of the attacks has been followed by one month or more of the persistent concern about having additional attacks, worry about implications of the attack and a significant change in behavior related to the attacks. There may be presence or absence of agoraphobia (DSM-IV, American Psychiatric Association 1994; 1999)

Panic disorder is common in patients with heart symptoms in the sitting of an emergency department (18%). Additionally, its prevalence in other populations was found higher such as 33 to 59% with negative coronary angiography, 29 to 38% with irritable bowel syndrome and 5 to 15% with migraine headache (Langewitz *et al*., 1995). Unexpected panic attacks and then worry about having more attacks are common experience for the patients with panic disorder. The prevalence of these conditions is about 3% for panic disorder and 13% for social anxiety disorder in the United States and is higher in women than in men (Westenberg and Liebowitz, 2000). CBT (Cognitive Behavior Therapy) is currently considered as a primary treatment option for panic disorder. The treatment focuses on the elimination

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of the patterns that underlie and perpetuate the disorder (Rayburn and Otto, 2000).

Several research works have been done in finding the relationship between the immunology and the psychiatric disorders. Immunological research studies in psychiatric disorders shows a possible relationship between psychiatric symptoms and acute infectious diseases. But evidence has been shown that the aetiopathological explanations for psychiatric disorders are no longer closely related to acute infection (Sperner-Unte wager, 2005). Immunoglobulin levels can be altered during depression and anxiety (Frasure *et al*., 2000). It has been reported that level of IgA, IgG, IgM in serum has been risen in schizophrenia (Tiwari *et al.*, 1989). Study conducted with schizophrenic patients found that the serum immunoglobulin concentrations (IgA, IgM and IgG) were unchanged when compared with cohort control (Karim *et al.*, 2005). Autoimmune factors are also have been reported in the aetiopathology of schizophrenia (Taylor, 2000). Another study has found that the positive emotions or negative emotions create a significant change in IgA level. Negative emotions are also associated with the depressed immune functions (Frasure *et al*., 2000). Low IgM concentrations were also observed in major depression and chronic schizophrenia when compared with healthy controls (Delsi *et al*., 1984). From the previous study with manic patients, significant increase of the serum concentration of IgA was observed while the concentrations of IgG and IgM remained unchanged (Baker *et al*., 2005). Interestingly, significant decrease in serum level of IgA was found in somatization disorder patient when compared with healthy control whereas the change of IgM and IgG was not significant (Hossain *et al*., 2006).

It has been reported from many investigators that there is a involvement of immunoglobulins in some psychiatric disorders such as schizophrenia, somatization disorder, mania, depression, anxiety etc (Bergquist *et al*., 1993; Hossain *et al*., 2007; Tiwari *et al*., 1998). But little work has been reported regarding the relationship between immunoglobulins and panic disorder patients. So the study has focused on immunoglobulins level in panic disorder patient and to assess its correlation with socioeconomic and nutritional status.

## MATERIALS AND METHODS

### *Subjects*

Forty four males and ten females having mean age of 29±7 yrs with panic disorder were randomly selected from Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College Hospital, Bangladesh by psychiatrist, expert in DSM IV from January to December in 2008. Fifty two healthy volunteers, (42 males and 10 females, mean age 30±6 yrs) matched by sex, education, and age were also recruited as control at the same time. Volunteers, both healthy and patients were informed about the objective of the research and written consent was obtained from all of them. Clinical examinations were performed to find out the existence of any patho-physiological conditions that might influence the level of immunoglobulin for all volunteers. Volunteers also had to go through a routine physical check up including their organ activity, weight, nutritional condition, blood pressure, chest X-ray and ECG. Patients, who were mentally retarded and suffered from co-morbid psychiatric disorders, diabetes, kidney failure, or any other diseases treated with drugs and mineral supplements, were excluded from the study. Sociodemographic data were also obtained in a questionnaire form that contains important information including socio-economic data, history of illness and family history. Ethical approval was obtained from the BSMMU authority (Nahar *et al.*, 2010)

### *Blood Analysis*

A 5 ml of venous blood was collected from all volunteers. The blood sample was then kept at room temperature for about 1 hr to clot and centrifuged at 3000 rpm for 15 minutes. After centrifugation the serum was taken into eppendorf tubes and kept at -80ºC until further analysis (Nahar *et al.*, 2010).

### *Immunoglobulin profiling*

The serum immunoglobulin level (IgG, IgM, IgA) were measured for all volunteers by the turbidimetric method (Dati *et al*., 1996, Tietz *et al*., 1983 and Pesce *et al*.,1987) using immunoglobulin kit (Chronolab, Switzerland). In this method the anti-human IgG, IgM, IgA antibodies were allowed to react with samples to form insoluble antigen-antibody complexes. These complexes then cause an absorbance change that depends on the IgG, IgM, IgA, concentration of the subjects. The change of absorbance was quantified by the calibrator of known IgG, IgM, IgA concentration and the serum level of immunoglobulins were measured for patients and healthy volunteers. All the serum samples of patients and controls have been centrifuged and the supernatant serum samples were then diluted to 1:4 with saline water i.e. 50 µl serum was added to 200 µl saline water making the volume 250 µl and vortexed for proper mixing. 10 µl of the diluted serum was pipetted into microtitre plate. Separate microtitre plate has been used for each of the immunoglobulin (IgG, IgA, IgM). 10 µl, 25 µl, 50 µl, 75 µl and 100 µl of the calibrator protein were also pipetted into marked wells of each of the microtitre plate for calibration. 230 µl of reagent $R_1$ (tris-buffer) was added to each serum present in wells of the microtitre plate to make the total volume of 240 µl. The tris-buffer was also added to calibrator protein containing well to make the volume 240 µl. The plate content was mixed well by a vortex mixer. Then 15 µl diluted respective antihuman IgA, IgG and IgM (1:1

diluted with Saline water) were added to the respective wells of the microtitre plate. Then the plates were incubated for 2-5 minute to react with antihuman immunoglobulin with the test serum and calibrator protein. After proper mixing absorbance were taken at 630 nm for IgG and IgA and at 405 nm for IgM respectively.

## STATISTICAL ANALYSIS

For statistical analysis, SPSS software package (Version 11.5, SPSS Inc. Chicago, USA) was used. For all variables, descriptive statistics were used and expressed as percentage, mean and standard deviation. For serum level of immunoglobulins, comparison between panic disorder patients and control subjects were performed by cross-table variables, independent sample t-test, correlative analysis and regression analysis.

## RESULTS

It was found that majority of the panic disorder patients were educated and it was more common in low income group (Nahar *et al.*, 2010). The average age of patient and control group was 29 ± 7 yrs and 30 ± 6 yrs respectively. The mean BMI of patients (22.62 ± 3.74 Kg/m$^2$) was not significantly different from that of the controls (23.74 ± 2.71 Kg/m$^2$) ($p > 0.05$). The mean serum immunoglobulin concentrations of IgG, IgM and IgA of panic disorder patients were found to be 0.999±0.26 (g/L), 0.1±0.028 (g/L), 0.194±0.066 (g/L) whereas the serum concentration of IgG, IgM and IgA of control subjects were 1.24± 0.039 (g/L), 0.097±0.022 (g/L), 0.194±0.053 (g/L) respectively. The results showed that the concentration of IgG decreased significantly (p=0.000) when compared with cohort controls but the concentration of IgM had a tendency to increase and IgA remain unchanged (p=0.497, p=0.962) (table 1). A significant effect of income had also been found in decreasing the serum IgG levels of panic disorder patients (table 2 and table 3).

## DISCUSSIONS

In the present study, the serum IgG, IgA and IgM levels were measured and it had been found that the serum IgG levels were significantly decreased in panic disorder

**Table 1**: Serum immunoglobulin concentration of panic disorder patients (n=54) and controls (n=52)

| Immunoglobulins (g/L) | Patients n (%) | Mean ± SD | Controls n ( % ) | Mean ± SD | Physiological concentration (g/L) [a] |
|---|---|---|---|---|---|
| IgG † | | | | | |
| 0 – 1.0 | 33 (61.11) | | 21 (40.38) | | |
| 1.1 – 1.5 | 19 (35.18) | 0.999 ± 0.26 | 14 (26.92) | 1.24 ± 0.39 | 1.00 |
| 1.6 – 4.5 | 2 (3.7) | | 17 (32.69) | | |
| IgA†† | | | | | |
| 0.05 - 0.15 | 13 (24.07) | | 10 (19.23) | | |
| 0.151 -0 .250 | 31 (57.40) | 0.194 ± 0.066 | 32 (61.53) | 0.194 ± 0.053 | 0.20 |
| 0.251 -0 .40 | 10 (18.51) | | 10 (19.23) | | |
| IgM††† | | | | | |
| 0.05 – 0.10 | 33 (61.11) | | 29 (55.76) | | |
| 0.101 -0 .150 | 18 (33.33) | 0.1 ± 0.028 | 21 (40.38) | 0.096 ± 0.022 | 0.12 |
| 0.151 -0 .30 | 3 (5.55) | | 2 (3.8) | | |

Significance p < 0.05; For † p = 0.000; For †† p = 0.962; For ††† p = 0.497, a= Ganong, 2003

**Table 2**: Pearson correlation of serum immunoglobulin IgG with BMI, income, age

| | IgG | BMI | Age | Income |
|---|---|---|---|---|
| IgG | r = 1.000 | r = 0.154<br>p =0 .317 | r = -0.155<br>p = 0.277 | r = 0.285*<br>p = 0.047 |
| BMI | r = 0.154<br>p =0 .317 | r = 1.000 | r = 0.013<br>p =0 .929 | r = -0.104<br>p = 0.497 |
| Age | r = -0.155<br>p =0 .277 | r = 0.013<br>p =0 .929 | r = 1.000 | r = 0.051<br>p = 0.719 |
| Income | r = 0.285*<br>p =0 .047 | r = -0.104<br>p =0 .497 | r = 0 .051<br>p = 0.719 | r = 1.000 |

*Correlation is significant at the p = < 0.05 level (2-tailed)

patients than that of the control subjects whereas the serum IgM levels had a tendency to increase and IgA remain unchanged. These findings are similar to the findings of the studies in various psychiatric disorders where immunoglobulin levels decreased significantly compared to the control subjects (Balaita *et al.*, 1992; Hossain *et al.*, 2007; Marazziti *et al*., 1992; Mubarak *et al.*, 1999) and the tendency to increase the level of serum IgM suggested a possible immune dysfunction (Ramesh *et al.*, 1991). A possible effect of income on serum IgG level had also been found but BMI and age did not have any effect on serum IgG level in panic disorder patients (table 3). Additionally, the prevalence of panic disorder patients in educated and employed population (business and service holder) with lower income was found that was similar to the previous findings with other psychiatric disorders (Nahar *et al.*, 2010; Kaplan and Sadock, 1995). The decreased levels of serum IgG in panic disorder patients may be because of deficiency of immunity against any type of infection but the normal BMI indicates that the individuals are free from infections. So the change in serum IgG levels may suggest the disease condition than infection. Lower socioeconomic status may be the reason for reducing the access to the resources and prestige in the community that ultimately act as a threat against their self-esteem in panic disorder patients. Consequently, increased negative emotion and cognition may cause the immune dysfunction in panic disorder. Though 54 panic disorder patients were interviewed but they were recruited from only two tertiary hospitals, could be considered as a limitation of the study. Whether or not the change in immunoglobulin levels in panic disorder patient is a cause or an effect for the pathogenesis of the disease, it requires a large scale research activity.

**Table 3**: Regression analyses using IgG as dependent variable and BMI, Income, Age, Smoking habit as independent variable

| Parameter | t | P |
|---|---|---|
| BMI | 1.465 | 0.151 |
| Income | 2.036 | 0.049 |
| Age | -1.170 | 0.249 |
| SMK | -0.883 | 0.383 |

Dependent variable: IgG

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