

ORIGINAL ARTICLE

Immunoglobulins Level in Patients Suffering from Major Depressive Disorder (MDD) in Comparison with Normal Healthy Individuals: A Prospective Study

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ABSTRACT

Key words:

Major Depressive Disorder;
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Background: Previous studies demonstrated significant elevations of immunoglobulin levels in various psychiatric disorders, however, no enough data is present regarding this association with major depressive disorder (MDD). **Objectives:** To compare the serum levels of immunoglobulins in individuals with MDD to healthy control persons. **Methodology:** We included 70 participants divided into two groups including 35 MDD patients with MDD from the Psychiatry Outpatient Clinic at Misr University of Science and Technology Hospital and 35 healthy controls. The sera were investigated for the level of total IgA, IgD, IgM, and IgG using enzyme-linked immunosorbent assay (ELISA) ImuPro 50 test. **Results:** Mean age of the 35 MDD patients was 32 years old while the normal individuals were aged 31 ($P=0.621$). The study revealed substantially lower levels of IgG, IgM, and IgA in depressed patients compared to controls. On the other hand, there was a significantly higher concentration of IgE and IgD in MDD patients than in controls. **Conclusion:** Immunoglobulin levels in the blood were found to be significantly linked to MDD. However, Future research should be the logical forward step in order to improve the quality of data about the importance of immunoglobulin levels in MDD patients.

INTRODUCTION

Major depressive disorder (MDD) is a mental illness characterized by poor cognitive performance, decreased interest, and a gloomy mood.^{1,2} The etiology of MDD is multifactorial, and its heritability is estimated to be around 35%.³ Moreover, it was reported that women have a two-fold more risk of MDD than men and affect one out of every six adults during life.⁴ MDD is defined by the inability to enjoy family and personal life, sleep disorders, hunger, sexual desire disruption, and suicidal thoughts or intentions.^{5,6} MDD is deemed to be linked to impairments in non-specific, adaptive, and innate immune responses as well as inflammatory processes.⁷

The immune system and the central nervous system have a significant association between each other. Immune response dysregulation is frequently linked to psychiatric disorders. Further, the concentration of proinflammatory cytokines and their effects on the Central nervous system (CNS) leads to neuropsychological symptoms of MDD.^{8,9} At a clinical level, The high prevalence of depressive disorders in patients with chronic inflammatory illnesses can indirectly corroborate this relationship.¹⁰ Only a few studies have discovered a relationship between stress-induced changes in serum immunoglobulin M (IgM),

immunoglobulin G (IgG), and immunoglobulin A (IgA) levels (IgA).^{11,12} Although prior research have shown that IgM, IgA, and IgG levels are significantly elevated in patients with schizophrenia, unipolar depression, and bipolar depression, there is little evidence to link this to MDD.¹³ As a result, the goal of this study was to compare the serum levels of immunoglobulins in MDD patients and healthy control people.

METHODOLOGY

Study population

The study included 70 participants: 35 with MDD and 35 healthy volunteers. Patients with MDD were recruited from the Misr University of Science and Technology Hospital's Psychiatry Outpatient Clinic. Patients with autoimmune, oncological, or inflammatory conditions were not allowed to participate. Patients who were diabetic or who had previously been diagnosed with a mental disease other than depression were also excluded.

Patients with comorbidities related to brain dysfunction, smokers, and substance abusers were excluded. Furthermore, patients with weight extremities (BMI < 18.5 kg/m² and >30 kg/m²) were excluded. Patients who were using glucocorticosteroids, anti-

inflammatory medications, antibiotics, mood stabilizers, or antipsychotics were also excluded from the study. All subjects were required to sign written consent after a detailed illustration of the study protocol. The study has been approved by the local ethical committee of Misr University of Science and Technology.

Sera from all participants were tested for total IgM, IgG, IgE, IgD, and IgA levels using the manufacturer's recommended enzyme-linked immunosorbent assay (ELISA) ImuPro 50 test (R-Biopharm, Darmstadt, Germany).

Data analysis

The social sciences statistical program was used to analyze the data (SPSS version 22.0). Categorical data were presented in numbers and percentages. Continuous data were expressed in mean and standard deviation. An independent sample t-test was used to compare the levels of immunoglobulins (IgG, IgM, IgG, IgD, and IgA) in people with major depressive disorder with healthy people. The null hypothesis was rejected once a p-value of less than 0.05 was declared significant.

RESULTS

The current study included 70 subjects. Thirty-five patients suffered from major depressive disorders, and 35 were normal and healthy individuals. Regarding the cases, the average age of the patients who suffered from depression was 32±6 years old. While the normal individuals were aged 31±6 on average (P-value = 0.621). Males represent 57.1% of the depressive patients, while they represent 51.1% subjects in the normal group, with a difference between both groups regarding gender distribution (P- value = 0.631).

Immunoglobulin levels

There were substantially lower levels of IgA, IgM, and IgG in depressed patients compared to controls (table 1). On the other hand, there was a significantly higher concentration of IgD and IgE in depressed patients compared to controls (Figure 1).

Table 1: Immunoglobulin levels in both cases and controls

Parameters	Cases (n= 35) mean (±SD)	Controls (n= 35) mean (±SD)	P value
IgG, mg/dl	703.1(±249.1)	997(±251.4)	< 0.001
IgM, mg/dl	83.5 (±72.6)	122.1(±54.1)	0.001
IgA, mg/dl	109.1(±84.1)	189.1(±86.7)	< 0.001
IgE, mg/dl	106.7 (±44.9)	60.9 (±40.9)	< 0.001
IgD, mg/dl	7.7 (±4.2)	4.6 (±3.3)	0.003

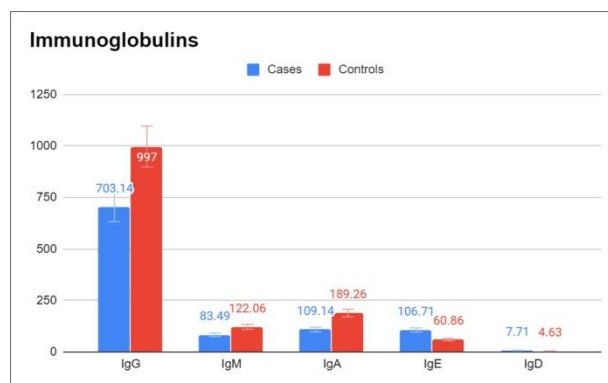


Fig. 1: Immunoglobulin levels in both cases and controls

DISCUSSION

In our work, we noticed that depressive patients had considerably lower levels of IgG, IgM, and IgA than healthy controls. Depressed patients, on the other hand, had considerably greater IgE and IgD concentrations than controls. In contrast, Nasreen et al. conducted a cross-sectional study on 88 MDD patients to assess serum immunoglobulin concentrations and compare them to 89 healthy controls. Their findings revealed that the patients' group had higher blood IgM, IgG, and IgA levels than the control group; however, this difference was not statistically significant.¹³ Similarly, in Al-Hakeim's study, he found a substantial rise in blood levels of C3, C4, cortisol, and IgG in the depressed patients' group compared to the control group, but no significant variations in IgA levels and IgM.¹⁴ The rise in C3 and C4 could be due to a variety of factors, however it has been discovered that intravenous immunoglobulins, primarily polyclonal IgG, block complement activation by preventing C3 and C4 absorption onto target cells and tissues.¹⁵ As a result, the observed rise in complements in the Al-Hakeim study might be due to an increase in serum IgG in depressed patients. These findings suggest that immunoglobulins could be employed as a treatment for depression and other disorders involving the activation of the classical complement system.

Park et al. discovered a significant change in the N-linked glycosylation profile in MDD patients, which could explain why immunoglobulins are biologically altered in this group of individuals.¹⁶ N-glycosylation has a critical impact on immune system modulation. IgG is highly impacted by the structure of its N-glycans.¹⁷ The anti-inflammatory cascade is triggered when sialic acid moieties and galactose are added to IgG N-glycans.¹⁷ In addition, a meta-analysis found that people with MDD had less T lymphocytes and natural killer cells than healthy people.¹⁸ Tumor necrosis factor and interleukin-1 and 6 have been associated with depression and have been discovered to alter the

neurotransmitter release and hypothalamic-pituitary-adrenal (HPA) axis.^{19,20}

Another perspective links increased Gram-negative gut commensal bacteria translocation to altered serum immunoglobulin levels in MDD patients.²¹ In comparison with controls, IgA- and IgM-mediated immune responses to gut commensal bacteria endotoxins (LPS) are considerably higher in individuals with MDD.^{22,23} These data suggest that Gram-negative bacteria, such as *Klebsiella pneumoniae*, *Citrobacter koseri*, *Pseudomonas putida*, *Morganella morganii*, *Pseudomonas aeruginosa*, and *Hafnia alvei*, have enhanced LPS translocation, and that the pathogenesis of MDD is associated to increased gut dysbiosis.²⁴

Many research have looked into how immunoglobulin production is affected in people with psychiatric diseases such schizophrenia, unipolar depression, and bipolar depression.^{25,26} Legros and colleagues discovered that all patients with bipolar and unipolar depression had considerably higher levels of IgM concentration than controls and that IgM levels were higher in female patients than males. IgG and IgA levels, on the other hand, showed no significant changes.²⁵ Another study found that depressed people had lower percentages of circulating lymphocytes, higher concentrations of circulating neutrophils, and significantly weaker in vitro lymphocyte responses to mutagenic stimulation than healthy people.²⁷ IgG levels were found to be considerably lower in panic disorder patients than in controls, despite no significant differences in IgA and IgM concentrations. This observation could be used as a criterion for diagnosing and treating panic disorder patients.²⁸

The serum concentrations of IgM and IgA were much higher in patients with obsessive conversion disorder (OCD) than in healthy controls, while the change in IgG was not significant.²⁹ Patients with generalised anxiety disorder (GAD) had significantly higher serum IgM levels than controls, despite the fact that IgA and IgG levels were insignificant.³⁰ All these changes in immunoglobulin levels could be considered risk factors for the diagnosis and treatment of mental illnesses. The single immunoglobulin evaluation, the lack of food intake data, and the limited sample size are all limitations of this study.

CONCLUSION

In conclusion, our findings point to a link between immunoglobulin concentration and MDD. In the case of MDD, future research should look at the predictive and prognostic value of high immunoglobulin levels.

This manuscript has not been previously published and is not under consideration in the same or substantially similar form in any other reviewed media. I have contributed sufficiently to the project to be

included as author. To the best of my knowledge, no conflict of interest, financial or others exist. All authors have participated in the concept and design, analysis, and interpretation of data, drafting and revising of the manuscript, and that they have approved the manuscript as submitted.

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