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SERUM CORTISOL, IMMUNOGLOBULINS AND SOME COMPLEMENTS AMONG DEPRESSED PATIENTS

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ABSTRACT

Psychiatric disorders especially depression are associated with a variety of changes in immunity parameters. In this work, an attempt was carried out to make estimation about the correlation between immunity and depression through the measuring of IgG, IgA, and IgM and complements (C3 and C4) levels in the serum of patients and comparing them with the corresponding levels of healthy control group. The results showed a significant increase in serum level of C3, C4, cortisol, IgG and no significant differences were noticed in the level of IgA and IgM in the depressed patients group as compared with control group. A slight positive correlation was observed between cortisol versus IgG in depressed patients that is not found in normal subjects. Thus in depression, human body defenses psychologically and sometimes this defense transformed into immunological resistance that is expressed as different measurable changes in immunological parameters.

KEY WORDS

Depression, Immunoglobulin, Complements, Cortisol.

INTRODUCTION

The term depression used variously to describe an emotional state, a syndrome and a group of specific disorders. Feeling of depression is synonymous with sad, blue, and miserable (1). It can be formulated as a malady of stress adaptation in the brain (2). There is a wide range of evidences about the correlation between depression or its symptoms and different physical illnesses. Depression is associated with different diseases. It is most common among the endocrine abnormalities such as diabetes mellitus (10), Cushing's disease (3), cardiovascular diseases (4, 5) and CNS disorders such as cerebrovascular diseases and Parkinson's disease (6). Psychiatric disorder especially depression and other central nervous system disorders are associated with a variety of changes in immunity parameters (7,8).

Evidence for immune activation in depressed patients initially collected by Maes (9) based on the measurement of acute phase proteins and cytokines in the plasma of patients with major depressive disorders and treatment resistant depression (9). The association between depression and altered immunological activities has repeatedly been suggested, but experimental data show contradictory results (10, 11, 12). At the clinical level, the higher than normal prevalence of depressive disorders in individuals who are afflicted with chronic inflammatory diseases indirectly supports such an association (13).

The circulating immune complexes comprising complement and immunoglobulins are reported to change with the prognosis of different diseases but their diagnostic role is not clear (14, 15). The immune-inflammatory system response in depression is accompanied by secretion of cytokines like interlukin-1, interlukin-2, interlukin-6, interlukin-8, and interferon etc. (16, 17). These cytokines stimulate the production and secretion of acute phase proteins in the liver (18). In this work, an attempt is made to relate the circulatory level of IgG, IgA, and IgM and complements (C3 and C4) among the subjects undergoing depression and comparing them with that of normal individuals.

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MATERIALS AND METHODS

This study included thirty-seven depressed patients aged (38.7±16.4 years) in addition to sex and age matched thirty-six healthy control subjects. The patients were diagnosed by the psychiatrists using a semi-structured psychiatric interview schedule for the diagnosis of depressive disorder based on the ICD-10. Patients were evaluated for medical history to exclude any existing systemic disease that may affect the parameters to be measured, particularly diabetes, liver disease, renal disease and chronic drug intake, otherwise, the patient was excluded from the study. Consent was obtained from the patient or his close relatives. The sex and age of the two groups are comparable to those of patients. None of these subjects was obese, alcoholic, or having a history of heart diseases other metabolic disorders and none of the females was on contraceptive pills. Venous blood samples were collected from patients between (9-12AM) before taking any medications. Sera were separated and stored at (-20°C) until analysis.

Immunoglobulins and Complements assay : After placing 5 µl of serum on each cavity on plates IgA, IgG, and IgM as well as C3 and C4 levels of both groups were quantitatively studied with immunodiffusion plates (Biomaghreb ®). Serum samples were incubated on plates for 72 hours at room temperature. At the end of this period, the diameter of precipitation was measured and converted to mg/dl units using table supplied by the manufacturer. Normal values of the plates used are as follows; IgG (710-1520mg/dl); IgA (90-310mg/dl), IgM (40-250mg/dl), C3 (84-193mg/dl), C4 (20-40mg/dl). The student's 't'-test assessed comparisons between groups.

Cortisol: Serum cortisol was measured using radioimmunoassay kit (CORT-CT2®) for the quantitative determination of cortisol in human supplied by ORIS group-France.

RESULTS

Level of serum components (cortisol, IgA, IgG, IgM, C3, and C4) in depressed patients group and control group are presented in Table 1 expressed as Mean±SD. The comparison between depressed patients and healthy control groups in the level of these parameters showed significant increase in serum level of C3, C4, cortisol, IgG while no significant differences were noticed in the level of IgA and IgM in the two compared groups as concluded from p-values. Correlation coefficient values of the relationship between each immune parameters and serum cortisol in patients and controls showed no correlation. However, in depressed patients a slight positive correlation (r=0.59) was found between cortisol and IgG.

DISCUSSION

The data of the present work indicated a change in immune system response/status in depressed patients (Table 1) and these results are in accordance with the hypothesis that moderate-severe depression disease is associated with an inflammatory response. Extensive evidences exist associating depression with changes in the immune system (7, 9, 19, 20).

Although one study showed that immunoglobulin titers (IgG, IgM, and IgA) were similar in depressed and healthy individuals (21) and another research demonstrate that depressed mood was not associated with secretary IgA in saliva (22). The depressed men had significantly elevated levels of the acute phase proteins, haptoglobin and alpha-1-antichymotrypsin, and of immunoglobulin G(23). In one research, no significant difference between the mean levels of C3 could be detected between depressed patients and controls, the levels of C4 (23, 24). C-reactive protein was significantly raised in the group with a depressive disorder. Our study suggests an interaction between psychological state and immune system operative in host defenses as noticed previously (24).

Table 1 : Serum cortisol, IgA, IgG, IgM, C3, and C4 in depressed patients and control group expressed (Values are Mean±SD)

Parameter	Control (n=36)	Patient (n=37)	p-value
C3 (mg/dL)	133.8±29.7	171.3±81.2	0.00007*
C4 (mg/dL)	26.8±7.9	5.6±21.7	0.004*
Cortisol (nmol/L)	341.3±81.5	409.7±73.4	0.00046*
IgA (mg/dL)	218.9±127.6	235.3±188.7	0.425
IgG (mg/dL)	1128.4±413.7	1652.4±849.5	0.024*
IgM (mg/dL)	176.4±92.3	158.5±83.4	0.196

Statistical comparison was done between control & patients; * P<0.05

The increase in the C3 and C4 can be explained by a variety of explanations. One interesting mechanism depends on the results of Miletic et al (25). He noticed that intravenous immunoglobulins, composed principally of polyclonal IgG, prevent complement attack by inhibiting C3 and C4 uptake onto target cells and tissues. Therefore, the increase in serum IgG in depressed patients may be the source of the noticed increase in the complements in our patients group. These consequences suggest that immunoglobulins can also be considered for active therapy in diseases accompanied by the activation of classical complement pathway and depression may be one of these disorders (25).

An acute phase protein response has been reported in major depression. Depressed subjects had significantly higher plasma haptoglobin, fibrinogen, C3, C4 and α1-acid-glycoprotein than normal controls. No significant differences in the above acute phase protein could be found between normal volunteers and depressed patients who underwent chronic treatment with psychotropic drugs. Plasma haptoglobin, fibrinogen, C3, C4, and α1-acid-glycoprotein, were significantly higher in untreated depressed patients than the treated patients (18, 26). The immunological changes accompanying depression may facilitate heart disease, infection, parasitic infestation or other ill health, so that depression is a mechanism for those least resilient or faced with most adversity to succumb to illness (19).

An alternative explanation of the changes in the concentration of the immunological factors obtained from the fact that the cytokines affect acute phase proteins and other immunological parameters (12, 27). Capuron et al (28) findings provide important information concerning the relationship between cytokines and depression.

The changes in immunity related parmeters in depression is not fully understood. However, this may attributed to somatic symptoms of depression particularly the decrease in physical activity and weight loss in depressed patients. The main mediator of the acute-phase response is IL-6, which, in turn, is regulated by IL-1 (29). The elevation of IL-6 helps induce synthesis of acute-phase proteins (inflammatory). Depending on these findings, the inert lifestyle of most depressed patients and decrease in their muscular movements lead to decrease cytokines production. Hence, the increase in acute phase proteins, as observed in present study may not due to the normal pathway for inflammation. Furthermore IL-6 enhances lipid turnover stimulating lipolysis as well as fat oxidation (30) which may be responsible for weight loss in depressed patients.

The increase in serum cortisol noticed in this work are in accordance with different other studies (31, 32). Cortisol hypersecretion in depressed patients has been documented by elevated plasma corticosteroid concentrations (31) and increased levels of cortisol metabolites (33). Elevated cortisol is recognized as a transient response to stress that is usually found among patients with major depressive disorder. An alternative interesting explanation is that impaired brain serotonin function in depression may be a consequence of cortisol hypersecretion (34).

In a pilot study (35), my colleagues and I noticed an increase in serum total sialic acid in depressed patients and this increase can be explained using the finding of many researchers who showed an immune response (16, 17) and increase in acute phase reactants (18) in depression because more than half of sialic acids in serum are derived from acute phase proteins (36).

Although, the result of the present work showed a slight relationship between cortisol and immunological parameters, many studies showed different correlations between these parameters and the tributaries of stress related endocrine systems. Cortisol has been shown to mobilize neutrophils from the bone marrow to the circulation in some studies (37).

From the results of this work and all the results from other researches surveyed in this article and discussions, it can be concluded consistently that there are various immunological changes in depression. There is also an interesting conclusion of Konsman et al (38) that the peripheral immune message is relayed to the brain via a fast neural pathway and a slower humoral pathway, resulting in the expression of pro-inflammatory cytokines in macrophage-like cells and microglia in the brain. Furthermore, the great work of Dantzer (39, 40) related to the interleukins and sickness behavior changes have great motive for connecting immunity with depression via a different hypothesized pathway. Hence, immune system can be well thought-out to be erring and fabricate an inflammatory like response in depression. These responses appeared and expressed as different immunological changes as recorded in different papers (7, 8, 12, 16-18, 27, 28). It's hypothesize that, in depression, human body defenses psychologically against what this paper suggests a (psychological pain) and sometimes this defense is transformed into real physical noticeable immunological resistance that is expressed as different measurable changes in immunological parameters. The present suggested possible phenomenon can explain the controversy and inconsistent findings in the researches studied the immunological parameters in depression. Furthermore,

any future work with immunity in depression will find various results depending on the special characteristics of personality and the sensitivity of the body immune system of the patients. These ideas need to be elucidated and confirmed and this is the project of the future works.

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