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# A Study Of Il-6 Levels In Schizophrenia Patients

Dr. Varsha Chowdhry
*-Associate professor, Department of Biochemistry, JLN Medical College, Ajmer.*
Dr. Harshvardhan
*-Senior demonstrator, Department of Biochemistry, JLN Medical College,Ajmer.*
Dr. Deepa
*- Senior demonstrator,Department of Biochemistry, JLN Medical College,Ajmer.*
Dr. Debina Sarkar
*-Assistant professor, Department of Biochemistry, Tripura Medical College*

***Abstract***
*The Functional Dichotomy Of Il-6 May Play A Critical Role In Maintaining The Balance Between Pro- And Anti-Inflammatory Responses. It Seems That Il-6 Can Have A Phase Specific Role In Schizophrenia Evolution, In The Context Of Acute Inflammation, Chronic Inflammation, And/ Or Autoimmunity. There Is Some Evidence That The Pathophysiology Of Schizophrenia Is Related To Activation Of The Inflammatory Response System (Irs), As Indicated By Increased Serum Concentrations Of Interleukin-6 (Il-6). Using Chemiluminescent Immunoassay , We Measured Serum Interleukin-6 (Il-6) Concentration In 50 Schizophrenic Patients And In 50 Normal Control Subjects. Mean Serum Il-6 Concentration Was Significantly Higher In The Schizophrenic Patients As Compared With The Control Subjects (P = 0.009). Thus, Elevated Serum Il-6 Levels In Schizophrenia Develop During The Course Of Illness And May Be Related To Treatment Or To Disease Progression.*

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## I. INTRODUCTION

The immune system could be described as a sensory system whose primary purpose is identifying the foreign (“non-self ”) substances, referred to as antigens. The mechanisms of innate immunity are physical and chemical barriers, cellular components, and soluble molecules. Cytokines are chemical messengers or hormones of the immune system. They mediate cell–cell interactions in immune responses and induce the movement of cells toward sites of inflammation, infection, and trauma. Thus, these soluble molecules regulate and coordinate many activities of the cells of innate and acquired immunity. Interleukin-6 has been widely studied in different aspects of schizophrenia: its onset and progression, association with different clusters of symptoms, response and resistance to the Interleukin-6 has been widely studied in different aspects of schizophrenia: its onset and progression, association with different clusters of symptoms, response and resistance to the treatment, and metabolical and other comorbid states. IL-6- 174G/C polymorphism showed to be associated with increased IL-6 plasma levels and represent a risk factor for schizophrenia . IL-6 gene expression in first-episode psychosis is in significant negative correlation with BDNF gene expression and associated with a smaller left hippocampal volume. The meta-analysis of Baumeister et al provide strong evidence that traumatic events have significant impact on the inflammatory immune system. Further, IL-6 is included in potential molecular pathway that leads to development of mental disorders and somatic states later in life. Plasma concentrations of interleukin-6 (IL-6) and the soluble IL-6 receptor (sIL-6R) are higher in schizophrenic patients than in normal volunteers (Maes et al., 1994a, Maes et al., 1995, Maes et al., 1996; Naudin et al., 1996). IL-6 is a pleiotropic cytokine that plays an important role in the immune and acute phase response, hematopoiesis, and the function of the (central) nervous system [for a review, see Maes et al. (1993)]. IL-6 exerts its biological effects by binding to a cell surface receptor complex consisting of two subunits, i.e. the IL-6R and gp130, a signal-transducing molecule (Yamasaki et al., 1988). Gp130 is a common signal transducer for IL-6, leukemia inhibitory factor, oncostatin M, IL-11 and ciliary neurotrophic factor (Gearing et al., 1992; Ip et al., 1992; Yin et al., 1993). The sIL-6R in serum has the potential to mediate IL-6 signals (even in IL-6-insensitive cells) by forming a complex with IL-6, which, in turn, associates with gp130 on the responding cells (Saito et al., 1993; Benigni et al., 1996). Serum sgp130 may compete with its membrane-bound counterpart for binding to the sIL-6/IL-6R complex, which may result in an inhibition of IL-6 signalling in some responding cells (Murakami-Mori et al., 1996).

The aims of the present study were to evaluate the values of serum IL-6 in schizophrenic patients and compare it to normal controls.

## II. MATERIALS & METHODS

The present work was carried out in JLN Medical Hospital, Ajmer on patients attending outpatient department and admitted in the psychiatry & neurology Department of the same college and Hospital, in the period of March 2022 to March 2023. The study type was case-control. The study included 50 subjects who were diagnosed as having schizophrenia based on the International Classification of Diseases-10 (ICD-10). Rest 50 subjects were non psychiatric patients who were considered as controls.

Inclusion criteria was as follows 1) age 18–65 years; 2) being admitted or hospitalized with a primary diagnosis of schizophrenia (ICD-10 codes between F20.0–F20.9).

Exclusion criteria for schizophrenia patients were as follows: presence of a comorbid psychiatric disorder, presence of a systemic disease that may influence inflammatory status such as diabetes mellitus, hepatic or renal failure, hypertension, acute infection, acute or chronic immuno- inflammatory disease or pregnancy, obesity or being underweight (body-mass index >29.9 $kg/m^2$ or <18.5 $kg/m^2$, respectively), heavy smoking (20>cigarettes per day), being under an anti-inflammatory or immunosuppressive medication or psychotropic medication other than antipsychotics, documented laboratory findings of liver or renal pathology, nutritional deficiency of vitamin B12 or folate and iron-deficiency anemia, and not having a laboratory screening at the admission. Method of analysis was by taking 2 ml of venous blood sample was drawn from cases and controls and serum was separated. IL-6 measurements were performed using Chemiluminescence immunoassay methods with Maglumi 800. All statistical analyses were performed using the SPSS. A chi-square test and an independent sample t-test were used for comparisons of categorical and parametric variables between the patient and the control groups. For the comparison of inflammatory markers amongst the schizophrenia and control group, one-way analysis of variance (ANOVA) was used. A p-value of less than 0.05 was considered statistically significant.

## III. RESULTS

43% of patients with schizophrenia had elevated and IL-6 values

The mean value of IL-6 values were 6.63 ± 5.6 vs 3.37 ± 4.0 pg. Serum IL-6 was also statistically significantly higher among patients with schizophrenia ($p = 0.009$)

There were no associations between IL-6 and age of onset, duration of current episode, , and smoking status.

## IV. DISCUSSION

There are genetic, environmental, and functional immunologic factors involved inthe induction of autoimmunity (Sinha et al., 1990). Cytokines play an important rolein the initiation, maintenance, modulation, and localization of normal and abnormalimmune responses. In this study, with sample of schizophrenic patients to have serum IL-6 measured, we found that schizophrenic patients had higher serum IL-6 than control subjects. Within schizophrenic patients, however, this increase could be fullyexplained by duration of illness. Other factors related to disease progression might also have to be considered toaccount for the increase in serum IL-6 in schizophrenia. IL-6 is found in many tissues besides those of the immune system. In the brain pituitary cells, neurons and astrocytes are all affected by IL-6 (Frei et al., 1989). IL-6 has been shown to be produced by microglia and astrocytes following central nervous system (CNS) viral infections (Frei et al, 1989), and IL-6 messenger ribonucleic acid (mRNA) transcripts are induced in glial cells following IL-1 stimulation. Since abnormalities of neural development have been postulated to underlie the pathogenesis of schizophrenia (Hyde and Weinberger, 1990) it is also ofinterest that IL-6 has been shown to support the growth of a number of neuronal celllines in synergy with nerve growth factor (Hama et al., 1991). In the latterexperiment, IL-6 was shown to improve survival and increase the dopamine contentof tyrosine hydroxylase-positive mesencephalic neurons. Thus, IL-6 is capable ofplaying a role in both the development and functioning of neurons and other cells ofthe CNS. Whether IL-6 changes in schizophrenia can be linked to the role of thislymphokine in CNS function and growth remains to be investigated. IL-6 orchestrates the innate and acquired immunity, but all these effects are context dependent and tissue-specific role of IL-6 in central nervous system and other metabolite tissues must be considered.IL-6 and leptin activity in hypothalamus could explain co-occurrence of schizophrenia and metabolic syndrome. Current research data about the role of microbiome in schizophrenia is still modest, but antipsychotic-induced alterations of the gut microbiota and metabolic changes should also be thoroughly explored. Beneficial effects of immunomodulatory therapy in schizophrenia have been already shown and the use of tissue-specific inhibitors of IL-6 or other IL-6-targeted therapy could possibly be useful in the treatment of schizophrenia and comorbid somatic states.

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