A K Kala Award

C-Reactive Protein (CRP) in patients with schizophrenia: Are they related with symptomatology ?

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Abstract : *The aim of this study was to assess, compare and corre the plasma levels of C-reactive protein with severity of psychop ogy in schizophrenia. Cross-sectional study carried out on inpatients at psychiatric centre, dept. of psychiatry, SMS Medical College, Jaipur, India. We measured the levels of CRP in N=30 individuals with schizophrenia and in N=15 healthy control subjects as APP. The positive and negative syndrome scale [PANSS] was used in order to rate psychopathology. The data collected on above tools, were analyzed by using Pearson's correlation coefficient. The schizophrenic patients (5.93± 8.101) had significantly high CRP levels as compared to healthy control subjects (2.53± .816). However , CRP value did not show any correlation with ANSS positive symptom subscale, negative symptom scale, general psychopathology and total score. Elevated plasma levels of C-reactive protein in schizophrenia are not associated with the severity of symptoms. The long term consequences of elevated levels of CRP require further investigation.*

Keywords: *Acute phase protein, C-reactive protein, PANSS, Inflammation.*

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INTRODUCTION

Schizophrenia is a serious neuropsychiatric disorder of uncertain etiology, with a lifetime prevalence of approximately 1% in the United States. While a number of genetic risk factors for schizophrenia have been found, most have relatively low odds ratio.[1] In addition to genetic factor, viral infections, neuro-endocrine and biochemical disorders and immune system disorders are also found.[2] Study conducted by Yolken and Torrey [3] supports the fact that infectious and inflammatory processes are potential contributing factor to disease etiology and pathogenesis. Among many inflammatory markers, there is particular interest in C-reactive protein (CRP). CRP is an acute phase reactant protein that originates in the liver and has many pathophysiological roles in the inflammatory process.[4] The measurement of C-reactive protein in the blood provides a reliable marker of chronic inflammation caused by infections and other inflammatory agents. Increased levels of C-reactive protein have been associated with chronic infections and inflammatory conditions, as well as with increased risk of inflammatory cardiovascular disorders.[5] In addition, elevated levels of CRP have been associated with depression [6,7] and cognitive impairment. [8,9]

Increased levels of inflammation have been found in many individuals with schizophrenia leading to the concept that immune mechanisms are important in pathogenesis of schizophrenia. However, there has been little investigation of the association between CRP levels and clinical characteristics in schizophrenia. Recently Fan et al [10] reported that

patient with elevated CRP levels also had significantly more severe psychiatric symptoms as measured by negative, positive, total and general psychopathology scales of the Positive and Negative Syndrome Scale.

The purpose of our study was to assess, compare and correlate the plasma levels of C-reactive protein to the severity of psychopathology in patients with schizophrenia. There is hardly any study available in India. This would help to understand the etiogenesis of symptoms of schizophrenia and to plan better intervention as well as management.

MATERIAL & METHODS

This study was conducted at department of psychiatry, SMS Medical College, Jaipur. Thirty male schizophrenic inpatients and fifteen normal healthy accompanying subjects, preferably 1st degree relatives, participated in this study. The diagnosis was on the basis of ICD-10 criteria by two psychiatrists. All the experimental and control subjects were registered after written informed consent.

Inclusion criteria were patients fulfilling diagnostic criteria for schizophrenia as per ICD-10 and between 18-60 years of age. Exclusion criteria were significant physical or neurological illness, diabetes and hypertension, history of head injury, evidence of neurodegenerative disorder, mental retardation and endocrinal abnormality, history of substance abuse/ dependence within the past 6 months, history of other psychiatric disorder. A control Group of normal healthy accompanying subjects, preferably 1st degree relatives between the age group (18-60) years was taken.

INSTRUMENTS OF STUDY

1. A specially designed pro forma was used for thorough evaluation of the patients. It included the socio demographic data sheet & clinical profile sheet.
2. **CRP-turbilatex method (Latex turbidimetry):** It is a quantitative turbidimetric test for the measurement of CRP in human serum or plasma. Latex particle coated with specific anti-human CRP are agglutinated when mixed with samples containing CRP. The agglutination causes an absorbance change, dependent upon the CRP contents of the patient's sample that can be quantified by comparison from a calibrator of known CRP concentration. Normal value of CRP up to 6mg/L and linearity limit of this assay is up to 150 mg/L.
3. **Positive and Negative Syndrome Scale (PANSS)[11] -**This 30 item, 7 point rating instrument was conceived as a carefully defined and operationalized method that evaluates positive, negative or other symptom dimension on the basis of a formal semi-structured clinical interview and other informational sources. In the 30 items, 7 are grouped to form a positive scale, measuring symptoms that are superadded to a normal mental status, and 7 items constitute negative scale, assessing features absent from a normal mental status, remaining 16 items constitute general psychopathology scale that gauges the overall severity of schizophrenic disorder by summation of remaining 16 items.

The day after their admission, psychopathology was evaluated by using the positive and negative syndrome scale.

SAMPLE COLLECTION

Blood samples for routine investigations and CRP measurement were drawn in the morning after an overnight fast between 9.00 am to 10:00 am. The routine laboratory analysis included blood sugar, hemoglobin (Hb), total leucocytes count (TLC), renal function test, liver function test and lipid profile levels. CRP was measured

by CRP turbilatex method.

Statistical Analysis

Mean (SD/Range) and percentages were used for descriptive purpose. Chi-square test & independent t-test was used for comparison of both the groups. The relationships between variables were studied with Pearson's correlation coefficient.

RESULTS

The mean age of schizophrenic patients was 32.93 (17-45) years and of control subjects was 38.40 [23-45] years. Most of respondents included in our study were married (study group 60%, control 66.6%), belonged to Hindu religion ((both groups 93.3%), nuclear extended families (Study group 46.6%, control 60%) and of rural background (both groups 93.3%). There was no statistically significant difference in the two groups with respect to socio-demographic variables.

Biochemical profile of schizophrenic patients and control subjects were depicted in Table-1. Besides blood sugar, uric acid and creatinine there were no significant difference observed & these levels were also within normal range.

There was statistically non-significant correlation of CRP value with disease duration and age of onset. The mean age of onset was 25.53 [12-48] years and disease duration was 7.16 [1-20] years.

TABLE 1

BIOCHEMICAL PROFILES OF SCHIZOPHRENIC PATIENTS (N=30) AND CONTROL SUBJECTS (N=15)

Variable	Patients	Controls	Significance
Blood Sugar (mg %)	74.76±21.05	89.26±14.04	.020*
Hb (gm/dl)	13.08±1.40	13.84±.97	.068
TLC (/cumm)	7.40±2.25	7.20±1.95	.765
Creatinine (mg %)	.82±.19	.99±.23	.014*
Uric Acid (mg %)	5.40±1.33	4.47±.78	.017*
SGOT (U/l)	42.93±23.63	38.66±20.69	.555
SGPT (U/l)	31.68±16.04	32.88±18.81	.825
ALP (U/l)	211.90±63.68	223.02±57.69	.572
Total Protein (gm %)	6.87±.65	7.20±.51	.097
Albumin (gm %)	4.34±.44	4.40±.27	.616
Total Cholestrol (mg %)	140.35±41.53	155.36±25.49	.207
Triglyceride (mg %)	139.27±105.28	136.78±27.77	.929

* Difference is significant at the 0.05 level (2-tailed)

The mean CRP level of schizophrenic patients group was 5.93±8.101 mg/L, which varied from 1.1 to 38 mg/L. Out of the 30 patients 5 patients had CRP level above the normal range [up to 6mg/L]. In healthy control subjects, observed mean CRP level was 2.53 ± .816 mg/L, which ranged from 0.8 to 3.2 mg/L. Mean CRP values were significantly high [t=2.29; p<0.05] in schizophrenic patients group as compared to healthy control subjects.

Table-2 shows the correlation between the acute phase reactant protein-CRP and PANSS score.CRP had no significant correlation with negative, positive, total and general psychopathology subscale score.

Table-2

Correlation of CRP with PANSS score

Variable	CRP	
	Pearson Correlation	Sig. (2–tailed)
Positive Symptom Score	.123	.518
Negative symptom Score	.036	.850
General Psychopathology score	-.060	.755
Total Score	**.025**	**.897**

DISCUSSION

To our knowledge, this is the first Indian study, directly examining the relationship between plasma level of CRP and the psychopathology profile of schizophrenia. The present study found that elevated level of CRP were not associated with severity of clinical symptoms in schizophrenia as reflected by the PANSS negative, positive, total and general psychopathology subscale score.

Our results are consistent with previous finding, which did not represents the correlation of CRP with the severity of psychiatric symptoms in individuals with schizophrenia,[12] individual recovering from cardiac surgery [13] and elderly without clinically apparent vascular disease. [14]

Our result differed from those of Fan et al,[10] who reported greater severity of negative and general symptoms in schizophrenia patients with higher CRP levels. An inflammatory process as reflected by elevated serum levels of CRP might be associated with more severe psychopathology in patients of schizophrenia. During the past decade experimental, epidemiological and clinical evidence links inflammation to development of metabolic complications with schizophrenia patients. Inflammation might be an important common pathophysiological process related to both schizophrenia psychopathology and metabolic disturbances. Further studies targeting proinflammatory cytokines and their molecular signaling pathways may give important lead to novel pharmacological interventions.

Further prospective studies are needed to examine the relationship between inflammation, as reflected by elevated serum levels of CRP, and treatment response as well as the moderating role of specific antipsychotic medications, in patients with schizophrenia.

LIMITATION

The result of the current study should be interpreted in background of following methodological limitation, which might have affected the observations. 1. Firstly, participants in this study were a group of inpatients with schizophrenia. 2. Patients were either continued or restarted with previously used antipsychotic medication or switched over between regular treatments. 3. We did not measure other factors which might contribute to elevated CRP such as diet or allergies.

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