

## Relationship of Blood C - reactive protein (CRP) Level and Cognitive Deficit in Patients with Schizophrenia

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### Abstract

**Introduction/Background:** Increasing blood serum CRP level (C - reactive protein) in schizophrenic patients has been shown in recent studies and there have more emphasis on inflammatory aspects of schizophrenic disease.

**Aim & Objective:** In current study, the purpose is to find and show the relationship between cognitive deficits in schizophrenic patients with blood serum CRP level.

**Methods/Study:** The statistical community, including patients with schizophrenia in the age range 18 to 65 years admitted to the Razi hospital in their diagnosis by an expert-based psychiatric diagnostic criterion (DSM-IV-TR) is definitive. Exclusion criteria for patients from the study is: 1) primary diagnosis of drug dependence, or sign of taking them, 2) a history of mental retardation, 3) having any history of clinical disorders that effect on cognitive vision, such as epilepsy and seizures, history of encephalitis or trauma (physical damage) to the skull or any central nervous system disorder. Using MMSE (Mini-Mental State Examination Questionnaire), 75 severely impaired cognitive patients were randomly selected. Also, in order to determine CRP serum, sample blood for fasting through immunoassay was measured, then through descriptive and inferential statistics, also showed and analyzed. In order to analyze the data in the description of frequency, percentage, mean and standard deviation, and in statistical inference of correlation, regression, ANOVA and t-test was used.

**Results/Finding:** The results show that there is a positive significant correlation between cognitive deficit and serum CRP( $r=0.18$ ,  $p<0.05$ ). Also there is a significant correlation between cognitive deficit and age of schizophrenia onset( $r=0.22$  and  $p<0.01$ ). Regression analysis was used to assess the role of serum CRP concentration to forecast cognitive deficit of the patients with schizophrenia ( $t=-2.2$  &  $f=5$  and  $p<0.05$ ). Comparison of cognitive deficit between two high and low groups of CRP, Based on cut-off point of CRP test, subjects were divided into two groups and t-test was used to compare their cognitive deficit( $t=2$  &  $f=2.36$  and  $p<0.05$ ).

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**Discussion/Conclusion:** Generally, such findings show the necessity to assess CRP in the patients with schizophrenia. Increased CRP is due to inflammation in patient's body, thereby using anti-inflammatory drugs may establish a path towards decreased effects of schizophrenia or even improvement of the disease.

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**Keywords:** Blood, high CRP serum, low CRP serum, cognitive deficit, schizophrenia

## **Introduction**

Clinical syndrome schizophrenia includes a variable but deeply destructive psychopathology which involves cognition, emotion, perception and other aspects of behavior. The incidence of these pretenses is variable in different people over time but the effect of disease is permanently sever and usually lasting. Such diseases start from 25 years old and will be stable lifetime. Besides, no social class is immune from catching it. Schizophrenia affects approximately 1% of the world population.<sup>1</sup> This disorder has a progressive and debilitating process which is along with pretenses and various approaches in psychiatry such as cognitive deficit (including disturbances in memory, orientation, visual - spatial and structural abilities, abilities in reading, writing and arithmetic actions), mood disorders, perceptual disorders and also disorder in how to communicate with others. The main specification of this disease is delusions and hallucinations of vision and hearing.<sup>2</sup> Diagnosis of schizophrenia is based on psychiatric biography and mental status examination. This diagnosis is performed according to diagnostic criteria DSM-IV-TR.<sup>1</sup> Generally, causes of schizophrenia can be classified into three following categories:

- A. Neurobiology (Chemistry of Nerves) which includes:
  1. Neurotransmitters (i.e. particles which are incorporated in chemical relation of neurons in Synapses or they are well-known neurotransmitters such as dopamine)
  2. Neuropeptides (e.g. Cholecystokinin)
  3. Neuropathology (i.e. studying structure of different parts of brain such as Limbic nuclei)
  4. Psychoneuroimmunology (i.e. studying immunity system of body such as lymphocytes and white blood cells)
  5. Psych neuroendocrinology (i.e. Studying hormones of body such as follicle motive hormone and its psychological effects on human being)
- B. Genetic Factors
- C. Psychological Factors<sup>1</sup>

In damage creation of schizophrenia, a special attention has been paid to CRP, which is a main indicator showing inflammation or infection in the blood and body. Studying blood serum CRP is inserted in neurobiology category of psychoneuroimmunology section. CRP is a kind of protein which is produced by some liver cells which are a type of white blood cells and are considered as a part of immunity system of body and are also existed in body at normal state.

But it increases rapidly during inflammation or infection and is an important indicator to demonstrate inflammation or infection in blood. This protein is produced due to inflammation and/or tissue destruction such as bacterial infections and/or heart attack in liver.<sup>3</sup>

CRP plays an important role in pathogenesis of many diseases including cardiovascular diseases and metabolic disorders.<sup>4,5</sup> Recently, its relationship with some psychiatric diseases such as depression and cognitive deficit has been proved.<sup>6,7</sup> Measurement of this indicator in blood serum is a reliable marker for diagnosis of chronic inflammatory processes caused by infections and other chronic inflammatory disorders. Recent researches have revealed increased serum CRP level in schizophrenic diseases.<sup>3</sup> This issue emphasizes more on inflammatory aspects of schizophrenia.<sup>8</sup> Komulainen conducted a study aimed by assessing the relationship between CRP serum level and cognitive deficit severity in old ladies. In this regard, a prospective study was designed with 12 years follow up on an instance of old ladies in the community. 97 ladies were chosen in the range from 60 to 70 years whose base serum level was measured. Also, cognitive deficit (using MMSE test) and memory deficit were evaluated against them. The study showed that there exists a positive statistical correlation- at 12 years after assessment- between base level of CRP serum and disorder severity. However, there was no significant relation between CRP level and cognitive deficit score of MMSE. Results suggest that long-term memory of old ladies can be evaluated and forecasted through serum CRP measurement.<sup>9,10</sup> Akanji conducted a study aimed by measuring serum level of CRP in the patients with schizophrenia. In this study, two identical groups were compared: (Health people in control group including 165 persons, the patients with schizophrenia including 207 persons). General information of patients was collected through a specific inventory. Serum level of CRP was measured using immunoassay method. The study showed that the group with schizophrenia significantly has a higher than control group. The results implied that schizophrenia can be accompanied with inflammatory processes.<sup>11</sup>

Also, Dickerson measured serum level of CRP in a study on 413 patients with schizophrenia. Severity of disease symptoms were evaluated using positive and negative signs criterion of schizophrenia. Cognitive performance of patients was also evaluated through neuropsychological status.

Results demonstrated that the patients with a CRP level higher than 0.5 have considerably lower cognitive ability scores than other patients. However, there was no difference in terms of positive and negative signs between two groups having a CRP higher and lower than 0.5. This study revealed that there is a significant relation between CRP level and cognitive deficit in schizophrenia. However, CRP level has no significant relation with psychological disorders.<sup>12</sup>

Currently, there are about 70 million patients with schizophrenia in the entire world and this disease is the main reason of founding psychiatric institutions. Although it has been more than a hundred years that research on schizophrenia has been conducted, still its causes have been largely unknown. Unfortunately, until the time schizophrenia is known, finding some construction to prevent is impossible. So, any research which goes towards reveal schizophrenia causes will find new horizons of correct and deep understanding about schizophrenia.<sup>13</sup>

Therefore, present research aims to specify serum level of CRP and its relationship with cognitive deficit in the patients with schizophrenia. Do inflammatory processes have any roles on

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perception and cognitive deficit in the patients with schizophrenia? Is it possible to prevent forming and development of cognitive deficit by using anti-inflammatory drugs?

## **Material and Method**

This study is a basic-applied research based on purpose whose method is descriptive and sectional survey type. The statistical society is formed by all patients with schizophrenia (in 18 to 65 years old range) who had been hospitalized in Razi Psychiatric Hospital in Iran. Participants were 75 patients who met DSM-IV criteria for schizophrenia. Exclusion criteria of patients from the study were as follows:

Initial diagnosis of drug dependence or its use- History of mental retardation- History of any clinical disorder which is effective on cognitive insight (including Epilepsy and seizures, encephalitis or trauma to the skull history or any central nervous system disorders); any changes in stability or need to change drugs during two recent months- high level of sugar or fat in the blood.

Sampling was targeted and a total of 75 patients were chosen randomly from statistical society. In present study, MMSE (Minutes Mental Status Examination) inventory is used to measure cognitive deficit.

This test is going to assess orientation, information registering, attention and calculation, reminding, verbal, movement, and design skills.<sup>14</sup> The reliability of this test for patients with schizophrenia and affective disorders (depression and Mania) and similar disorders has been reported of 88 percent.<sup>15</sup> "MMSE" inventory was also filled by subjects individually. Also, personal specifications of sample persons (including age of patient, age of illness onset, and duration of illness) were of variables assessed by the researcher. Venous blood samples of instances were taken in fasting form and between 8 am to 10 am and serum level of CRP is measured by immunoassay procedure.

### ***Immunoassay method***

To measure blood C-reactive protein (CRP) they first take blood serum that is a transparent liquid. The CRP obtains by passing the serum through a centrifuge machine and then by using the Immunoassay method (a method with high sensitivity and accuracy) they Count that. It can be briefly explained in this way through a series of materials that are called antibodies of CRP and have the ability of connecting to it they count them on a certain level of blood.<sup>3,8</sup> Then by help of SPSS software, findings were analyzed. Used tests in this investigation were as follows: Pearson correlation index, regression analysis, one-way analysis of variance, and independent T-test. Statistical software SPSS version 13.0 for windows (SPSS Inc., Chicago, IL) was used.

## **Results**

Table 1 shows mean and standard deviation of studied variables. In Table 2, research findings suggest that there is a positive significant correlation between cognitive deficit and serum CRP concentration i.e. higher the concentration level of serum CRP is along with increased deficit in

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cognitive efficiency and cognitive performance ( $r=0.18$  and  $p<0.05$ ). Also, there is a significant correlation between cognitive deficit and age of schizophrenia onset ( $r=0.22$  and  $p<0.01$ ). In other words, if age of illness onset was higher, then cognitive deficit would be lower. But, duration of illness has inverse correlation with cognitive deficit which means that longer disorder duration, more intense cognitive deficit. Of course, this disorder has not been statistically significant.

Regression analysis was used to assess the role of serum CRP concentration to forecast cognitive deficit of the patients with schizophrenia whose results are shown in Table 3 ( $t=-2.2$  &  $f=5$  and  $p<0.05$ ). Regression analysis shows that serum CRP concentration will explain 3 percent of cognitive deficit variance.

Comparison of cognitive deficit between two high and low groups of CRP: Based on cut-off point of CRP test, subjects were divided into two groups and t-test was used to compare their cognitive deficit whose results have presented in Table 4 ( $t=2$  &  $f=2.36$  and  $p<0.05$ ). There is a significant difference between mean cognitive deficit of two groups such that cognitive deficit rate is higher in the group having high concentration CRP. Results reveal that homogeneity condition of groups' variance is satisfied.

## **Discussion**

Importance of clinical issue on schizophrenia entire the history has caused to attract interest of great scholars in psychiatry and neurology towards this disorder, though schizophrenia is discussed in such a way that it apparently is a single disease but probably is a combination of disorders with heterogeneous etiology and includes some patients who are different in terms of clinical presentation, treatment response and the disease process. Role of immunologic and inflammatory disorders in schizophrenia cause has been evaluated in several studies; however, corresponding results have been different. Most of studies were about to identify individual inflammatory indicators for schizophrenia.<sup>16,17</sup> It is worth noting that inflammation is sign of local reaction to a foreign agent, one of important phenomena against foreign agents is response of acute phase in body<sup>18</sup>. Acute phase in body is a systematic response to foreign agents. CRP is a protein which is produces in response of acute phase in body against foreign agents. Changes made in host are occurred in such organs as liver, hematopoietic system, endocrine system, nervous system and finally immune system.<sup>19</sup>

As assessed in previous studies, schizophrenia can be accompanied with inflammatory processed that among different agents, a considerable interest has been to serum level of "CRP". Akanji<sup>11</sup> showed that serum level of CRP in the patients with schizophrenia is higher than control group. Komulainen in 2007 also addressed that memory deficit in patients with schizophrenia have positive correlation with CRP rate of blood such that long-term memory can be evaluated and forecasted by measuring CRP of blood. Dickerson<sup>12</sup> represented CRP level as an effective factor on cognitive deficit of the patients with schizophrenia so that by increased CRP level in blood of the patients with schizophrenia, cognitive deficit of them will be increased as well.

In present paper, also statistical findings showed that with increased CRP, cognitive deficit of the patients with schizophrenia will be increased as well. As another finding of this study, the relationship between age of illness onset and rate of cognitive deficit in the patients with schizophrenia i.e. lower age of schizophrenia onset, higher severity of cognitive deficit. On the other hand, also illness duration of schizophrenia is related with cognitive deficit and this relationship is in such a way that longer illness duration of schizophrenia, higher severity of cognitive as well.

Generally, such findings show the necessity to assess CRP in the patients with schizophrenia. Increased CRP is due to inflammation in patient's body; thereby using anti-inflammatory drugs may establish a path towards decreased effects of schizophrenia or even improvement of the disease. Since schizophrenia is debilitating, the investigations in this regard shall be wider and effective possible factors associated with this disease shall be identified.

### **Acknowledgement**

Authors would like to express their gratitude to the "DaneshAban" Educational, Research and Treatment Institute which has been instrumental in executive stages, preparation and the successful completion of this project.

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**Table 1:** Mean and standard deviation of studied variables

Variables	Min	Max	Mean	Sd
Age	25	60	45.5	8.4
Age of illness onset	15	48	29.9	7.9
Duration of illness	1	35	15.4	9.5
CRP	0.1	60.3	5	8.7
Cognitive Deficit Score	6	30	21	5.7

Data are presented as mean  $\pm$  SD or n (%)

**Table 2:** Correlation matrix of variables

Variables	CRP	Cognitive Deficit Score
Cognitive Deficit Score	*0.18	1
Age	0.001	0.07
Age of illness onset	0.05	**0.22
Duration of illness	0.05	-0.11

\*\* Significant =0.01      \*significant =0.05

**Table 3:** Regression analysis of CRP serum for cognitive deficit

Variable	R	R <sup>2</sup>	F	F Significant	B	Beta	t	P value
CRP	0.18	0.03	5	0.03	-0.12	-0.18	-2.2	0.000

**Table 4:** Comparison of cognitive deficit between two high and low groups of CRP

Groups	N	Mean	SD	Variance Homogeneity		df	T	P value
				F	significant			
High CRP	14	18.43	4.4	2.36	0.13	73	2	0.05
Low CRP	61	21.75	5.9					