

# Association of Serum Proteins among Acute Schizophrenic Patients -A case control study

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## Abstract

**Background:** Etiological research in schizophrenia is actively exploring biochemical toxic factor that may be result of an innate metabolic error - that factor is thought to be abnormal protein factor.

**Aim:** The present study was undertaken to study the concentration of various protein fractions in acute schizophrenics, to find out the association of serum proteins in acute schizophrenia patients and to find out in what fraction of proteins an abnormality lies.

**Methods:** Study consists of two groups, group one formed by healthy individuals, acting as controls and group two by acute schizophrenia patients. With all aseptic precautions, blood was collected and subjected to electrophoresis and for biuret reaction to find out fractional proteins and total proteins respectively. Analysis was done using Students "t" test.

**Results:** In acute schizophrenics, decrease in albumin fraction was seen compared to control group, and increase in the ALPHA 1 and ALPHA 2 Fraction was seen in patients of acute schizophrenia as compared to healthy controls.

**Conclusion:** Observation showed that there exists an abnormal protein fraction in acute schizophrenia patients. As seen in present research, there is decreased albumin level and increase in both Alpha -1 and Alpha-2 globulin fraction significantly as compared to controls. Alpha -2 fraction was more increased in patients with increased psychomotor activity.

**Key words:** Acute schizophrenia, Proteins fraction, Electrophoresis.

## Introduction

The spectrum of schizophrenia disease still presents an enigma and challenge for enormous proportions to medical research. Of the so called functional disorder, this disorder, as a spectrum of disease entities, must be considered the most malignant. Biochemistry, which has had notable successes in other areas of medicine, has appropriately been brought to bear on this one too. Study of the serum proteins in functional psychosis has been extensively carried out by research workers. Russian and European workers have done major work in this area.

Currently two concepts appear prominent in all biochemical studies done in case of schizophrenia. The first involves the study of plasma proteins

abnormalities and the second the amine metabolic disturbances. It is thought that an abnormal protein fraction exists in schizophrenia patients which interfere with normal metabolic path way of neuroamines resulting in the formation of abnormal biologically active metabolites or it acts as antibody to highly specific septal caudate region of brain.<sup>1</sup>

Thus ability of simple chemical substances to produce a toxic psychosis (psychotomimetic), which simulates Schizophrenia in some aspects, has generated hopes that a relatively simple chemical substance may prove to be the etiological agent.<sup>2,3</sup> In 1940 research done in Germany claimed that elevated levels of copper were responsible for some Schizophrenia symptoms but further study failed to replicate the results, hence

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refuted this claim.

In 1958 Heath<sup>2</sup> and his colleague found an abnormal protein fraction in the blood of schizophrenic patients and were capable of producing some of symptoms of that disorder, when injected into the non-schizophrenic volunteers.<sup>3</sup> Hadded and Rabe<sup>4</sup> found some evidence for an antigenic abnormality in the pooled serum of chronically ill schizophrenics. Abnormal spiking and slow wave activity were observed consistently in electroencephalograms from the septal region of patients during psychotic behavior.<sup>5</sup>

Study by Heath<sup>2</sup> reports intravenous injection of a globulin fraction of the sera of psychotic schizophrenic patients induced similar abnormal EEG changes and catatonia in rhesus monkeys, and caused behavioral symptoms resembling those of psychotic schizophrenic patients in volunteer recipients. Neither whittingham<sup>6</sup> nor Logan and Deodhar<sup>7</sup> (1970) could demonstrate it. Cepulic et al found elevation of Beta and Gamma globulins in schizophrenics. Hippus<sup>8</sup> emphasized about the elevations in Alpha-1 and Alpha-2 globulins. Janik<sup>9</sup> and Pospisilva considered that Beta globulin elevated in paranoid schizophrenia and Alpha-2 was highest in psychomotor agitation and puerperal psychosis. Bergen<sup>10</sup> and Frohman<sup>11</sup> and Lozovsky<sup>12</sup> shown abnormal protein is Alpha and Beta globulin of high lipid content. Similar observations were made by Pennel.<sup>13</sup> Similar observation made by Europeans. Fessel and Grambaum<sup>14</sup> found significant rise in Gamma globulin in chronic psychotics and according to Fessel<sup>15</sup> presence of S<sub>19</sub> microglobulin –an autoimmune factor may be responsible for the pathogenic chain of events leading to functional psychosis.

Similarly other workers have commented on variations in Alpha and Gamma globulins. (Frohman<sup>11</sup>, Kuruvilla<sup>16</sup>, Rudraprakash<sup>17</sup>, Gammock<sup>18</sup> and Hector, Alias et al<sup>19</sup>). All these observations suggested a possible relation between abnormal protein and clinical manifestations of schizophrenia.<sup>1</sup> The epidemiologic Catchment Area study sponsored by the National Institute of Mental Health, reported a lifetime prevalence of schizophrenia is 0.6 to 1.9 percent and the annual incidence ranges from 0.5 to 5.0 per 10,000.

Schizophrenia is found in all societies and geographical areas, and incidence and prevalence rates are roughly equal worldwide. Lifetime prevalence in United States of schizophrenia is about 1%. In the United States, about 0.05 percent of the total population is treated for schizophrenia in any single year and the direct and

indirect costs of schizophrenia in the United States alone are estimated to be in the tens of billions of dollar every year.<sup>20</sup> Keeping all these controversial finding in the background of mind it was decided to take up a comparative study to find out abnormal serum proteins fraction in acute schizophrenics blood and compare with healthy individuals. Today etiological research is actively exploring four areas namely genetic, biochemical, psychodynamic and social factors. In present study association of biochemical factors such as serum proteins in acute schizophrenia patients and plasma proteins abnormality, amine metabolism disturbances are being explored.

### Objectives

1. To study the concentration of various protein fractions in the sera of acute schizophrenic patients.
2. To compare the levels of serum proteins of acute schizophrenia patients with a control group of healthy subjects
3. To study in which fraction of serum proteins an abnormality exists.

### Materials and Methods

**Study design:** Case control study.

**Sampling method:** Universal Sampling

**Collection of samples:** The study was done at Department of Psychiatry in Khaja Bande Nawaz institute of medical sciences, Gulbarga.

**Participants:** The study participants in the age group of 17 to 50 years, consisted of two groups, first group was formed by healthy individuals acting as controls who were selected from the relatives of the patients who had accompanied patients at the time of hospitalization and the second group was formed by study group diagnosed to have acute schizophrenia according to ICD-10 criteria by a Psychiatrist.

**Data collection:** Ethical clearance from the ethical committee of Khaja Bande Nawaz institute of medical sciences, Gulbarga was taken. It was conducted in the Department of Psychiatry, written consent was obtained from each participant regarding willingness in participating in the study after explaining it to them in their own language. It was strictly observed that none of the individuals from controls as well as the experimental group had received any drugs including antipsychotics during past 12-14 weeks. Physical examination and laboratory investigations like x-ray chest, Haemogram, ECG, Urine examination were done to rule out possible evidence of physical illness.

Under aseptic conditions 5 ml of venous blood was collected from all participants. Subsequently sera was subjected for paper electrophoresis using Watman no.1 chromatograph paper and for biuret reaction. Photoelectric densitometer was used for optical density percentage, from which the total proteins of each fraction was calculated. Total proteins estimation was done by biuret reaction. Globulin value was calculated by subtracting albumin from total proteins.

**Statistical analysis:** Data was collected and entered in Microsoft Excel sheet. Data was tabulated with variables. Data was presented in Mean and Standard deviation for quantitative data using Microsoft Excel and Open Epi software. The analysis of descriptive statistics and the difference between the two given groups was done by using Chi square test and Student's "t" test.

### Results

A total of 74 patients were included in the study. Results showed total Albumin (128.02) in healthy individuals with mean value of 2.56 was more compared to acute schizophrenics with mean value of 2.38. Increase in Alpha 1 (mean-0.33) and Alpha 2 (mean-0.64) globulin fraction was seen in acute schizophrenia patients as compared to control group (mean-0.60)(Table1, Figure1).

Among the protein fractions results (Table 1) serum Albumin in acute schizophrenics was significantly t value=4.25,  $p < 0.001$  decreased compared to healthy controls. Increase in Alpha-1 t value=4.58,  $p < 0.00$  and Alpha-2 t value=3.77,  $p < 0.00$  in study group was significant compared to control group.

Acute schizophrenia was associated (Table 2) with significant decrease in total serum Albumin level in study group compared to healthy controls  $\chi^2 (2) = 29.37$ ,  $P=0.001$ .

Acute schizophrenics (Table 3) had significant increase in Alpha 1 fraction of serum Globulins  $\chi^2 (2) = 34.4$ ,  $P=0.0001$  when compared to control group and increase in Alpha 2 fraction of serum Globulins (Table 4) in acute schizophrenia patients was also found to be significant  $\chi^2 (2) = 42.0$ ,  $P=0.0001$  compared to healthy individuals.

**Table 1. Serum protein fractions in acute schizophrenics and healthy controls**

Protein fraction	Healthy controls		Acute schizophrenics	
	Total	Mean	Total	Mean
Albumin	128.02	2.56	59.64	2.38*
Alpha-1	16.53	0.33	9.50	0.38*
Alpha-2	32.44	0.64	15.04	0.60*
Beta	54.89	1.08	23.44	0.93
Gamma	78.95	1.57	37.88	1.51

\* p value – statistically significant

**Table 2. Total Albumin levels in healthy controls and acute schizophrenics**

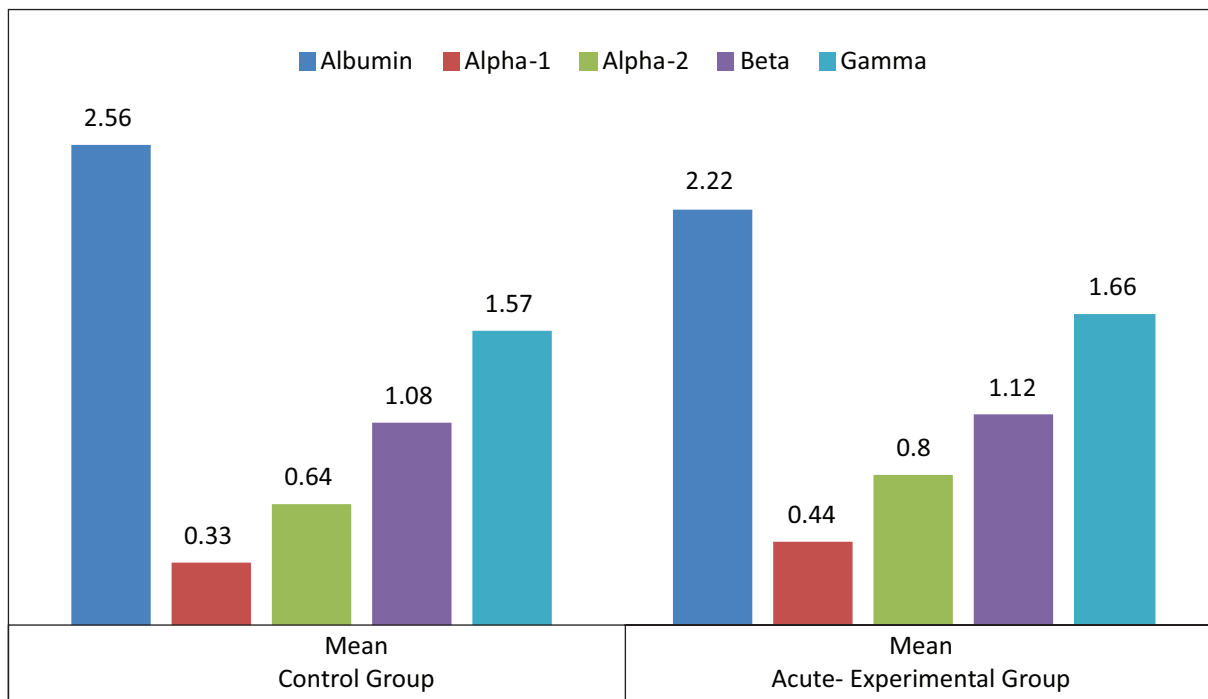
Albumin level	Acute Schizophrenics	Healthy controls	Total	Chi-square value	P value
Normal (3.8 gm)	5	41	50	29.37	0.001
Abnormal (<3.8gm)	19	9	24		
Total	24	50	74		

**Table 3. Alpha 1 fraction of Globulin in healthy controls and acute schizophrenics**

Globulin-Alpha-1	Acute Schizophrenics	Healthy controls	Total	Chi-square value	P value
Normal (0.3gm)	4	38	42	34.4	0.0001
Abnormal (> 0.3gm)	20	12	32		
Total	24	50	74		

**Table 4. Alpha 2 fraction of Globulin in healthy controls and acute schizophrenics**

Globulin-Alpha-2	Acute Schizophrenics	Healthy controls	Total	Chi-square value	P value
Normal (0.6gm.)	4	46	50	42.0	0.0001
Abnormal (> 0.6gm)	20	4	24		
Total	24	50	74		



**Figure 1. Mean values of serum protein fractions in control and acute experimental group (acute schizophrenics) group**

## Discussion

Present study was undertaken with aim of studying the concentration of various protein fractions in acute schizophrenics, to find out the association of serum proteins in acute Schizophrenia and the fraction of proteins which is abnormal in the disease. In this study compared to healthy controls, it was observed that acute schizophrenia patients had decrease in Albumin fraction of serum proteins. Acute schizophrenia was also associated with significant increase in Alpha -1 and Alpha-2 globulin fraction as compared to healthy individuals. This finding of present study is in agreement with the general notion held by other workers-Cepulic, Domec, v, Consbruch and Faust<sup>8</sup>, Fessel.<sup>14,15</sup> Fessel correlated this to nonspecific stress. In present study a quantitative and significant decrease in albumin fraction may be there for the same reason. But we cannot say this firmly because nutrition also plays an important part as far as protein levels are concerned. More over subjects under this study were coming from low socio economic class. However our findings are in keeping with the above reports of other authors.

A perusal of literature shows a good deal of evidence that Alpha Globulin is consistently elevated in schizophrenia in studies of Hippus,<sup>8</sup> Fessel,<sup>14</sup> Bergen,<sup>21</sup> Pennel<sup>13</sup> and Lozovsky et al.<sup>12</sup> In present study also Alpha-1 and Alpha-2 fraction was found to be

significantly high, however, our findings of alpha -1 elevation is not substantiated by an Indian report, Rudraprakash<sup>17</sup> and Alpha-2 are not consistent with report of Kuruvilla et al<sup>16</sup> in which Alpha-2 globulin was not significantly raised in schizophrenic patients.

Alpha-2 fraction was highest in patient with increase psychomotor agitation Hippus<sup>11</sup> Fessel<sup>24</sup>. It was corroborated in present study as most of our acute schizophrenia patients were agitated. It is generally agreed that gamma globulin is raised in schizophrenia-Cepulic et al, Hippus<sup>11</sup>, Fessel<sup>24</sup>, Frohman et al<sup>22</sup>, Rudraprakash.<sup>17</sup> However, our present study did not confirm these widely documented findings. But an Indian study by Kuruvilla<sup>16</sup> was consistent with present study, there was no significant rise in gamma fraction. Present study did agree as far as the abnormality in the serum globulins in schizophrenia, but not in which fraction of the protein the abnormality lays.

**Limitations:** Our study had its limitations as the study population was from one hospital. As no comparable data for all the variables studied by us are available in other studies, observations of this study and their implications are restricted across different populations.

**Conclusion:** Research done in past many decades have revealed some of the biological and genetic links to the origins of schizophrenia. Present study supports hypothesis of biochemical impairment in

acute schizophrenia. Further research in etiological role of abnormalities in serum albumin and Alpha 1 and Alpha 2 fractions of serum globulins in acute schizophrenia will establish their association with the disease and will be helpful in prognosticating the course of the disease.

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