ORIGINAL RESEARCH PAPER

Psychiatry

"TO COMPARE LEVELS OF C-REACTIVE PROTEIN (CRP) IN DRUG NAĎVE PATIENTS OF FIRST EPISODE OF SCHIZOPHRENIA, FIRST EPISODE OF BIPOLAR DISORDER (MANIA) AND HEALTHY CONTROLS"

KEY WORDS: First Episode Of Schizophrenia ,first Episode Of Bipolar Disorder (mania),c- Reactive Protein.

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ABSTRACT

Background:-. Schizophrenia, bipolar disorder are severe mental disorders with complex etiology and pathophysiology that are far from being established. Infectious and inflammatory processes could potentially play an important role in the etiology and pathogenesis of psychotic disorders. Results of studies are mostly conclusive and show raised level of CRP in these disorders. However, fewer are studies comparing CRP levels in drug naive patients of these diagnostic groups.

AIM:- To compare levels of C-reactive protein (CRP) in drug naive patients of first episode of schizophrenia, first episode of bipolar disorder (mania) and healthy controls.

Methodology – A cross sectional hospital based Analytic type of Observational study was carried out between September 2017 and MAY 2018 Which included drug naive thirty cases each of first episode of schizophrenia(FES),first episode bipolar disorder (mania) (FEBP)patients with thirty age and sex matched healthy controls. Blood samples of these groups were taken for measurement of serum CRP levels.

Results:-

FES patients show significant raised serum C-reactive protein as compared to FEBP patients (mean diff. 5.90 and P <0.001) and healthy controls (mean diff.8.48 and P <0.001), while FEBP patients also show significant raised serum C-reactive protein as compared to healthy controls (mean diff. 2.58 and P <0.001).

CONCLUSION:- This present study adds to the growing body of literature indicating that schizophrenia is associated with immune activation and elevated CRP.

INTRODUCTION:-

Schizophrenia, bipolar disorder are severe mental disorders with complex etiology and pathophysiology that are far from being established. Infectious and inflammatory processes could potentially play an important role in the etiology and pathogenesis of psychotic disorders. Different biological mechanisms have been associated with different mood states in bipolar disorder and phases of symptomatic stability and acute relapse in schizophrenia. Various evidence indicates the involvement of immune-inflammatory processes in the pathophysiology of both disorders and mediate illness relapse[1]. Initially, the involvement of these processes has been proposed on the basis of epidemiological studies which showed higher rates of autoimmune disorders in patients of schizophrenia[2]. Emerging evidence also indicates that this observation holds true for BD[3].

Various studies have shown alterations in cellular component of immune systems[4,5], indices of microglial activation[6], alterations in cytokine levels[1,7]. and elevated c-reactive protein (CRP) levels[8], in patients of schizophrenia and bipolar disorder.

C-reactive protein is one of positive acute phase protein and it is synthesized in the liver and then excreted in the blood. CRP levels can be increased more than 10000 times as a response to an infection and represent direct and quantitative measure of acute inflammatory reaction. Increased CRP levels are associated not only with acute but with chronic infections too. There are many studies showing that patients in acute manic phase have increased levels of CRP and other inflammatory markers compared to depressive, euthymic patients and healthy controls[9,10,11] and that the intensity of manic symptoms is associated with CRP levels. Inflammatory markers in patients with bipolar disorder and schizophrenia (TNF -1 and CRP) are significantly higher than in healthy controls[12]

Results of studies are mostly conclusive and show raised level of crp in these disorders but there are very few,studies, comparing crp levels in drug naive patients of these diagnostic groups.

AIM:-

To compare levels of c-reactive protein (CRP) in drug naive patients of first episode of schizophrenia(FES),first episode of bipolar disorder (mania) (FEBP) and healthy controls.

METHODOLOGY –

- A cross sectional hospital based analytic type of observational study was carried out between september 2017 and may 2018 in department of psychiatry of SMS medical college,jaipur. Ethical consideration was taken from research review board & ethical committee of the institution.
- Patients having age between 18–65 years, either sex, meeting the icd-10 criteria for schizophrenia disorder and bipolar disorder (mania),only first episode patients,no history of any psychoactive drug,willing to participate in the study were included in the study. Patients having history of any neuropsychiatric illness or any significant substance abuse, in last 3 months, except nicotine (icd-10) or neurological disorder/ significant head injury or any history of chronic medical illness and mental retardation were excluded from the study. substance use disorder and any other psychiatric illness were ruled out by clinical interview based on icd-10 criteria. medical illness, neurological disorder and mental retardation were ruled out by clinical examination and history.
- Control group included normal and healthy persons who were taken from hospital staff and bystanders of hospitalized patients (not first degree relatives) and was screened for psychiatric illness by two psychiatrists independently.Drug naive thirty cases each of first episode of schizophrenia (FES),first episode bipolar disorder (mania) (FEBP)patients with thirty age and sex matched healthy controls. Blood samples of these groups were taken for measurement of serum CRP levels before initiating the treatment.

STATISTICAL ANALYSIS

Statistical analyses were done using computer software (SPSS version 20 and primer). the qualitative data were expressed in percentages and the quantitative data expressed as mean and standard deviations. the difference between mean value of the three groups was analyzed using ANOVA one way test, which were further analysed by using post hoc test (tukey test).Significance level for tests were determined as 95% ($p < 0.05$).

RESULTS:

TABLE 1 Comparison of Socio-demographics between group A (Schizophrenia patients), B (Bipolar patients) and C (healthy controls)

Parameter	Group A(N=30) Mean (SD)	Group B(N=30) Mean (SD)	Group C(N=30) Mean (SD)	P value
AGE	32.56 (7.84)	32.80 (7.29)	32.63 (7.21)	0.815
GENDER Male Female	24 6	25 5	23 7	0.812
MARITAL STATUS Married Unmarried	22 8	20 10	21 9	0.853
EDUCATION Illiterate Primary Secondary Graduate or P.G	6 16 4 4	8 14 5 3	8 14 4 4	0.990
RELIGION Hindu Muslim	25 5	22 8	26 4	0.39
LOCALITY Rural Urban	26 4	26 4	22 8	0.149
FAMILY TYPE Nuclear Nuclear Extended Joint	14 6 10	18 2 10	19 2 9	0.214
SOCIOECONOMIC CLASS Lower Middle	25 5	22 8	26 4	0.39

Table 1 is showing that three groups were comparable to each other according to the socio-demographic data as no statistically significant difference was found among these three groups (P >.05). Majority of the patients were married, Hindu males of rural background belonging to lower socioeconomic class and living in a nuclear family.

TABLE 2:- comparison of the Peripheral biomarkers among groups A (Schizophrenia patients), B (Bipolar patients) and C (healthy controls).

	Group A(N=30)		Group B(N=30)		Group C(N=30)		P Value
	Mean	SD	Mean	SD	Mean	SD	
CRP (mg/L)	10.25	2.43	4.35	1.45	1.77	0.54	<0.01

Table no 2 shows that Serum C-reactive protein was significantly increased in FES as compared to FEBP and healthy controls but serum TSH level was significantly higher in FEBP as compared to FES and healthy controls (P<0.01).

TABLE 3:- Inter group comparison of the Peripheral biomarkers among groups A (Schizophrenia patients), B (Bipolar patients) and C (healthy controls)

	Group A vs B		Group A vs C		Group B vs C	
	Mean diff	P Value	Mean diff	P Value	Mean diff	P Value
CRP	5.90	<0.01	8.48	<0.01	2.58	<0.01

Table no 3 shows that serum CRP levels are significantly deranged in FES patients as compared to FEBP patients but both FES and FEBP patients have significantly deranged peripheral biomarkers (P<0.01).

DISCUSSION:-

Table 1 is showing that three groups were comparable to each other according to the socio-demographic data as no statistically significant difference was found among these three groups. Majority of the patients were married, Hindu males of rural background belonging to lower socioeconomic class and living in a nuclear family. The mean age of the SZ, BD patients and healthy controls were 32.56 (7.84), 32.80(7.29) and 32.63(7.21) respectively, which were not significantly different on statistical analysis (P=0.815). There was no statistically significant differences in gender composition of three groups in this present study (P=0.812).There were overall 63 (70%) married, 27 (30%) were unmarried. All three groups did not differ significantly in terms of marital status (p value=.853) and educational status (p=0.99).

In present study, serum C-reactive protein were significantly elevated in the schizophrenic patients compared to the bipolar patients and healthy controls (P<0.01). While assessing inflammatory markers, the mean scores of serum C-reactive protein in the FES, FEBP patient group and healthy controls were 10.25.±2.43mg/L, 4.35±1.45mg/L, 1.77±0.54mg/L, respectively. Studies on antipsychotic-naive patients with first episode psychosis find that inflammation is present already at this stage, some of these abnormalities resolve after the initiation of treatment, suggesting that they are state markers of acute psychosis, but other abnormalities persist[13].For this reason continuous monitoring of laboratory parameters is imposed as necessary already at the very beginning of the treatment, in order to clearly distinguish those abnormalities that are direct consequences of the disease itself, from the disorders or due to antipsychotic therapy.[14]

FES patients show significant raised serum C-reactive protein as compared to FEBP patients (mean diff. 5.90 and P <0.001) and healthy controls (mean diff.8.48 and P <0.001), while FEBP patients also show significant raised serum C-reactive protein as compared to healthy controls (mean diff. 2.58 and P <0.001). Our results are not in line with the results of other studies showing no differences in CRP levels between patients with bipolar disorder and schizophrenia[15,12].Several methodological differences between the studies is present and this present study include first episode and younger patients which may account for the inconsistent results.

LIMITATION:-

This study has several limitations, and results should therefore be interpreted with caution. The first limitation is the relatively small sample size of patients: future studies should be conducted on larger samples in order to confirm our findings. Moreover,Recruitment of patients took place exclusively in a psychiatry centre and so are not representative of whole psychiatric population as only moderate to severe cases have chance to be selected. We did not measure waist circumference or other measures of body fat so we cannot determine if differences that in the distribution or metabolism of body fat might explain differences in CRP levels measured in the study populations. Because our study was cross sectional in nature, we could not determine the temporal sequence of immune activation as reflected in higher levels of CRP and the development of schizophrenia and the clinical course of the disorder.

CONCLUSION AND FUTURE DIRECTIONS

The present study supports the hypothesis that inflammation is involved in the etiopathogenesis of psychotic disorders, which also supported by numerous studies[13,16,17].Our results are also consistent with the investigation of Suvisaari[13] in showing elevated CRP to schizophrenia and schizophrenia-spectrum disorders. Additional studies should be directed at the factors which determine CRP levels and at the effects of elevated CRP in this population. Additional studies including longitudinal and cohort studies should be performed to determine the relationship between genetic susceptibility, environmental exposures, and increased levels of CRP in schizophrenia and bipolar disorder.

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