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Original Article

Psychiatry/Mental Health Section

Haematological Parameters and Serum Osmolality in Patients with Bipolar Affective Disorder and Schizophrenia: A Cross-sectional Study

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ABSTRACT

Introduction: Schizophrenia (SCZ) and Bipolar Affective Disorder (BPAD) are psychiatric disorders affecting an estimated 1-2% of the population worldwide. Inflammatory reactions such as cytokine cascades, cellular immune responses and increased levels of acute phase proteins and complement factors are associated with many psychiatric disorders, including SCZ and BPAD.

Aim: To compare peripheral inflammatory indices in patients with SCZ and BPAD.

Materials and Methods: This hospital-based, cross-sectional study was conducted during the period of October 2023 to August 2024 at the Department of Psychiatry, Balvir Singh Tomar Institute of Medical Science, Research and Hospital, Jaipur, Rajasthan, India which included 162 participants comprising 72 patients with BPAD, 90 patients with SCZ, aged 18-60 years. A semi-structured proforma was used to assess clinical characteristics. Blood samples were collected for various haematological and serum osmolality parameters. Statistical significance was set at $p<0.05$.

Results: All groups were matched for gender, age, caste, religion and residence. The majority of patients were married. There was no significant difference in neutrophils, lymphocytes, platelets, Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), Haemoglobin (Hb), haematocrit, Mean Platelet Volume (MPV), or Erythrocyte Sedimentation Rate (ESR) ($p>0.05$). However, monocyte percentage was significantly higher (p-value <0.001) in BPAD patients (8.60±1.22) compared to SCZ patients (7.59±2.41). Although BPAD patients had slightly higher mean blood urea nitrogen and serum osmolality values, these differences were not significant.

Conclusion: The present study found that most haematological, biochemical, inflammatory and serum osmolality parameters were similar in both groups. These suggest that these laboratory parameters alone may not be useful in differentiating BPAD from SCZ.

Keywords: Cytokine cascade, Inflammatory indices, Psychiatric disorder

INTRODUCTION

The SCZ and BPAD are multi-factorial mental disorders affecting approximately 1-2% of the world population and in India this prevalence is between 0.5% and 0.7% [1].

The SCZ is generally characterised by fundamental and distinctive distortions of thinking and perception, along with inappropriate or blunted affect [2]. Consciousness and intellectual capacity are usually maintained, although certain cognitive deficits may be observed [3]. The disturbance affects the most basic functions that give a person a sense of individuality, uniqueness and self-direction. Paranoid SCZ, hebephrenic SCZ and catatonic SCZ are the common types of SCZ [4].

The BPAD is characterised by repeated (i.e., at least two) episodes in which the patient's mood and activity levels are significantly disturbed, this disturbance consisting on some occasions of an elevation of mood and increased energy and activity (mania or hypomania) and on others of a lowering of mood and decreased energy and activity (depression). Characteristically, recovery is usually complete between episodes and the incidence in the two sexes is more nearly equal than in other mood disorders. The exact underlying mechanism in the development of SCZ and BPAD remains obscure [4].

Recent evidence suggests that inflammatory processes are associated with psychiatric disorders such as SCZ and BPAD [5,6]. Activated macrophages and T lymphocytes lead to release of proinflammatory cytokines and these cytokines play a role in attenuating the release of neurotransmitters such as noradrenalin and serotonin in the brain [7].

The neuro-pathological studies found associations between SCZ and both abnormal levels of inflammatory cytokines and increased frequency of activated lymphocytes [5-8]. Higher Monocyte-Lymphocyte Ratio (MLR) and PLR values have been determined in the euthymic and manic periods in patients with bipolar disorder. Increased neutrophil counts and decreased lymphocyte counts have been shown in bipolar disorder patients in comparison with a control group [9]. This finding supports the hypothesis of a fluid and electrolyte imbalance during acute episodes. Decreased serum osmolarity might be a reflection of a relative haemo-dilution in mania [10].

Although growing evidence implicates inflammation in the pathophysiology of SCZ and BPAD, findings on routinely available haematological markers remain inconsistent and limited, particularly in the regional level [6]. Most studies focus on isolated parameters or single diagnostic groups, with scarce comparative data across SCZ, BPAD and control [11,12]. Therefore, study was planned to compare the BPAD and SCZ to assess the differences in haematological and biochemical parameters, as well as serum osmolality levels, in the Rajasthan region of India.

MATERIALS AND METHODS

The present hospital-based, cross-sectional study was conducted during the period of October 2023 to August 2024 at the Department of Psychiatry, Balvir Singh Tomar Institute of Medical Science, Research and Hospital, Jaipur, Rajasthan, India. Permission was obtained from the Research review board and Ethics Committee of the college (No.1294/MC/ECA/2023).

Inclusion and Exclusion criteria: The study included all clinically diagnosed cases of SCZ and BPAD, identified according to the International Classification of Diseases (ICD)-10 diagnostic criteria, aged between 18 and 60 years [13]. Participants were recruited from the Psychiatry Outpatient Department (OPD) of the institution. Patients receiving antipsychotic, anti-inflammatory, or immunosuppressive medications, or those on any concomitant drug therapy for the past six months were excluded. Individuals with a history of heavy smoking (more than 15 cigarettes per day), significant alcohol or other substance use, other psychiatric disorders, or any acute/chronic medical conditions such as coronary heart disease, diabetes mellitus, or Chronic Obstructive Pulmonary Disease (COPD) were also excluded from the study. All participants provided informed consent before inclusion in the study.

Sample size calculation: A minimum sample of 70 cases in each group was required to verify the expected difference of 6.6±14.4 g/L in haemoglobin level in between group, as per seed article [14].

$n=2(Z\alpha/2+Z\beta)^2\sigma 2/d^2$ (where n is sample size required per group, $Z\alpha/2$: desired significance level (1.96), $Z\beta$: study power (0.84), σ = pooled standard deviation (14.4), d = expected difference between the two means (6.6).

Study Procedure

A semi-structured, pre-validated questionnaire was used as a tool for data collection. The blood samples were collected early from the subjects who were identified as included in the study, the specimen containers were labelled appropriately before specimen collection. Container label includes details like subject name, age and identification number, for proposed blood investigations like Complete Blood Count (CBC), serum electrolytes, blood glucose, albumin and Blood Urea Nitrogen (BUN), venous blood samples sent to the hospital laboratory and thereafter, the laboratory reports were analysed. NLR, PLR ratios were assessed by using cells value from CBC.

STATISTICAL ANALYSIS

Quantitative data were summarised as mean and standard deviation and analysed using Student's t-test. A p-value <0.05 was taken as statistically significant. Data were analysed using Stata version 5.0 and Statistical Package for the Social Sciences (SPSS) version 22.0.

RESULTS

A total of 162 patients were enrolled in the study, including 72 patients with BPAD and 90 patients with SCZ. The differences in the proportions of participants with respect to age, gender, caste, religion and residence between the groups were not statistically significant (p>0.05). A higher proportion of BPAD patients were married 63 (87.5%) compared to SCZ patients 61 (67.8%). Conversely, divorced/separated/widowed status was more common among SCZ patients 11 (12.2%) than BPAD patients 2 (2.8%) [Table/Fig-1].

There was no statistically significant difference in neutrophils, lymphocytes, platelets, NLR, PLR, haemoglobin, haematocrit, MPV, or ESR (p>0.05). However, monocyte percentage was significantly higher in BPAD patients (8.60±1.22) compared to SCZ patients (7.59±2.41), with a highly significant p-value (p=0.0007). Overall, except for monocytes, haematological profiles were similar in both groups [Table/Fig-2].

Serum albumin, blood urea nitrogen, serum sodium and serum osmolality levels were similar in both study groups (p>0.05). Although BPAD patients had slightly higher mean blood urea nitrogen and serum osmolality values, these differences were not statistically significant. Overall, the serum biochemical profile did not differ significantly between BPAD and SCZ patients in the present study [Table/Fig-3].

Variables	BPAD (n=72)	Schizophrenia (SCZ) (n=90)	p-value*
Gender			
Male	50 (69.4%)	59 (65.6%)	0.722
Female	22 (30.6%)	31 (34.4%)	
Age (years)			
Mean±SD	33.84±9.44	32.17±8.81	0.247
Religion			
Hindu	71 (98.6%)	90 (100%)	0.911
Muslim	1 (1.4%)	0 (0%)	
Marital status			
Married (P1)	63 (87.5%)	61 (67.8%)	P1 vs P2: 0.062 P1 vs P3: 0.032 P2 vs P3: 0.641
Unmarried (P2)	7 (9.7%)	18 (20.0%)	
Divorced/separated/ widow (P3)	2 (2.8%)	11 (12.2%)	
Residence			
Rural	63 (87.5%)	76 (84.4%)	0.744
Urban	9 (12.5%)	14 (15.6%)	
Family type			
Nuclear (P1)	52 (72.2%)	68 (75.6%)	P1 vs P2: 0.89 P1 vs P3: 0.89 P2 vs P3: 0.99
Joint (P2)	10 (13.9%)	11 (12.2%)	
Extended (P3)	10 (13.9%)	11 (12.2%)	

[Table/Fig-1]: Socio-demographic characteristic of the study groups.
*Chi-square test Values presented as n (%) N=162

Parameters	BPAD (n=72) Mean±SD	Schizophrenia (SCZ) (n=90) Mean±SD	p-value*
Neutrophils (%)	63.38±8.31	63.41±7.59	0.9811
Lymphocytes (%)	26.47±7.01	26.64±8.24	0.8874
Platelets (10^5/µL)	3.05±0.77	2.90±0.75	0.2146
Monocytes (%)	8.60±1.22	7.59±2.41	0.0007
NLR	2.68±1.21	2.73±1.26	0.7978
PLR	158.82±82.98	156.44±75.28	0.8504
Hb (g/dL)	13.26±1.99	13.10±2.01	0.6134
Haematocrit (%)	40.76±5.51	40.03±5.73	0.4117
MPV (fL)	10.89±1.94	11.04±1.79	0.6136
ESR (mm/hr)	15.57±8.08	16.08±9.00	0.7049

[Table/Fig-2]: Comparison of various haematological parameters between groups.
*independent "t-test N=162

Parameters	BPAD (n=72) Mean±SD	Schizophrenia (SCZ) (n=90) Mean±SD	p-value*
Serum albumin (g/dL)	3.72±0.43	3.76±0.43	0.557
Blood urea nitrogen (mg/dL)	10.78±3.00	10.27±2.93	0.145
Serum sodium (mEq/L)	137.26±2.33	137.10±2.31	0.479
Serum potassium (m.eq./L)	4.13±0.50	4.09±0.43	0.585
Serum osmolality (mOsm/kg)	291.76±4.81	291.01±4.74	0.561

[Table/Fig-3]: Comparison of serum osmolality in between groups.
*Independent t-test N=162

DISCUSSION

In the present study, all groups were matched for socio-demographic characteristics like gender, age, caste, religion and residence of participants, showed the comparability of the groups for different parameters. A higher proportion of BPAD patients were married (87.5%) compared to SCZ patients (67.8%). Conversely, divorced/separated/widowed status was more common among SCZ patients (12.2%) than BPAD patients (2.8%). Pair-wise comparison showed a statistically significant difference between married and divorced/separated/widowed groups (p=0.032), while

differences between married and unmarried (p=0.062) and between unmarried and divorced/separated/widowed (p=0.641) were not statistically significant. Similarly, Tandon R et al., highlighted the substantial social and functional impairment associated with SCZ, contributing to poor marital outcomes [15]. Indian studies, such as those by Thara R and Srinivasan TN have also documented significant marital disruption and separation among patients with SCZ, particularly among women [16]. Furthermore, the World Health Organisation (WHO) cross-national studies have consistently shown that SCZ is associated with greater long-term social disability compared to mood disorders (WHO, 1979; 1992) [17,18].

In present study, inflammatory parameters were elevated in both BPAD and SCZ patients supporting the growing evidence that immune dysregulation plays a role in the pathophysiology of major psychiatric disorders. Markers such as neutrophils, NLR, PLR and ESR were present at comparable levels in both groups, suggesting a similar underlying inflammatory burden. On comparison between the two groups, most haematological parameters including neutrophils, lymphocytes, platelets, NLR, PLR, haemoglobin, haematocrit, MPV and ESR did not show statistically significant differences (p>0.05). This indicates that the overall systemic inflammatory profile was largely similar in BPAD and SCZ patients. However, monocyte percentage was significantly higher in BPAD patients compared to SCZ patients (p=0.0007). Since monocytes are important mediators of innate immune activation and cytokine production, this finding may reflect differential immune activation patterns between the two disorders. This observation is supported by the study of Çakır U et al., and Kalelioglu T et al., concluded that Neutrophil (%), Monocyte (%), NLR, MPV show the higher mean value in BPAD and Schizophrenic group [19,20]. The study of Sahpolat M et al., also concluded that the monocyte counts was in SCZ, however they did not compare this with BPAD group [21].

Similarly, most studies have investigated T-cell subgroups in patients with SCZ but have reported inconsistent results. Some have found a decrease in T-cell counts (Mazzarello V et al., Steiner J et al., [22,23]), while others have observed an increase in T-cell numbers among schizophrenic patients (Sperner-Unterweger B [8]).

Serum biochemical parameters were quite similar in both BPAD and SCZ patients as the difference of these parameters were not statistically significant (p>0.05). Although BPAD patients demonstrated slightly higher mean blood urea nitrogen and serum osmolality levels, these differences were not statistically significant. Similarly, serum sodium and albumin levels were almost identical in both groups, indicating stable electrolyte balance and protein status across the study populations. The absence of significant differences suggests that fluid balance and osmotic regulation are not markedly altered between BPAD and SCZ patients in this sample. These findings indicate that serum osmolality and related biochemical parameters may not serve as distinguishing biomarkers between the two disorders, though further studies with larger sample sizes are recommended for confirmation. However the study by Kalelioglu T et al., who reported that serum osmolality in manic patients (295.34±4.90 mOsm/L) was significantly lower than that of controls (298.46±5.33 mOsm/L) [20]. Similarly, Hochman E et al., demonstrated a significant reduction in serum fluid-balance indices during manic episodes compared to depressive episodes [24]. These studies reinforce the possibility that fluid balance disturbances and haemodilution may play a role in the biological profile of patients with bipolar disorder and SCZ. These changes could reflect underlying hypothalamic pituitary adrenal axis dysregulation, stress response abnormalities, or medication effects influencing water balance. Although mild dilution may not be clinically overt, it could contribute to the biological profile associated with these psychiatric disorders [25].

Limitation(s)

The present study was conducted at a single centre and therefore the results may not represent the broader population. Only selected haematological and biochemical parameters were assessed, while other potential inflammatory or immunological markers were not evaluated. Finally, the cross-sectional design of the study limits the ability to establish causal relationships between the observed laboratory findings and the psychiatric disorders.

CONCLUSION(S)

The present study found that most haematological, biochemical, inflammatory and serum osmolality parameters were comparable between patients with BPAD and SCZ. These findings suggest that these laboratory parameters alone may not be useful in differentiating BPAD from SCZ. However, monocyte levels were significantly higher in BPAD patients, which may indicate a possible difference in immune activation between the two disorders.

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