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Original Research Article

Association of Serum IL-6, CRP(Q) and Ferritin Levels among Acute Transient Psychotic Disorder, Cannabis-Induced Psychotic Disorder and Healthy Controls: A Cross-Sectional Study

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Abstract: ***Background***: Growing evidence suggests that immune dysregulation and systemic inflammation play a significant role in the pathophysiology of psychotic disorders. Acute Transient Psychotic Disorder (ATPD) and Cannabis-Induced Psychotic Disorder (CIPD) represent clinically distinct yet overlapping psychotic conditions, and differentiation from primary psychotic disorders remains challenging. Inflammatory biomarkers such as interleukin-6 (IL-6), C-reactive protein (CRP) and ferritin may offer objective biological insights. ***Aim Of the Objective:*** To evaluate and compare serum IL-6, CRP(Q), and ferritin levels among patients with ATPD, CIPD, and healthy controls, and to assess their potential role as biomarkers in transient psychotic disorders. ***Material & Methods:*** This cross-sectional study was conducted at a tertiary care teaching hospital. A total of 90 participants were recruited and divided equally into three groups: ATPD (n=30), CIPD (n=30), and normal population (n=30). Psychiatric diagnoses were made using ICD-10 criteria. Serum IL-6, CRP(Q), and ferritin levels were measured using standardized laboratory techniques. Statistical analysis was performed using SPSS, employing ANOVA, post-hoc tests, and correlation analysis. ***Results***: Mean serum IL-6, CRP(Q), and ferritin levels were significantly elevated in ATPD and CIPD groups compared to healthy controls ($p < 0.001$). CIPD patients demonstrated higher inflammatory marker levels than ATPD patients, though differences were variable across markers. Positive correlations were observed between inflammatory markers and severity of psychotic symptoms. ***Conclusion***: ATPD and CIPD are associated with heightened systemic inflammation. Inflammatory biomarkers may aid in understanding disease mechanisms, improving diagnostic precision, and guiding future immunomodulatory interventions in psychotic disorders.

Keywords: ATPD, CIPD, IL-6, CRP, Ferritin, Neuroinflammation.

INTRODUCTION

(ATPD) and Cannabis-Induced Psychotic Disorder (CIPD) remain less clearly understood from a biological perspective.

ATPD is characterized by the sudden onset of psychotic symptoms including hallucinations, delusions, and disorganized behavior, typically resolving within weeks to months[2]. Unlike schizophrenia, ATPD often follows acute psychosocial stressors and shows a favorable prognosis. CIPD, on the other hand, is precipitated by cannabis use and presents with psychotic features that may resolve after abstinence or progress to chronic psychotic illness in vulnerable individuals.

Differentiating transient psychoses from emerging primary psychotic disorders is clinically challenging. Current diagnostic approaches rely heavily on phenomenology and longitudinal follow-up, which may delay targeted interventions. Therefore,

identifying objective biological markers that reflect underlying pathophysiology is of paramount importance.

In recent years, the role of inflammation in psychiatric disorders has gained increasing attention. Neuroinflammatory processes are believed to influence neurotransmitter systems, synaptic plasticity, neurodevelopment, and blood-brain barrier integrity. Elevated levels of inflammatory cytokines and acute-phase reactants have been consistently reported in schizophrenia and mood disorders with psychotic features [3].

Interleukin-6 (IL-6) is a pro-inflammatory cytokine involved in immune regulation and neuroimmune communication. It can cross the blood-brain barrier and influence dopaminergic and glutamatergic neurotransmission. Elevated IL-6 levels have been linked to symptom severity, cognitive deficits, and poor treatment response in psychotic disorders [4].

C-reactive protein (CRP) is an acute-phase protein synthesized by the liver in response to systemic inflammation. Increased CRP levels have been associated with psychosis risk, metabolic abnormalities, and cognitive impairment [5]. Ferritin, an iron-storage protein, also acts as an inflammatory marker and reflects oxidative stress and immune activation, both of which are implicated in psychotic pathology[6].

Despite growing evidence linking inflammation to psychosis, limited studies have simultaneously examined IL-6, CRP, and ferritin in transient psychotic disorders such as ATPD and CIPD. Understanding inflammatory profiles across these conditions may provide insights into disease mechanisms, prognosis, and potential therapeutic targets.

The present study aims to compare serum IL-6, CRP(Q), and ferritin levels among ATPD patients, CIPD patients, and healthy controls in a tertiary care setting, thereby contributing to the emerging field of psycho neuroimmunology.

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional observational study was conducted at the Department of Psychiatry, SCB Medical College and Hospital, Cuttack, Odisha, a tertiary care teaching hospital.

Study Population

A total of 90 participants were enrolled and divided into three groups:

- **Group A:** Acute Transient Psychotic Disorder (ATPD) – 30 patients
- **Group B:** Cannabis-Induced Psychotic Disorder (CIPD) – 30 patients
- **Group C:** Normal Population (NP) – 30 healthy controls

Inclusion Criteria

- Age between 18 and 60 years
- Diagnosis of ATPD or CIPD as per ICD-10 criteria
- For controls: absence of psychiatric illness
- Written informed consent

Exclusion Criteria

- History of chronic psychotic disorders
- Acute or chronic inflammatory or autoimmune diseases
- Current infection or fever
- Substance use other than cannabis (for CIPD group)
- Use of anti-inflammatory or immunosuppressive drugs

Clinical Assessment

Psychiatric evaluation was performed by qualified psychiatrists. Severity of psychotic symptoms was assessed using the Brief Psychiatric Rating Scale (BPRS). Cannabis use was evaluated using the Cannabis Use Disorder Identification Test-Revised (CUDIT-R).

Laboratory Assessment

Venous blood samples were collected under aseptic conditions. Serum IL-6 levels were measured using enzyme-linked immunosorbent assay (ELISA). CRP(Q) and ferritin levels were estimated using standardized automated biochemical methods.

Statistical Analysis

Data were analyzed using SPSS software. Descriptive statistics were expressed as mean ± standard deviation. Group comparisons were performed using one-way ANOVA followed by post-hoc tests. Correlation analysis was conducted using Pearson's correlation coefficient. A p-value < 0.05 was considered statistically significant.

RESULTS

Table-1. Sociodemographic profile of the study participants

	Overall(N=90)
Age	
Mean (SD)	29.36(7.80)
Range	18.00-49.00
Age group	
18-22	19(21.1%)
23-27	25(2708%)
28-35	22(24.4%)
36-49	24(26.7%)
Gender	
Female	30(33.3%)
Male	60(66.7%)

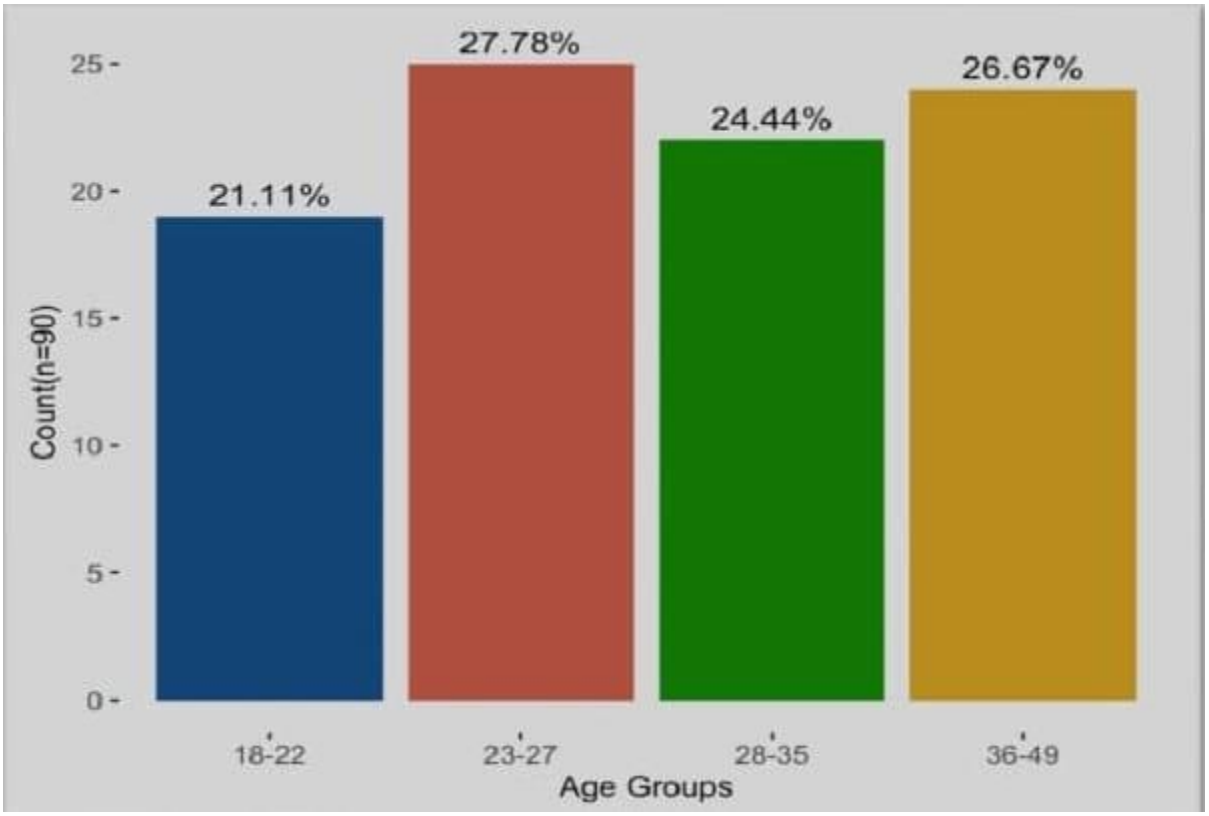

Figure1 Age distribution of the study participant

Table 2. Comparison of socio-demographic profile of the study participants

	ATPD(N=30)	CIPD (N=30)	Control (N=30)	P value
Age				0.14
Mean (SD)	27.03 (8.13)	30.60 (6.51)	30.43 (8.36)	
Range	18.00 - 42.00	23.00 - 45.00	18.00 - 49.00	
Age group				0.001
18-22	11 (36.7%)	0 (0.0%)	8 (26.7%)	
23-27	8 (26.7%)	14 (46.7%)	3 (10.0%)	
28-35	3 (10.0%)	8 (26.7%)	11 (36.7%)	
36-49	8 (26.7%)	8 (26.7%)	8 (26.7%)	
Gender				<0.001
Female	15 (50.0%)	0 (0.0%)	15 (50.0%)	
Male	15 (50.0%)	30 (100.0%)	15 (50.0%)	

Table 3. Comparison of socio-economic characteristics between three groups

	ATPD (N=30)	CIPD (N=30)	Control (N=30)	P value
Education				0.24
Graduate	3 (10.0%)	7 (23.3%)	8 (26.7%)	
Illiterate	0 (0.0%)	1 (3.3%)	1 (3.3%)	
Primary	12 (40.0%)	5 (16.7%)	5 (16.7%)	
Secondary	15 (50.0%)	17 (56.7%)	16 (53.3%)	
Occupation				0.001
Housewife	6 (20.0%)	0 (0.0%)	7 (23.3%)	
Semi-skilled	2 (6.7%)	7 (23.3%)	5 (16.7%)	
Unemployed	13 (43.3%)	3 (10.0%)	9 (30.0%)	
Unskilled	9 (30.0%)	20 (66.7%)	9 (30.0%)	
Marriage				0.006
Married	13 (43.3%)	18 (60.0%)	25 (83.3%)	
Unmarried	17 (56.7%)	12 (40.0%)	5 (16.7%)	
Socio-economic status				0.24
Lower	5 (16.7%)	6 (20.0%)	1 (3.3%)	
Lower middle	9 (30.0%)	9 (30.0%)	13 (43.3%)	
Upper	1 (3.3%)	0 (0.0%)	0 (0.0%)	
Upper lower	13 (43.3%)	9 (30.0%)	9 (30.0%)	
Upper middle	2 (6.7%)	6 (20.0%)	7 (23.3%)	
Domicile				0.061
Rural	10 (33.3%)	15 (50.0%)	13 (43.3%)	
Semi-urban	12 (40.0%)	6 (20.0%)	3 (10.0%)	
Urban	8 (26.7%)	9 (30.0%)	14 (46.7%)	
Type of family				0.012
Compound family	0 (0.0%)	4 (13.3%)	0 (0.0%)	
Extended family	7 (23.3%)	10 (33.3%)	7 (23.3%)	
Joint family	20 (66.7%)	12 (40.0%)	13 (43.3%)	
Nuclear family	3 (10.0%)	4 (13.3%)	10 (33.3%)	

Table 4. Comparison of clinical presentation among three groups

	ATPD (N=30)	CIPD (N=30)	Control (N=30)	P value
H/O Medical Psychiatry Illness				1.00
No	30 (100.0%)	30 (100.0%)	30 (100.0%)	
Substance use				<0.001
Cannabis	0 (0.0%)	10 (33.3%)	0 (0.0%)	
Cannabis and Nicotine	0 (0.0%)	20 (66.7%)	0 (0.0%)	
No substance	30 (100.0%)	0 (0.0%)	30 (100.0%)	
BPRS				<0.001
Moderate psychosis	10 (33.3%)	5 (16.7%)	0 (0.0%)	
Normal	0 (0.0%)	0 (0.0%)	30 (100.0%)	
Severe psychosis	20 (66.7%)	25 (83.3%)	0 (0.0%)	
CUDITR				<0.001
Cannabis use disorder	0	30 (100.0%)	0	
GHQ12				<0.001
Moderate mental health issues	11 (36.7%)	5 (16.7%)	0 (0.0%)	
Normal	0 (0.0%)	0 (0.0%)	30 (100.0%)	
Severe mental health issues	19 (63.3%)	25 (83.3%)	0 (0.0%)	

Table 5. Comparison of IL6 levels among the three groups

	ATPD (N=30)	CIPD (N=30)	Control (N=30)	P value
Sr. IL-6 level				<0.001
Mean (SD)	9.71 (2.65)	1.82 (0.54)	2.46 (0.64)	
Range	4.53 - 16.90	0.88 - 2.62	1.81 - 4.97	

Mean serum IL-6 levels were significantly higher in the ATPD and CIPD groups compared to the healthy control group ($p < 0.001$). CIPD patients showed higher IL-6 levels than ATPD patients, though the difference did not reach statistical significance.

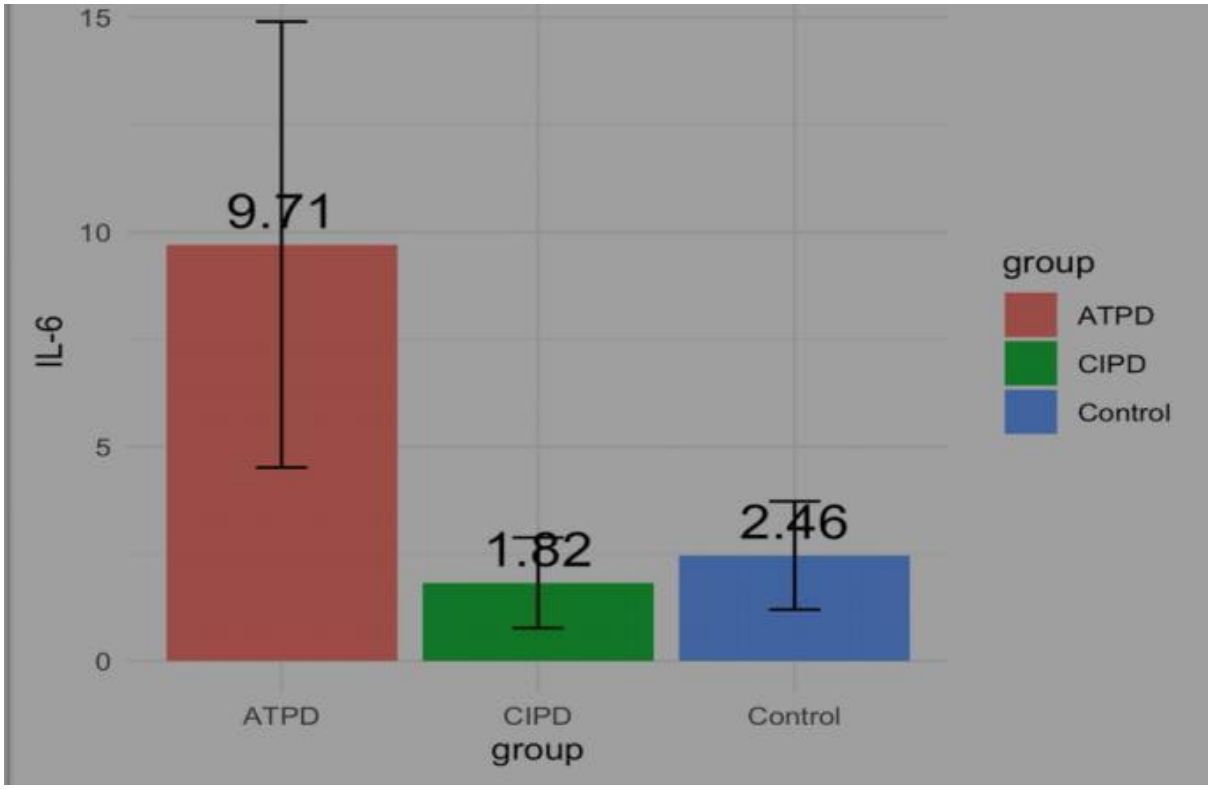

Figure2

Table 6. Comparison of CRP(Q) levels among the three groups

	ATPD (N=30)	CIPD (N=30)	Control (N=30)	P value
Sr. CRP(Q)				<0.001
Mean (SD)	3.61 (1.48)	1.41 (0.45)	2.05 (0.64)	
Range	1.81 - 7.60	0.69 - 2.43	0.92 - 3.02	

CRP(Q) levels followed a similar pattern, with significantly elevated values in both psychotic groups compared to controls ($p < 0.001$). CIPD patients demonstrated the highest mean CRP levels.

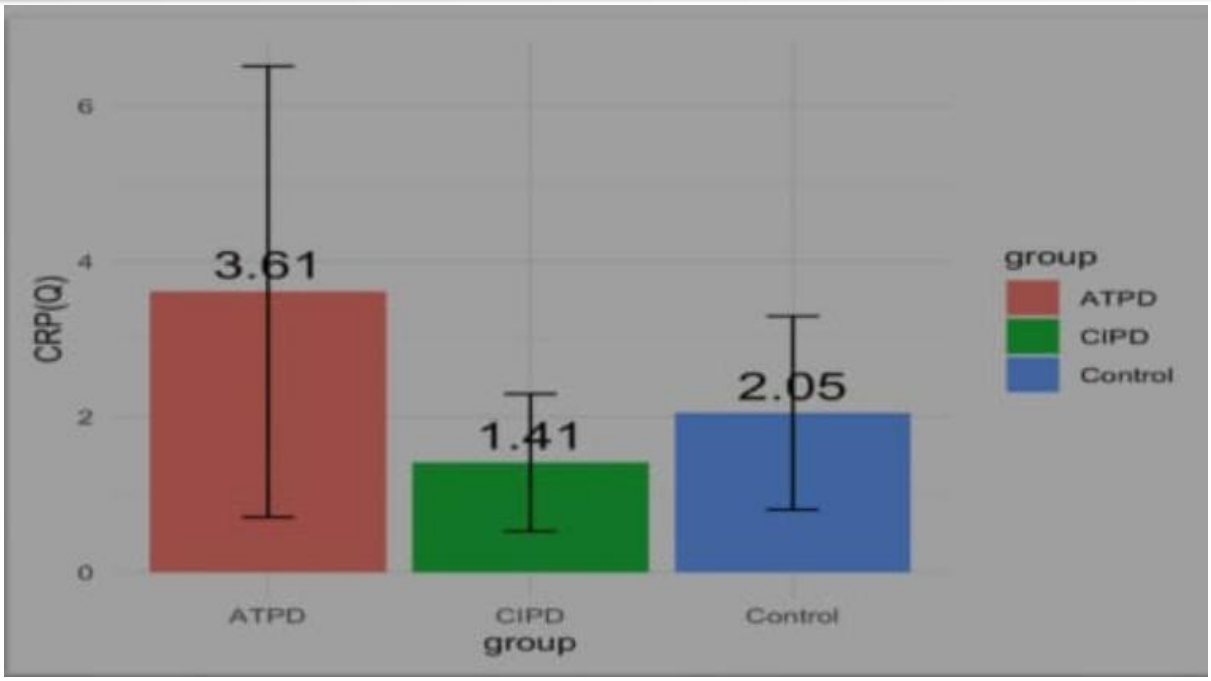

Figure3

Table 7. Comparison of Serum Ferritin levels among the three groups

	ATPD (N=30)	CIPD (N=30)	Control (N=30)	P value
Sr. Ferritin				<0.001
Mean (SD)	58.69 (18.45)	52.39 (14.59)	80.74 (23.12)	
Range	30.62 - 102.06	34.01 - 89.11	39.98 - 124.61	

Ferritin levels were also significantly increased in ATPD and CIPD groups compared to the normal population ($p < 0.001$). The CIPD group showed relatively higher ferritin levels, suggesting greater inflammatory and oxidative stress burden.

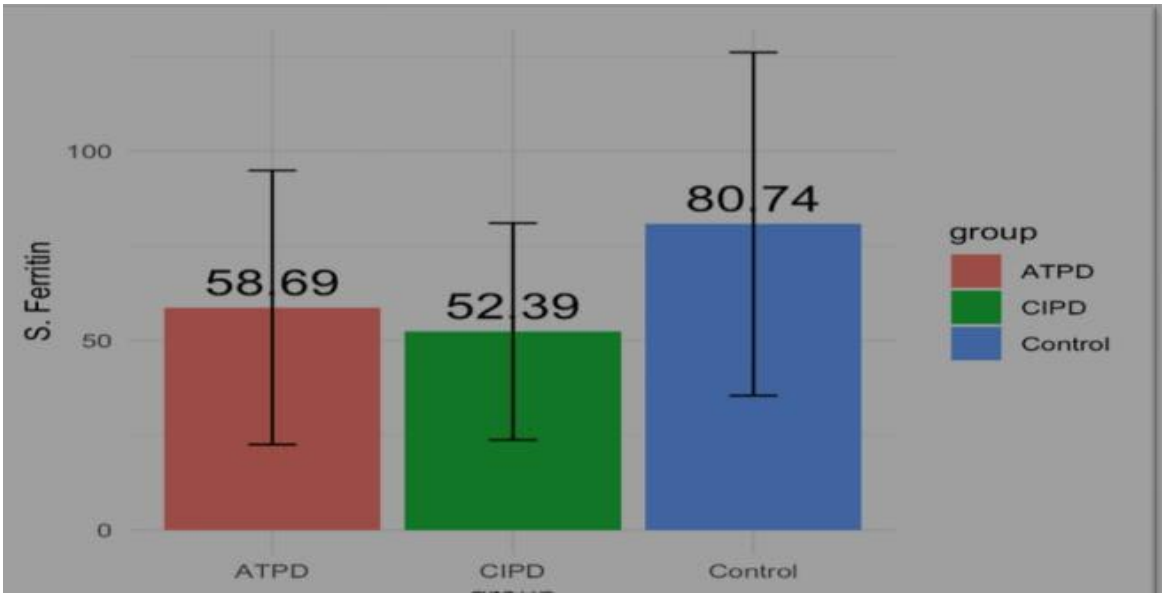

Figure 4

DISCUSSION

The present study demonstrates that patients with ATPD and CIPD exhibit significantly elevated serum IL-6, CRP(Q), and ferritin levels compared to healthy individuals, supporting the hypothesis that systemic inflammation plays a role in transient psychotic disorders.

Elevated IL-6 levels observed in both psychotic groups align with previous studies in first-episode psychosis and schizophrenia. IL-6-mediated neuroinflammation may influence dopamine dysregulation and glutamatergic dysfunction, contributing to psychotic symptomatology.

Higher inflammatory marker levels in CIPD patients may reflect the immunomodulatory effects of cannabis. Chronic cannabis use has been shown to alter cytokine balance, activate microglia, and increase oxidative stress, potentially exacerbating inflammatory responses in vulnerable individuals.

Ferritin elevation suggests dysregulated iron metabolism and increased oxidative stress, which may contribute to neurotoxicity and symptom severity. The observed correlations between inflammatory markers and symptom severity further reinforce the clinical relevance of immune activation in psychosis. These findings highlight the potential utility of inflammatory biomarkers in differentiating transient psychoses and identifying individuals at risk for progression to chronic psychotic disorders.

CONCLUSION

This study provides evidence that ATPD and CIPD are associated with increased systemic inflammation, as reflected by elevated serum IL-6, CRP(Q), and ferritin levels. The findings support the role of immune dysregulation in the pathophysiology of transient psychotic disorders and suggest that inflammatory biomarkers may serve as valuable adjuncts in diagnosis, prognosis, and treatment planning.

Clinical Implications and Future Directions

Routine assessment of inflammatory markers may enhance early identification of high-risk psychotic states. Future longitudinal studies are needed to determine whether these biomarkers predict conversion to chronic psychosis and to explore the role of anti-inflammatory interventions in improving outcomes.

Strengths and Limitations

The study's strengths include a well-defined sample and simultaneous evaluation of multiple inflammatory markers. Limitations include its cross-sectional design, modest sample size, and lack of longitudinal follow-up.

Conflict of interest: Nil
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