ORIGINAL RESEARCH

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Inflammatory Indices and Clinical Indication for Hospitalization in Patients Presenting with Acute Psychosis

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Abstract

Objective: Growing evidence suggests that inflammatory mechanisms may contribute to psychotic disorders, and hematologic indices derived from routine complete blood count parameters may offer practical biomarkers in emergency settings. This retrospective, single-center, observational study evaluated the relationship of the systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune-inflammation value (PIV) with clinical outcomes in adults presenting to the emergency department with acute psychosis.

Materials and Methods: Adult patients presenting between January 1, 2021, and December 31, 2023, were included. The primary outcome was the clinical indication for hospitalization after emergency department assessment, defined as either completed admission or refusal of a recommended admission. Patients discharged without a recommendation for admission constituted the no-indication group. Secondary outcomes were inpatient length of stay, emergency department length of stay, and 12-month revisits.

Results: A total of 260 patients were analyzed (mean age, 36.89±12.29 years; 43.1% female). A clinical indication for hospitalization was documented in 201 patients (77.3%): 176 were admitted, and 25 declined the recommended admission. SII was higher in the indication group in the unadjusted analysis (1084.57±828.79 vs 884.53±590.99; p=0.045), but this association was not retained after multivariable adjustment. SIRI and PIV were not associated with the clinical indication for hospitalization. ROC analysis showed limited discriminative performance for SII (AUC, 0.586; 95% CI, 0.523–0.646; p=0.041). No significant associations were found between the inflammatory indices and inpatient length of stay or revisit frequency.

Conclusion: Although SII showed a modest unadjusted association with the clinical indication for hospitalization, its limited discrimination and lack of an independent association after adjustment do not support its clinical use. These exploratory findings do not support SII, SIRI, or PIV as triage biomarkers in acute psychosis at present.

Keywords: Acute psychosis, biomarkers, clinical indication for hospitalization, disposition, emergency department, inflammatory indices

Introduction

Acute psychosis is a psychiatric condition characterized by marked disturbances in thought content, perception, behavior, and reality testing, often requiring urgent evaluation and intervention [1]. Patients commonly present to emergency departments with agitation, disorganized behavior, risk of harm to self or others, impaired insight, and an inability to maintain self-care [2]. Emergency assessment is primarily aimed at excluding underlying medical causes, ensuring safety, determining clinical severity, and making appropriate disposition decisions regarding hospitalization or discharge. However, the heterogeneous presentation of acute psychosis and the frequent lack of reliable collateral history may complicate early risk stratification.

In recent years, increasing evidence has suggested that psychotic disorders may involve not only neurochemical abnormalities but also immune and inflammatory mechanisms [3,4]. Alterations in peripheral inflammatory markers, elevated cytokine levels, and dysregulated immune responses have been reported during psychotic episodes in schizophrenia spectrum disorders and mood disorders with psychotic features [5–7]. These findings raise the possibility that systemic inflammation may accompany acute psychiatric exacerbations.

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Composite inflammatory indices derived from routine complete blood count parameters, including neutrophils, lymphocytes, monocytes, and platelets, have attracted growing interest as practical biomarkers [8–10]. Among these, the systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune-inflammation value (PIV) may provide a more integrated reflection of the inflammatory burden than single laboratory parameters alone. Their low cost, rapid availability, and ease of calculation make them potentially attractive for investigation in emergency settings, where timely decision-making is essential [11,12].

Nevertheless, the potential investigational relevance of these indices in patients presenting with acute psychosis remains uncertain. Previous studies have largely focused on specific diagnostic categories, involved relatively small samples, or provided limited data regarding emergency department outcomes [13–15]. In particular, the relationship between inflammatory indices and disposition-related endpoints, such as the clinical indication for hospitalization, length of stay, and revisit rates, has not been sufficiently clarified [16].

The aim of this study was to evaluate SII, SIRI, and PIV in patients presenting to the emergency department with acute psychosis and to examine their associations with emergency department disposition, particularly the clinical indication for hospitalization. We also investigated whether these indices were related to inpatient length of stay and subsequent revisits.

Methods

Study Design and Setting

This retrospective, single-center, observational study was conducted in the emergency department of İzmir Katip Çelebi University Ataturk Research and Training Hospital Training and Research Hospital. Adult patients presenting with acute psychosis between January 1, 2021, and December 31, 2023, were eligible for inclusion.

Data Collection

Potential cases were identified through the hospital information system using ICD-10 diagnostic codes F20, F23, F25, F28, F30, and F32. Diagnoses were verified through a review of electronic medical records, emergency physician notes, and available psychiatric consultation records.

Demographic variables included age and sex. Clinical variables comprised emergency department length of stay, the documented clinical recommendation regarding hospitalization, actual disposition, inpatient length of stay among admitted patients, and post-discharge revisits. Admission recommendations were made jointly by the emergency medicine and psychiatry teams according to routine clinical assessment. The documented clinical recommendation was abstracted separately from actual disposition so that patients who declined a recommended admission could be classified according to the clinical indication.

Laboratory analyses were based on the first complete blood count obtained at presentation. SII was calculated as platelet count×neutrophil count/lymphocyte count, SIRI as neutrophil count×monocyte count/lymphocyte count, and PIV as platelet count×neutrophil count×monocyte count/lymphocyte count. Cell counts were entered as $\times 10^9$/L. Because these are calculated composite indices without standardized clinical units, SII, SIRI, and PIV are reported as arbitrary units (AU).

Study Population

Patients younger than 18 years; those with suspected alcohol- or substance-induced psychosis, psychosis secondary to an organic medical condition, active infection, or pregnancy; those with incomplete clinical or laboratory data; and those transferred to another institution with unavailable outcome data were excluded. During the study period, 663 records were screened; after application of the exclusion criteria, 260 patients were included in the final analysis. Analyses were conducted on complete cases, and no missing-value imputation was performed.

Outcome Measures

The primary outcome was the presence or absence of a clinical indication for hospitalization after emergency department assessment. The indication-present group included patients who were admitted and patients who declined a documented recommendation for admission. The no-indication group comprised patients discharged from the emergency department without a recommendation for hospitalization. Actual disposition (hospitalized, discharged, or refused recommended hospitalization) was reported separately. This pragmatic endpoint reflected real-world clinical decision-making but was not considered a validated measure of psychosis severity. Secondary outcomes were inpatient length of stay among admitted patients, emergency department length of stay, and revisits within 12 months.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Distributional assumptions for continuous variables were assessed using the Shapiro–Wilk test together with visual inspection of histograms and Q–Q plots. Continuous variables are presented as mean±standard deviation for consistent descriptive reporting. Group comparisons were performed using the independent-samples t test when parametric assumptions were met and the Mann–Whitney U or

Kruskal–Wallis test when they were not. No logarithmic or other transformation was applied to SII, SIRI, or PIV. Categorical variables were compared using the chi-square test. Associations between continuous variables were examined using Spearman correlation analysis. Multivariable logistic regression was used to evaluate factors associated with the clinical indication for hospitalization; SII was entered on its original scale and reported per 100-AU increase. Receiver operating characteristic (ROC) curve analysis was used to assess discrimination. Missing data were handled by complete-case analysis without imputation. A two-sided p value of <0.05 was considered statistically significant.

Results

A total of 260 patients were included in the study. Of these, 112 (43.1%) were female and 148 (56.9%) were male. The mean age was 36.89±12.29 years. Diagnostic categories were manic episode in 50 patients (19.2%), depressive episode in 42 (16.2%), schizophrenic episode in 74 (28.5%), and nonorganic psychotic disorder in 94 (36.1%). Mean neutrophil, lymphocyte, platelet, and monocyte counts were 6.71±2.78×10^9/L, 2.15±0.80×10^9/L, 283.38±77.75×10^9/L, and 0.71±0.27×10^9/L, respectively. Mean SII, SIRI, and PIV values were 1039.18±784.66 AU, 2.74±2.49 AU, and 784.35±771.92 AU, respectively (Table 1).

Table 1. Baseline characteristics of the study population

Variable	Total (n=260)
Age, years	36.89±12.29
Female sex, n (%)	112 (43.1)
Male sex, n (%)	148 (56.9)
Manic episode, n (%)	50 (19.2)
Depressive episode, n (%)	42 (16.2)
Schizophrenic episode, n (%)	74 (28.5)
Nonorganic psychotic disorder, n (%)	94 (36.1)
Neutrophil, ×10^9/L	6.71±2.78
Lymphocyte, ×10^9/L	2.15±0.80
Platelet, ×10^9/L	283.38±77.75
Monocyte, ×10^9/L	0.71±0.27
SII, AU	1039.18±784.66
SIRI, AU	2.74±2.49
PIV, AU	784.35±771.92
Emergency department stay, days	1.40±1.85
Hospital stay, days*	32.29±19.14

*Among hospitalized patients. AU: arbitrary units; PIV: pan-immune-inflammation value; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index.

A clinical indication for hospitalization was documented in 201 patients (77.3%). Of these, 176 (67.7% of the total cohort) were hospitalized, and 25 (9.6%) declined the recommended admission. The remaining 59 patients (22.7%) had no indication for hospitalization and were discharged from the emergency department. Among hospitalized patients, the mean inpatient length of stay was 32.29±19.14 days, whereas the mean emergency department length of stay in the total cohort was 1.40±1.85 days. During the 12-month follow-up period, 66 patients (25.4%) had at least one revisit (Table 2).

In sex-based comparisons, only SIRI was significantly higher in male patients than in female patients (2.98±2.78 vs 2.42±2.01 AU; p=0.017). No significant sex-related differences were observed for SII or PIV (p=0.724 and p=0.298, respectively).

No significant differences in SII, SIRI, or PIV were identified across diagnostic subgroups (all p>0.05). When patients were compared according to actual disposition status (hospitalized, discharged, or refused recommended admission), none of the inflammatory indices differed significantly among the three groups (SII, p=0.090; SIRI, p=0.245; PIV, p=0.161).

In the prespecified binary analysis based on the clinical indication for hospitalization, SII was higher in the indication-present group than in the no-indication group (1084.57±828.79 vs 884.53±590.99 AU; p=0.045). Neither SIRI nor PIV showed a significant between-group difference (p=0.107 and p=0.071, respectively) (Table 3).

In multivariable logistic regression analysis adjusting for age, sex, and diagnostic category, SII was not independently associated with the clinical indication for hospitalization (adjusted OR, 1.03 per 100-AU increase; 95% CI, 1.00–1.07; p=0.076) (Table 4). No other covariates were significantly associated with the outcome.

The discriminatory performance of SII for identifying a clinical indication for hospitalization was assessed using ROC analysis. The area under the curve was 0.586 (95% CI, 0.523–0.646; p=0.041), indicating limited

Table 2. Clinical outcomes and dispositions

Variable	n (%)
Clinical indication for hospitalization present	201 (77.3)
Hospitalized	176 (67.7)
Refused recommended hospitalization	25 (9.6)
No clinical indication; discharged from ED	59 (22.7)
No revisit within 12 months	194 (74.6)
≥ 1 revisit within 12 months	66 (25.4)

ED: emergency department. Patients who refused recommended hospitalization were included in the indication-present group for the primary analysis.

Table 3. Inflammatory indices according to clinical indication for hospitalization

Variable	Indication present (n=201)	No indication (n=59)	p
SII, AU	1084.57±828.79	884.53±590.99	0.045
SIRI, AU	2.84±2.60	2.41±2.03	0.107
PIV, AU	817.17±806.11	672.52±635.34	0.071

AU: arbitrary units; PIV: pan-immune-inflammation value; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index.

Table 4. Multivariable logistic regression analysis for clinical indication for hospitalization

Variable	Adjusted OR (95% CI)	p
Age (per 1-year increase)	1.00 (0.98–1.02)	0.910
Male sex	0.91 (0.53–1.56)	0.740
Manic episode	1.19 (0.46–3.04)	0.720
Schizophrenic episode	0.89 (0.41–1.96)	0.780
Nonorganic psychotic disorder	0.86 (0.39–1.88)	0.700
SII (per 100-AU increase)	1.03 (1.00–1.07)	0.076

AU: arbitrary units; CI: confidence interval; OR: odds ratio; SII: systemic immune-inflammation index. The outcome was the documented clinical indication for hospitalization (present vs absent).

Table 5. Correlation of inflammatory indices with outcomes

Variable	Hospital stay, rho / p	12-month revisit count, rho / p
SII	–0.060 / 0.501	–0.049 / 0.433
SIRI	–0.102 / 0.256	–0.084 / 0.174
PIV	–0.126 / 0.159	–0.060 / 0.336

PIV: pan-immune-inflammation value; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index.

discrimination. The optimal cutoff value was >668.42 AU, yielding a sensitivity of 69.15% and a specificity of 47.6% (Fig. 1).

Correlation analysis showed no significant association between the inflammatory indices and inpatient length of stay: SII (rho=–0.060, p=0.501), SIRI (rho=–0.102, p=0.256), and PIV (rho=–0.126, p=0.159). Similarly, no significant correlations were found between these indices and total revisit count: SII (rho=–0.049, p=0.433), SIRI (rho=–0.084, p=0.174), and PIV (rho=–0.060, p=0.336) (Table 5).

Discussion

Interest in inflammatory mechanisms in psychotic disorders has increased substantially in recent years [14,15]. In this cohort, SII

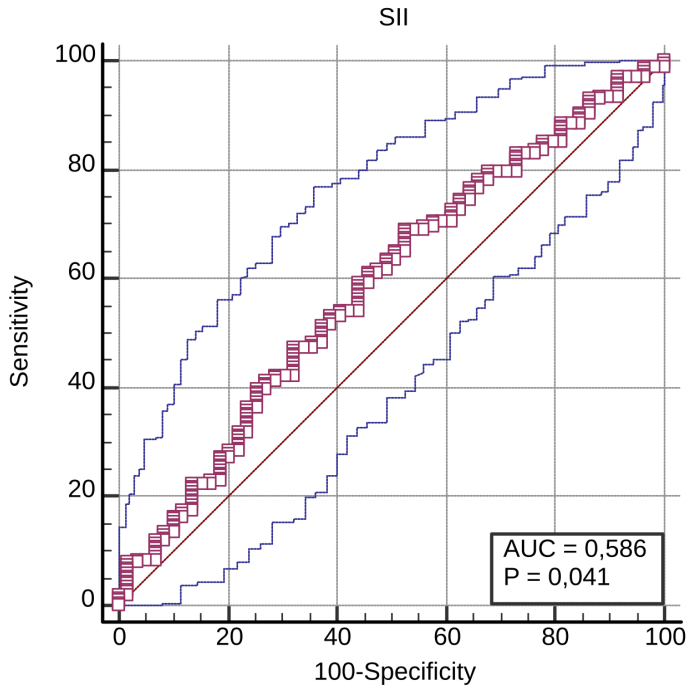

Figure 1. ROC Curve of SII for identifying a clinical indication for hospitalization

was the only composite index to show a nominal unadjusted difference according to the clinical indication for hospitalization. However, this association was not independent after adjustment, and none of the examined indices demonstrated clinically useful discrimination. The observed unadjusted SII difference may reflect the combined contribution of neutrophils, lymphocytes, and platelets to systemic stress and inflammatory responses [11,17], but the present study cannot establish a causal or clinically actionable relationship.

Inflammatory indices did not differ across diagnostic subgroups. In the emergency setting, acute agitation, behavioral dyscontrol, insomnia, autonomic arousal, and psychological stress may overlap across schizophrenia spectrum disorders, mood episodes with psychotic features, and brief psychotic presentations. Any biological signal captured by these indices may therefore relate to nonspecific acute decompensation rather than to formal diagnostic categories. This interpretation remains exploratory.

The clinical indication for hospitalization was used as a pragmatic disposition-associated endpoint. To avoid conflating the clinical recommendation with the disposition ultimately completed, the 25 patients who declined the recommended admission were included in the indication-present group, whereas actual disposition was reported separately. Although the endpoint reflects factors commonly considered in routine care—such as prominent psychotic symptoms, risk to self or others, impaired judgment, inability to meet basic needs, or poor treatment

adherence [18]—it is not a substitute for a standardized psychosis severity scale and may also be influenced by clinician judgment and contextual factors.

The predictive performance of SII was clearly limited. An AUC of 0.586, low specificity at the identified cutoff, and loss of significance after multivariable adjustment do not support SII as either an independent or supplementary triage biomarker. SIRI and PIV also showed no clinically meaningful associations. Accordingly, these findings should be viewed as exploratory and hypothesis-generating rather than as evidence for clinical implementation.

We did not observe associations between the inflammatory indices and either inpatient length of stay or revisit frequency. These outcomes are shaped by many determinants beyond the initial biological state, including treatment response, medication adherence, substance use, family support, housing stability, outpatient follow-up, and healthcare access [19]. Such factors may outweigh any contribution from baseline inflammatory activity.

Although CBC-derived indices are inexpensive and readily available, accessibility alone does not establish clinical value. The present results do not show that SII, SIRI, or PIV adds useful information beyond routine clinical assessment. At present, these indices should remain investigational and should not be used to determine psychiatric admission or discharge decisions.

Study Limitations

Several limitations should be acknowledged. The retrospective, single-center design limits causal inference and external validity. Standardized psychosis severity scales were not consistently available, necessitating the use of a clinician-determined disposition endpoint. Admission recommendations were made by different emergency medicine and psychiatry clinicians in routine practice; therefore, interclinician variability and the absence of a standardized admission algorithm or interrater reliability assessment may have affected classification. Although suspected substance-induced psychosis was excluded, substance exposure was based mainly on clinical documentation and was not systematically confirmed by toxicology testing. Data on smoking, body mass index or obesity, and psychotropic or anti-inflammatory medication exposure were not consistently available, leaving potential residual confounding. The inclusion of patients who refused recommended admission in the indication-present group preserves the documented clinical recommendation but does not equate refusal with completed hospitalization. The multivariable model may have been underpowered to detect small independent effects. Only the first blood sample was analyzed, temporal changes in inflammatory markers were not assessed, and the interval between symptom onset and emergency department presentation was unavailable.

Conclusion

In this exploratory study, SII showed a modest unadjusted association with the clinical indication for hospitalization, but the association was not independent after adjustment, and discrimination was limited. SIRI and PIV were not associated with the primary or secondary outcomes. These findings do not support the clinical use of SII, SIRI, or PIV as triage biomarkers in acute psychosis. Prospective, multicenter studies using standardized severity and disposition criteria would be required before any clinical role could be considered.

Ethics

Ethics Committee Approval: This study was approved by The Izmir Katip Celebi University Health Research Ethics Committee on 16 January 2025 (Approval No: 0038)

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

Use of AI for Writing Assistance: The authors declared that artificial intelligence was not used in the study.

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