



Original Research Article

Association of Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios with Quality of Life in Schizophrenia, Bipolar Disorder, and Major Depressive Disorder: A Cross-Sectional Study

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ABSTRACT

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Background: Quality of life is substantially impaired in schizophrenia and mood disorders. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are inexpensive peripheral inflammatory indices, but their relationship with patient-reported quality of life across major psychiatric diagnoses remains insufficiently characterized.

Aim: To examine the association of NLR and PLR with global and domain-specific quality of life in drug-naïve and drug-free adults with schizophrenia, bipolar disorder, and major depressive disorder.

Methods: This hospital-based cross-sectional study included 90 adults aged 18-60 years: 30 with schizophrenia, 30 with bipolar disorder, and 30 with major depressive disorder, diagnosed using ICD-11 clinical requirements. Quality of life was assessed using the 26-item WHOQOL-BREF. NLR and PLR were derived from complete blood counts. The article classified NLR as <3 versus >3 and PLR as <137 versus >137. Original analyses used IBM SPSS Statistics 26. For this article, Welch t tests, Satterthwaite degrees of freedom, 95% confidence intervals, Hedges g, and Holm-adjusted p values were reconstructed from the reported group-level data using Python 3.13.5, NumPy 2.3.5, and SciPy 1.17.0.

Results: Participants with NLR >3 had lower quality-of-life scores than those with NLR <3 for the article-defined global score (31.40 +/- 1.69 vs 45.86 +/- 1.82; mean difference 14.46, 95% CI 13.71-15.21; $t(73.9)=38.18$; $p<0.05$), physical health (mean difference 13.30), psychological health (9.30), social relationships (6.61), and environment (4.90); all Holm-adjusted $p<0.05$. PLR >137 was likewise associated with lower global quality of life (30.50 +/- 1.50 vs 39.70 +/- 7.02; mean difference 9.20, 95% CI 7.38-11.02; $t(80.5)=10.08$; $p<0.05$) and lower scores in all four domains. Quality-of-life scores also differed across diagnoses, with the lowest means in schizophrenia and highest means in major depressive disorder in this sample (all omnibus $p<0.05$).

Conclusions: Higher NLR and PLR categories were strongly associated with poorer quality of life across physical, psychological, social, and environmental domains. The cross-sectional design, diagnostic confounding, dichotomization of continuous biomarkers, and unusually small reported standard deviations require cautious interpretation. Participant-level multivariable verification is essential before journal submission.

INTRODUCTION

Schizophrenia, bipolar disorder, and major depressive disorder contribute substantially to disability, premature mortality, impaired social participation, and reduced occupational functioning worldwide [1,2]. Symptom reduction is important, but recovery is not adequately captured by clinician-rated psychopathology alone. Quality of life (QOL) incorporates the individual's appraisal of physical health, psychological well-being, social relationships, and environmental circumstances and is therefore a central patient-reported outcome in psychiatric care [3-5].

The World Health Organization defines QOL as an individual's perception of their position in life within their cultural and value context and in relation to their goals, expectations, standards, and concerns [3]. The WHOQOL-BREF was designed as a brief cross-culturally applicable instrument and provides four domain scores: physical health, psychological health, social relationships, and environment [4,5]. Studies in severe mental illness consistently demonstrate broad QOL impairment, although the relative burden across schizophrenia, bipolar disorder, and depression varies by symptom state, remission, resilience, functioning, and social context [12-16].

Inflammatory dysregulation has emerged as a transdiagnostic biological feature of major psychiatric disorders. Cross-disorder meta-analytic evidence supports alterations in peripheral cytokines and immune-cell measures, although effect sizes, specificity, and clinical utility remain heterogeneous [7]. Ratios derived from routine complete blood counts, particularly NLR and PLR, integrate components of innate immune activation, adaptive immune regulation, and platelet-linked inflammatory activity. Meta-analyses have reported higher NLR in non-affective psychosis and depression and elevations of NLR and PLR in mood disorders, supporting their use as low-cost research biomarkers [8-11].

A biologically plausible relationship may exist between inflammatory activity and QOL. Inflammation may contribute to fatigue, sleep disturbance, reduced motivation, cognitive inefficiency, anhedonia, somatic symptoms, and functional disability, each of which can lower patient-perceived well-being. Outside psychiatry, chronic inflammatory biomarkers have been associated with emotional and relational aspects of QOL [17]. However, direct cross-diagnostic evidence linking NLR and PLR to WHOQOL-BREF outcomes in drug-naïve and drug-free psychiatric samples remains limited.

Medication exposure is an important confounder in immune research. Antipsychotics, mood stabilizers, antidepressants, metabolic adverse effects, and treatment-related changes in symptoms may alter blood-cell indices and QOL. By enrolling drug-naïve individuals and patients who had been medication-free for prespecified periods, the present study attempted to reduce immediate pharmacological confounding. The QOL analysis addressed a article objective distinct from the diagnostic comparison of inflammatory ratios and from the association of inflammatory ratios with clinician-rated illness severity.

AIMS AND OBJECTIVES

Aim

To determine the association of NLR and PLR with quality of life in drug-naïve and drug-free adults with schizophrenia, bipolar disorder, and major depressive disorder.

Primary objectives

- To compare WHOQOL-BREF physical, psychological, social-relationship, and environmental domain scores between participants with NLR <3 and NLR >3.
- To compare the same WHOQOL-BREF outcomes between participants with PLR <137 and PLR >137.

Secondary objectives

- To compare quality-of-life scores across schizophrenia, bipolar disorder, and major depressive disorder.
- To estimate unstandardized mean differences, 95% confidence intervals, and standardized effect sizes for the inflammatory-ratio comparisons.
- To identify methodological priorities for participant-level adjusted analyses.

Hypoarticle

Participants with higher NLR and PLR categories were hypothesized to have lower WHOQOL-BREF scores across all domains.

MATERIALS AND METHODS

Study design, setting, and reporting

A hospital-based cross-sectional study was conducted over 12 months at the Institute of Mental Health, Erragadda, Hyderabad, affiliated with Osmania Medical College. Both inpatients and outpatients were recruited by convenience

sampling. The source article included 90 participants, with 30 participants in each diagnostic group. Reporting was organized in accordance with the STROBE framework for observational studies [24].

Participants and diagnostic procedure

Adults aged 18-60 years were eligible if they fulfilled ICD-11 diagnostic requirements for schizophrenia, bipolar disorder, or major depressive disorder [6]. Diagnostic classification was established through psychiatric clinical assessment. Drug-naïve participants had not previously taken psychiatric medication. Drug-free participants had discontinued oral psychiatric medication for at least 2 months or long-acting/depot preparations for at least 3 months before blood sampling.

Exclusion criteria were intellectual disability; harmful use or dependence involving psychoactive substances; organic or neurodegenerative disorders; current infection or fever; endocrine, inflammatory, autoimmune, cerebrovascular, renal, cardiac, or hepatic disease; diabetes mellitus; hypertension; cancer; body mass index >30 kg/m²; heavy smoking (>20 cigarettes/day); pregnancy or lactation; and use during the preceding 2 weeks of non-steroidal anti-inflammatory drugs, aspirin, corticosteroids, immunosuppressants, or antibiotics.

Assessment instruments

Table 1. Diagnostic, clinical, and quality-of-life assessment instruments

Instrument	Construct	Administration/scoring	Role in study	Reference
ICD-11 CDDR	Diagnostic classification	Clinical descriptions and diagnostic requirements for schizophrenia, bipolar disorder, and depressive disorders	Eligibility and diagnostic grouping	[6]
PANSS	Schizophrenia symptom severity	30 clinician-rated items covering positive, negative, and general psychopathology; higher scores indicate greater symptom burden	Diagnosis-specific clinical characterization	[20]
YMRS	Manic symptom severity	11 clinician-rated items; higher scores indicate more severe manic symptoms	Clinical characterization of bipolar mania	[21]
HAM-D	Depressive symptom severity	Clinician-rated depressive symptom scale; higher scores indicate greater depressive symptom burden	Clinical characterization of bipolar depression and MDD	[22]
CGI-S	Global clinical severity	Single clinician-rated item from 1 (normal) to 7 (among the most extremely ill)	Common severity measure across diagnoses	[23]
WHOQOL-BREF	Quality of life	26 items; four domains: physical, psychological, social relationships, and environment; higher transformed scores indicate better QOL	Primary patient-reported outcome	[3-5]

The article additionally reported a transformed "global QOL" score. Because the standard WHOQOL-BREF formally includes two general items rather than a universally defined global composite, the derivation of this article-defined global score should be confirmed from the original SPSS syntax before submission [3-5].

Blood collection and inflammatory ratios

Venous blood was collected into EDTA-containing vacutainers and analyzed using an automated hematology analyzer at the Institute of Mental Health diagnostic laboratory. Complete blood count parameters included total leukocyte count, hemoglobin, platelet count, and differential leukocyte percentages. NLR was calculated as neutrophil count divided by lymphocyte count. PLR was calculated as platelet count divided by lymphocyte count.

Exposure categories and outcomes

The article categorized NLR as <3 (n=37) versus >3 (n=53) and PLR as <137 (n=67) versus >137 (n=23). These thresholds were retained to reproduce the prespecified article analysis. The NLR threshold is broadly compatible with published healthy-population ranges, but neither threshold should be interpreted as a validated psychiatric QOL cut point [18]. The primary outcomes were the four WHOQOL-BREF domains. The article-defined global QOL score was treated as an exploratory secondary outcome.

Statistical analysis

The source article was analyzed in IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as n (%), and continuous variables as mean $\pm$ standard deviation. Diagnostic-group differences in QOL were assessed with one-way analysis of variance. For this manuscript, omega-squared effect sizes were reconstructed from the reported F statistics. Pairwise diagnostic contrasts were reconstructed using Welch t tests and corrected within each QOL outcome using the Holm procedure.

For the primary inflammatory-ratio analyses, Welch independent-samples t tests were reconstructed from the reported sample sizes, means, and standard deviations. Each comparison is reported with the lower-ratio minus higher-ratio mean difference, 95% confidence interval, Welch t statistic, Satterthwaite degrees of freedom, two-sided p value, and Hedges g. Holm adjustment was applied separately across the five NLR comparisons and the five PLR comparisons. Supplementary calculations used Python 3.13.5, NumPy 2.3.5, SciPy 1.17.0, pandas 2.2.3, and Matplotlib 3.10.8. Statistical significance was set at $p < 0.05$.

Because participant-level data were not available in the supplied article document, continuous correlations and multivariable regression adjusting for diagnosis, CGI-S, illness duration, employment, body mass index, and drug-naïve/drug-free status could not be performed.

Ethics

Institutional ethics committee approval was obtained from Osmania Medical College before recruitment, and written informed consent was obtained from all participants. The approval identifier and exact recruitment dates were not present in the supplied article record and must be inserted from the institutional documentation.

RESULTS

Participant characteristics

All 90 participants were included in the reported analyses: 30 with schizophrenia, 30 with bipolar disorder, and 30 with major depressive disorder. Mean age did not differ significantly across groups, whereas illness duration, age at onset, body mass index, occupation, inflammatory ratios, and quality-of-life scores differed in the source analysis. Sex distribution was balanced at 15 men and 15 women per diagnostic group.

Table 2. Selected participant characteristics by diagnostic group

Characteristic	Schizophrenia (n=30)	Bipolar disorder (n=30)	MDD (n=30)	Statistical result
Age, years	32.6 $\pm$ 5.6	31.7 $\pm$ 4.0	34.0 $\pm$ 3.2	F(2,87)=2.10; $p=0.129$
Male sex	15 (50.0%)	15 (50.0%)	15 (50.0%)	Equal distribution
Duration of illness, years	6.4 $\pm$ 5.6	6.9 $\pm$ 3.9	0.7 $\pm$ 0.2	F(2,87)=22.7; $p < 0.05$
Body mass index, kg/m ²	24.0 $\pm$ 0.3	26.0 $\pm$ 1.5	24.1 $\pm$ 0.5	F(2,87)=38.7; $p < 0.05$
NLR	3.23 $\pm$ 0.10	3.21 $\pm$ 0.50	2.30 $\pm$ 0.10	F(2,87)=77.7; $p < 0.05$
PLR	138.4 $\pm$ 2.6	131.6 $\pm$ 3.7	128.2 $\pm$ 2.1	F(2,87)=94.6; $p < 0.05$

MDD, major depressive disorder; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

Quality of life across diagnoses

WHOQOL-BREF scores differed across the three diagnostic groups for the article-defined global score and all four domains. In this sample, schizophrenia had the lowest mean QOL and major depressive disorder the highest mean QOL for every reported outcome. Omnibus effect sizes were large; however, these estimates are influenced by unusually low within-group standard deviations.

Table 3. WHOQOL-BREF scores by diagnostic group

Outcome	Schizophrenia	Bipolar disorder	MDD	ANOVA	p value	Omega squared
Global QOL	30.90 $\pm$ 1.72	35.60 $\pm$ 6.42	45.60 $\pm$ 1.90	F(2,87)=105.80	< 0.05	0.700
Physical health	38.40 $\pm$ 2.58	44.50 $\pm$ 5.35	53.10 $\pm$ 1.08	F(2,87)=135.20	< 0.05	0.749

Outcome	Schizophrenia	Bipolar disorder	MDD	ANOVA	p value	Omega squared
Psychological health	36.20 +/- 3.10	41.63 +/- 3.80	47.06 +/- 0.78	F(2,87)=105.02	<0.05	0.698
Social relationships	45.80 +/- 3.05	51.60 +/- 3.15	54.43 +/- 0.80	F(2,87)=87.40	<0.05	0.658
Environment	52.00 +/- 1.56	55.70 +/- 2.20	58.03 +/- 1.10	F(2,87)=98.50	<0.05	0.684

Table 4. Reconstructed pairwise diagnostic contrasts in WHOQOL-BREF scores

Outcome	Contrast	Mean difference	95% CI	Welch t (df)	Raw p	Holm p
Global QOL	Schizophrenia vs Bipolar disorder	-4.70	-7.17 to -2.23	-3.87 (33.1)	<0.05	<0.05
Global QOL	Schizophrenia vs MDD	-14.70	-15.64 to -13.76	-31.42 (57.4)	<0.05	<0.05
Global QOL	Bipolar disorder vs MDD	-10.00	-12.48 to -7.52	-8.18 (34.0)	<0.05	<0.05
Physical health	Schizophrenia vs Bipolar disorder	-6.10	-8.29 to -3.91	-5.63 (41.8)	<0.05	<0.05
Physical health	Schizophrenia vs MDD	-14.70	-15.73 to -13.67	-28.79 (38.9)	<0.05	<0.05
Physical health	Bipolar disorder vs MDD	-8.60	-10.63 to -6.57	-8.63 (31.4)	<0.05	<0.05
Psychological health	Schizophrenia vs Bipolar disorder	-5.43	-7.22 to -3.64	-6.06 (55.8)	<0.05	<0.05
Psychological health	Schizophrenia vs MDD	-10.86	-12.05 to -9.67	-18.61 (32.7)	<0.05	<0.05
Psychological health	Bipolar disorder vs MDD	-5.43	-6.87 to -3.99	-7.67 (31.4)	<0.05	<0.05
Social relationships	Schizophrenia vs Bipolar disorder	-5.80	-7.40 to -4.20	-7.25 (57.9)	<0.05	<0.05
Social relationships	Schizophrenia vs MDD	-8.63	-9.80 to -7.46	-14.99 (33.0)	<0.05	<0.05
Social relationships	Bipolar disorder vs MDD	-2.83	-4.04 to -1.62	-4.77 (32.7)	<0.05	<0.05
Environment	Schizophrenia vs Bipolar disorder	-3.70	-4.69 to -2.71	-7.51 (52.3)	<0.05	<0.05
Environment	Schizophrenia vs MDD	-6.03	-6.73 to -5.33	-17.30 (52.1)	<0.05	<0.05
Environment	Bipolar disorder vs MDD	-2.33	-3.24 to -1.42	-5.19 (42.6)	<0.05	<0.05

Mean difference is first diagnosis minus second diagnosis; negative values indicate lower QOL in the first diagnosis. Holm adjustment was applied to the three pairwise contrasts within each outcome.

Quality of life according to NLR category

Across all five outcomes, participants with NLR >3 had lower mean quality-of-life scores than participants with NLR <3. The largest unstandardized difference was observed for the article-defined global score, followed by physical health.

Table 5. WHOQOL-BREF outcomes according to NLR category

Outcome	NLR <3	NLR >3	Mean difference	95% CI	Welch t (df)	Raw p	Holm p	Hedges g
Global QOL	45.86 +/- 1.82 (n=37)	31.40 +/- 1.69 (n=53)	14.46	13.71 to 15.21	38.18 (73.9)	<0.05	<0.05	8.22
Physical health	53.10 +/- 1.23 (n=37)	39.80 +/- 2.91 (n=53)	13.30	12.41 to 14.19	29.69 (74.9)	<0.05	<0.05	5.56
Psychological health	47.10 +/- 0.75 (n=37)	37.80 +/- 3.34 (n=53)	9.30	8.35 to 10.25	19.58 (59.3)	<0.05	<0.05	3.53
Social relationships	54.51 +/- 0.76 (n=37)	47.90 +/- 3.84 (n=53)	6.61	5.52 to 7.70	12.19 (57.7)	<0.05	<0.05	2.19
Environment	58.10 +/- 1.04 (n=37)	53.20 +/- 2.14 (n=53)	4.90	4.22 to 5.58	14.41 (79.9)	<0.05	<0.05	2.74

Mean difference is lower-ratio category minus higher-ratio category; positive values indicate better QOL in the lower-ratio category. Hedges g values are exceptionally large for several outcomes because of the very small reported within-group standard deviations.

Quality of life according to PLR category

Participants with PLR >137 also had lower mean scores across the defined global outcome and all four WHOQOL-BREF domains. The largest difference was observed for physical health, followed by psychological health and social relationships.

Table 6. WHOQOL-BREF outcomes according to PLR category

Outcome	PLR <137	PLR >137	Mean difference	95% CI	Welch t (df)	Raw p	Holm p	Hedges g
Global QOL	39.70 +/- 7.02 (n=67)	30.50 +/- 1.50 (n=23)	9.20	7.38 to 11.02	10.08 (80.5)	<0.05	<0.05	1.49
Physical health	48.26 +/- 5.65 (n=67)	36.86 +/- 0.81 (n=23)	11.40	9.98 to 12.82	16.04 (73.4)	<0.05	<0.05	2.30
Psychological health	44.16 +/- 3.48 (n=67)	34.26 +/- 1.05 (n=23)	9.90	8.95 to 10.85	20.70 (87.2)	<0.05	<0.05	3.21
Social relationships	52.90 +/- 2.20 (n=67)	43.86 +/- 0.81 (n=23)	9.04	8.41 to 9.67	28.48 (87.5)	<0.05	<0.05	4.60
Environment	56.67 +/- 1.91 (n=67)	51.08 +/- 1.04 (n=23)	5.59	4.95 to 6.23	17.55 (70.8)	<0.05	<0.05	3.20

Mean difference is lower-ratio category minus higher-ratio category; positive values indicate better QOL in the lower-ratio category. Hedges g values are exceptionally large for several outcomes because of the very small reported within-group standard deviations.

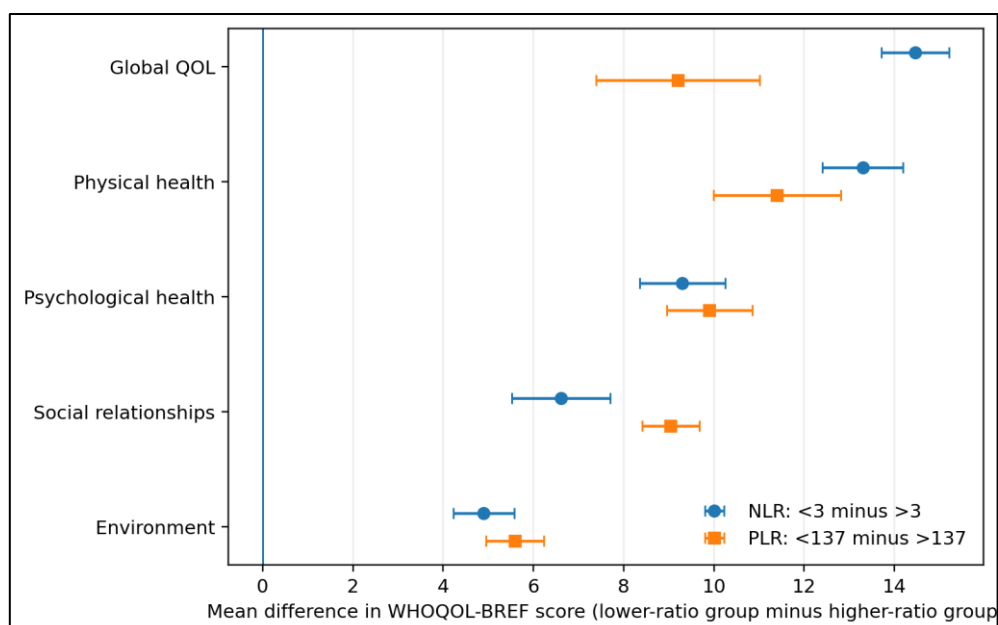


Figure 1. Mean differences and 95% confidence intervals in quality-of-life scores between lower and higher NLR/PLR categories. Positive values favor the lower inflammatory-ratio category.

DISCUSSION

Principal findings

In this cross-diagnostic sample of 90 drug-naïve and drug-free adults, higher NLR and PLR categories were consistently associated with lower QOL across physical, psychological, social, and environmental domains. The direction of association was uniform for both inflammatory ratios. NLR category showed the largest differences for the article-defined global score and physical health, whereas PLR category showed pronounced differences for physical, psychological, and social outcomes. QOL also differed substantially by diagnosis, with schizophrenia showing the lowest mean scores across all outcomes in this dataset.

The magnitude and consistency of the findings support the study hypothesis, but the statistical effects are substantially larger than typically observed in clinical psychiatry. This is driven partly by the unusually small standard deviations reported in several article tables. The results should therefore be regarded as a faithful reconstruction of the article summary data rather than definitive participant-level estimates.

Quality of life across diagnostic groups

The lower QOL observed in schizophrenia is broadly compatible with studies showing major impairment in psychological and social domains among people with schizophrenia compared with bipolar disorder and healthy groups [12-14]. Akvardar et al. reported lower WHOQOL-BREF physical scores in schizophrenia and bipolar disorder than in healthy participants and particularly low psychological and social scores in schizophrenia [12]. Hofer et al. further demonstrated that symptomatic remission and resilience are important correlates of QOL in both schizophrenia and bipolar disorder [13].

The finding that the MDD group had higher mean QOL than the schizophrenia and bipolar groups should not be generalized beyond this sample. QOL in depression is usually impaired and remains sensitive to residual symptoms, recurrence, chronicity, social support, and functional recovery [15,16]. In the present article, illness duration was much shorter in the MDD group than in the schizophrenia and bipolar groups, creating an important alternative explanation for the diagnostic gradient.

Inflammatory ratios and quality of life

Meta-analytic evidence indicates that NLR and related blood-cell ratios are elevated across non-affective psychosis and mood disorders [8-11]. These markers are nonspecific and cannot identify a single inflammatory pathway, but they may summarize the balance between innate immune activation, adaptive immune regulation, and platelet-associated inflammation. A higher ratio could therefore index a clinical state characterized by greater physiological stress, symptom burden, or medical vulnerability.

Direct psychiatric evidence connecting NLR or PLR to WHOQOL-BREF domains remains limited, making the present QOL-focused analysis potentially novel. In a broader aging sample, chronic inflammation predicted emotional and relational QOL outcomes [17]. The current pattern is consistent with a biopsychosocial model in which inflammatory activity may contribute to fatigue, sleep disruption, reduced energy, psychomotor changes, cognitive inefficiency, and

diminished social engagement. Nevertheless, the reverse direction is also plausible: severe illness, poor nutrition, inactivity, sleep disturbance, psychosocial adversity, and lower QOL may themselves promote inflammatory dysregulation.

Role of clinical severity and confounding

Clinical severity is a particularly important confounder. The same article found positive correlations of NLR and PLR with CGI-S, while symptom severity is independently associated with QOL. Accordingly, the observed biomarker-QOL differences may be partially mediated or confounded by illness severity. Diagnosis, illness duration, body mass index, occupation, inpatient status, smoking exposure, prior treatment, and drug-naïve/drug-free status may also influence both inflammatory ratios and QOL. Participant-level regression and mediation analysis are required to establish whether NLR or PLR contributes information beyond these factors.

Interpretation of cut points

The use of NLR <3 versus >3 and PLR <137 versus >137 simplified interpretation but sacrificed information and may inflate apparent differences. A healthy-adult study reported a wide NLR reference range and emphasized variation by population and laboratory context [18]. Neither threshold is a validated psychiatric QOL decision limit. Future analyses should retain NLR and PLR as continuous variables, inspect non-linearity, and report sensitivity analyses across alternative thresholds.

Clinical implications

NLR and PLR are inexpensive and routinely available, but the present data do not justify their use as stand-alone QOL screening tools or treatment targets. Their most appropriate immediate role is as research variables used alongside direct patient-reported outcome measures. Clinicians should continue to assess QOL explicitly rather than infer it from symptom severity or laboratory markers. A low QOL score should prompt evaluation of residual symptoms, physical illness, sleep, occupational functioning, relationships, financial and environmental stressors, and access to psychosocial rehabilitation.

Strengths

- The study examined a clinically important patient-reported outcome rather than relying exclusively on symptom scales.
- The sample included equal numbers of participants with schizophrenia, bipolar disorder, and major depressive disorder.
- Drug-naïve and prespecified drug-free recruitment reduced immediate psychotropic exposure as a source of confounding.
- QOL was assessed with the internationally developed WHOQOL-BREF across four domains.
- The manuscript adds confidence intervals, Welch degrees of freedom, multiplicity adjustment, and effect-size estimates to the original article reporting.

LIMITATIONS

- The cross-sectional design cannot determine temporal sequence or causality.
- Convenience sampling from one tertiary psychiatric institution limits generalizability.
- The study had no healthy control group and each diagnostic group contained only 30 participants.
- NLR and PLR were dichotomized using exploratory thresholds that are not validated psychiatric QOL cut points.
- Participant-level data were unavailable for continuous correlations, multivariable regression, interaction testing, mediation analysis, or robust sensitivity analyses.
- Diagnosis, CGI-S severity, illness duration, body mass index, employment, inpatient status, and drug-naïve/drug-free status could confound the observed relationships.
- The drug-naïve and drug-free subgroup counts were not reported separately in the article results.
- The reported standard deviations for multiple QOL and inflammatory variables are unusually small and generate extremely large standardized effect sizes; transcription, data coding, and SPSS output must be audited.
- Laboratory analyzer details, time of blood sampling, fasting status, absolute versus percentage differential counts, and short-term lifestyle factors were not documented in the supplied record.

Future Directions

- Reanalyze the participant-level dataset with NLR and PLR as continuous variables and WHOQOL-BREF domain scores as continuous outcomes.
- Fit multivariable linear models adjusted for diagnosis, CGI-S, age, sex, body mass index, illness duration, employment, smoking, inpatient status, and drug-naïve/drug-free status.
- Test diagnosis-by-biomarker interactions to determine whether the association differs among schizophrenia, bipolar disorder, and major depressive disorder.
- Evaluate whether clinical severity mediates the relationship between inflammatory ratios and QOL.
- Use prospective repeated measurements to determine whether changes in NLR or PLR track changes in QOL during treatment and recovery.
- Include healthy controls and additional inflammatory measures such as C-reactive protein and cytokines to improve biological interpretation.

- Replicate the findings in multicenter samples with preregistered outcomes, standardized blood collection, and culturally validated WHOQOL-BREF scoring.

CONCLUSION

Higher NLR and PLR categories were associated with lower WHOQOL-BREF scores across physical, psychological, social-relationship, and environmental domains in drug-naïve and drug-free adults with schizophrenia, bipolar disorder, and major depressive disorder. These findings support further investigation of low-cost inflammatory ratios as correlates of patient-reported functioning and well-being. They do not establish that inflammation causes poor QOL, and the magnitude of the reported effects requires confirmation using the original participant-level database and adjusted analyses.

DECLARATIONS

Ethics approval and consent to participate: Institutional ethics committee approval was obtained before recruitment, and all participants provided written informed consent. The approval identifier must be inserted from the institutional record.

Consent for publication: Not applicable; no identifiable individual information is presented.

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Competing interests: The authors declare no competing interests.

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