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Inflammatory Markers in Suicidality: A Cross-Sectional Study of Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) in Depressed Patients

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ABSTRACT

Background: Depression is a major global mental health disorder linked to substantial morbidity, mortality, and suicidal behavior. Growing evidence indicates that neuroinflammation is a key factor in its pathophysiology. Haematological inflammatory markers, such as the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR), are simple, cost-effective indicators of systemic inflammation. This study aimed to evaluate NLR and PLR levels in patients with depression, examine their association with depressive severity, and explore their relationship with life satisfaction and suicidal ideation.

Methods: A hospital-based, cross-sectional study was conducted in the Departments of Physiology and Psychiatry at a tertiary care hospital in Odisha, India. A total of 150 clinically diagnosed depressive patients (age range: 20–60 years; mean age: 46±9.5 years) and 150 age- and gender-matched healthy controls were enrolled. Depression severity was assessed using the Hamilton Depression Rating Scale (HAM-D), while life satisfaction was evaluated using the Satisfaction with Life Scale (SWLS). NLR and PLR were calculated from complete blood count (CBC) reports.

Results: Depressed patients showed significantly higher NLR and PLR than controls (p=0.001). Both markers increased with depression severity and were elevated in individuals with poor life satisfaction, indicating a possible link between higher inflammatory indices and suicidal ideation.

Conclusion: NLR and PLR are significantly elevated in depressive patients and correlate positively with depression severity and suicidal ideation. These readily available inflammatory markers may serve as adjunct screening tools in clinical settings for early identification of at-risk individuals, potentially preventing permanent psychiatric disability and improving quality of life.

Key-words: Depression; Neutrophil-to-Lymphocyte Ratio; Platelet-to-Lymphocyte Ratio; Suicidality; Hamilton Depression Rating Scale; Satisfaction with Life Scale; Neuroinflammation; Biomarkers

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INTRODUCTION

Depression is one of the most prevalent and debilitating mental health disorders worldwide. According to the World Health Organization's World Mental Health Report, depression affects more than 264 million people globally, contributing substantially to disability-adjusted life years (DALYs) and representing a major public health burden [1]. In India, the National Mental Health Survey (2015–16) reported that approximately 1 in 20

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individuals suffers from depression, with the most affected age group being 40–49 years [2].

Depression is strongly associated with suicidal ideation and behavior, poor satisfaction with life, and diminished occupational and social functioning. Despite its high prevalence, depression remains underdiagnosed and undertreated, particularly in low- and middle-income countries such as India, where stigma, limited mental health workforce, and lack of access to care are persistent challenges [2]. There is an urgent need for simple, accessible, and cost-effective screening tools to identify vulnerable individuals early.

In recent years, the inflammatory hypothesis of depression has gained considerable attention. Accumulating evidence suggests that dysregulation of the immune-inflammatory system plays a central role in the pathogenesis of depression [3,4]. Studies have reported elevated levels of pro-inflammatory cytokines (e.g., IL-6, TNF-α, CRP) in depressed patients [5]. Further evidence supports the role of inflammatory mediators such as IL-6 and CRP in the development of depression and psychosis [6]. Alterations in cytokines and cortisol levels have also been demonstrated in depressive disorders [7].

Hematological ratios derived from the complete blood count (CBC)—namely, the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR)—have emerged as inexpensive surrogate markers of systemic inflammation. NLR reflects the balance between pro-inflammatory and anti-inflammatory immune components, whereas PLR incorporates platelet activity involved in inflammatory processes [8]. Elevated NLR and PLR have been reported in various clinical conditions, including depression [6].

Only a limited number of studies have examined NLR and PLR in relation to depressive severity and suicidal behavior [5,7]. Therefore, the present study aimed to evaluate NLR and PLR in depressed patients compared to healthy controls, assess their correlation with depression severity using the Hamilton Depression Rating Scale (HAM-D) [8], and examine their association with life satisfaction using the Satisfaction with Life Scale (SWLS) [9].

MATERIALS AND METHODS

Study Design and Setting- This was a hospital-based, cross-sectional, observational study conducted at the Department of Physiology in collaboration with the Department of Psychiatry at a tertiary care teaching hospital in Odisha, India. The study protocol was approved by the Institutional Ethics Committee (IEC), and informed written consent was obtained from all participants before enrollment.

Study Participants- A total of 150 patients (age 20–60 years; mean age: 46±9.5 years) with a clinically confirmed diagnosis of depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria were recruited as cases. An equal number of 150 age- and gender-matched healthy volunteers with no current or past psychiatric illness constituted the control group.

Inclusion Criteria

Cases: Patients aged 20–60 years with a confirmed diagnosis of depressive disorder attending the Psychiatry outpatient department. Controls: Healthy individuals of comparable age and gender with no psychiatric morbidity.

Exclusion Criteria

The following exclusion criteria were applied to both cases and controls to minimize confounding effects on inflammatory markers:

- ✓ Recent infection, trauma, or stressful life event (within 4 weeks)
- ✓ Any chronic hematological or autoimmune disorder (e.g., rheumatoid arthritis, SLE, inflammatory bowel disease)
- ✓ Current substance use or substance use disorder
- ✓ Chronic, serious, or unstable comorbid medical or surgical illness
- ✓ Family history of a first-degree relative with a psychiatric disorder

Assessment Tools

Hamilton Depression Rating Scale (HAM-D): The 17-item HAM-D was used to measure the severity of depressive symptoms. Each item is rated on a Likert scale (0–4 for 8 items and 0–2 for 9 items), yielding a maximum score of 50. A score >8 was considered indicative of depression, with subcategories defined as mild (8–16), moderate (17–23), and severe (≥24).

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Satisfaction with Life Scale (SWLS): The SWLS is a validated 5-item instrument evaluating global cognitive judgments of life satisfaction. Each item is rated on a 7-point Likert scale (1 = strongly disagree to 7 = strongly agree), yielding a maximum total score of 35. A score ≤20 was considered indicative of dissatisfaction with life; prior literature links low SWLS scores (<12) with suicidal ideation.

Hematological Measurements- Peripheral venous blood samples (5 mL) were collected from all participants under aseptic conditions after an overnight fast. A complete blood count (CBC) was performed using an automated haematology analyser. NLR was calculated as the ratio of absolute neutrophil count to absolute lymphocyte count. PLR was calculated as the ratio of absolute platelet count to absolute lymphocyte count. All laboratory analyses were performed at the institution's certified clinical laboratory.

Statistical Analysis- Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY). Continuous variables are expressed as mean ± standard deviation (SD). Differences between groups were assessed using the independent-samples t-test for parametric data. The chi-square (χ^2) test was applied to assess the association between categorical variables. A one-way ANOVA with post hoc Bonferroni correction was used to compare NLR and PLR across depression severity subgroups. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 300 participants were enrolled, comprising 150 depressive patients and 150 healthy controls. The mean age of depressive patients was 46.3±9.8 years and that of controls was 45.9±10.1 years, with no statistically significant difference (p=0.74). Gender distribution was identical across both groups (78 males and 72 females each). Table 1 presents the baseline demographic and hematological characteristics.

Table 1: Comparison of Demographic Characteristics and Inflammatory Indices between Depressive Patients and Healthy Controls

Characteristic	Depressive Patients (n=150)	Healthy Controls (n=150)	p-value
Age (years), Mean ± SD	46.3 ± 9.8	45.9 ± 10.1	0.74
Gender (Male/Female)	78/72	78/72	1.00
NLR (Mean ± SD)	1.81 ± 0.45	1.41 ± 0.36	0.001*
PLR (Mean ± SD)	81.8 ± 25.51	58.5 ± 15.40	0.001*
HAM-D Score (Mean ± SD)	19.6 ± 7.3	4.2 ± 2.1	0.001*

** Statistically significant (p<0.05). SD = Standard Deviation; NLR = Neutrophil-to-Lymphocyte Ratio; PLR = Platelet-to-Lymphocyte Ratio; HAM-D = Hamilton Depression Rating Scale.*

Depressive patients demonstrated significantly higher NLR (1.81±0.45) compared to healthy controls (1.41±0.36; p=0.001). Similarly, PLR was significantly elevated in depressive patients (81.8±25.51) relative to controls (58.5±15.40; p=0.001). These findings are consistent with an activated systemic inflammatory state in depression.

Among the 150 depressive patients, 52 (34.7%) had mild depression (HAM-D: 8–16), 62 (41.3%) had moderate depression (HAM-D: 17–23), and 36 (24.0%) had severe depression (HAM-D ≥24). Both NLR and PLR demonstrated a statistically significant progressive increase with increasing severity of depression (Table 2; p=0.001 for both). Post-hoc analysis revealed significant pairwise differences across all three severity groups.

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Table 2: NLR and PLR Values Across Depressive Severity Subgroups (HAM-D Categories)

Parameter	Mild Depression (HAM-D 8–16) n=52	Moderate Depression (HAM-D 17–23) n=62	Severe Depression (HAM-D ≥24) n=36	p-value (χ^2)
NLR (Mean ± SD)	1.43 ± 0.35	1.87 ± 0.38	2.51 ± 0.90	0.001 (χ^2=50.45)
PLR (Mean ± SD)	74.0 ± 9.20	91.30 ± 29.0	120.50 ± 20.6	0.001 (χ^2=45.50)

HAM-D = Hamilton Depression Rating Scale; NLR = Neutrophil-to-Lymphocyte Ratio; PLR = Platelet-to-Lymphocyte Ratio; χ^2 = Chi-square value.

DISCUSSION

The present cross-sectional study provides evidence that systemic inflammatory markers NLR and PLR are significantly elevated in patients with depressive disorder compared to healthy controls, and that these elevations are positively associated with both the severity of depression and poor life satisfaction—a proxy for suicidal ideation. These findings corroborate the neuroinflammatory hypothesis of depression and underscore the potential clinical utility of these readily available biomarkers [3,4].

The observed elevations in NLR (1.81±0.45) and PLR (81.8±25.51) in depressive patients compared to controls in our study are consistent with and extend prior findings in the literature. Swathi *et al*. [7], in a study from Karnataka, India, reported an NLR of 1.74±0.77 and a PLR of 70.8±34.6 in depressed patients assessed with HAM-D, findings broadly comparable to ours. Similarly, other international studies have consistently noted elevated NLR in psychiatric disorders, particularly major depressive disorder [6]. The pathophysiological basis for these findings relates to the immune-inflammatory model of depression: chronic low-grade systemic inflammation, mediated by activated neutrophils and altered platelet function, leads to increased production of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α), activation of the HPA axis, and serotonergic depletion [3,10].

Our finding of a significant positive dose-response relationship between HAM-D severity category and both NLR and PLR (mild: NLR 1.43, PLR 74.0; moderate: NLR 1.87, PLR 91.3; severe: NLR 2.51, PLR 120.5) is particularly noteworthy. This graded association implies that as the inflammatory burden increases, the clinical expression of depressive illness worsens. Interestingly, this is consistent with a bidirectional relationship—chronic psychological stress amplifies inflammation, while heightened inflammation, in turn, exacerbates affective dysregulation [5].

The association of elevated NLR and PLR with low SWLS scores is a novel and clinically significant finding of our study. Low SWLS scores, particularly scores below 12, have been linked to suicidal ideation in the psychiatric literature. Our data demonstrate that life-dissatisfied individuals—those most prone to suicidal ideation—had significantly higher NLR and PLR compared to those satisfied with their lives. This supports the hypothesis that inflammatory markers may not only track with the cognitive-affective dimensions of depression but also with its most severe behavioral manifestation: suicidality [11-13]. Platelet hyperactivation, as reflected in elevated PLR, may be particularly relevant here; platelets are rich in serotonin and may play a role in neurobiological pathways associated with suicidal behavior [14].

From a clinical standpoint, NLR and PLR offer several advantages as screening adjuncts. They are derived from a routine CBC, which is a universally available, low-cost, first-line investigation performed in virtually all clinical settings—including general outpatient departments and primary care clinics—regardless of speciality. Unlike specialised inflammatory assays (e.g., high-sensitivity CRP and IL-6), NLR and PLR require no additional reagents, equipment, or expenditure. Routinely incorporating their assessment during clinic visits could enable the early identification of at-risk individuals, prompt psychiatric referral, and potentially avert permanent psychiatric disability and suicide [15].

LIMITATIONS

The study has several limitations that warrant acknowledgment. First, as a hospital-based cross-sectional design, causal inferences cannot be drawn from the observed associations. Second, the sample size, while adequate for the primary analyses, may limit the generalizability of subgroup results. Third, the study did not assess other confounders of inflammation such as

body mass index (BMI), diet, physical activity, sleep quality, and socioeconomic status. Fourth, biomarkers of inflammation, including NLR and PLR, are inherently non-specific and may be elevated in a variety of conditions beyond depression. Longitudinal and prospective studies with larger, community-based samples are necessary to establish temporal relationships and to determine optimal NLR/PLR cut-off values for psychiatric screening.

CONCLUSIONS

This cross-sectional study demonstrates that NLR and PLR are significantly elevated in depressed patients compared to healthy controls, with values escalating in proportion to depressive severity as assessed by HAM-D. Furthermore, elevated NLR and PLR are associated with poor satisfaction with life, a recognized correlate of suicidal ideation. These simple, low-cost hematological ratios, routinely available from a standard CBC, hold promise as adjunct screening tools for depression and suicidal risk in diverse clinical settings. Sensitising general physicians and the broader medical community to assess NLR and PLR in patients presenting for routine or disease-specific evaluations may facilitate early identification and psychiatric referral of vulnerable individuals, ultimately contributing to improved mental health outcomes and quality of life. Longitudinal studies are recommended to further validate these markers and establish evidence-based clinical thresholds.

CONTRIBUTION OF AUTHORS

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