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Neutrophil lymphocyte ratio: An accessible biomarker for suicide risk stratification in affective disorder

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Editorial

Suicide remains one of the most pressing public health crises, claiming more than 720.000 lives a year and is the third leading cause of death in people aged 15-29 especially in the middle-income countries.[1] In Indonesia, 600 suicide attempts were reported in 2018, with the highest suicide rates in Central Java, Special Region of Yogyakarta, North Maluku, and Riau Islands.[2,3,4] Many factors influence suicidal behavior, including biological, psychological, social, cultural, and environmental factors. In every suicide case, many other people are having suicidal thoughts and plans. Suicide attempts remain an important predictor of suicidal ideation in crucial because individuals at this stage are at a higher risk of progressing to suicide attempts. Unfortunately, in daily clinical practice, identification of suicide risk often still relies on the subjective assessment of a history. Biological biomarkers are essential for objective screening.

Inflammation has emerged as a key biological pathway in the pathophysiology of affective disorder and suicidal behavior.[5] The Neutrophil Lymphocyte Ratio (NLR), a simple metric derived from routine complete blood counts, has gained attention as an inexpensive and accessible inflammatory biomarker with potential applications in psychiatry.[6]

NLR and the pathophysiology of affective disorder are the most studied hematological parameters. Neutrophils are the first line of defense of the innate immune system and are active non-specific inflammatory mediators of phagocytosis and apoptosis. Lymphocytes themselves are regulatory or protective component of the immune pathways, reflecting the intensity of chronic stress.[7] Elevated NLR indicates a dominant nonspecific immune response over the adaptive immune response. Chronic stress or systemic inflammation may increase neutrophil counts and decrease lymphocyte counts, thus raising the NLR. In the context of affective disorders, these changes may reflect neuroinflammatory processes associated with an increased risk of suicide.[7]

Affective disorders such as depression and bipolar disorder are closely linked with immune system dysregulation. Increased proinflammatory cytokines such as IL-6, TNFα, and IL-1β have been reported in patients with major depression and suicidal behavior.[9] Inflammation can affect tryptophan metabolism, reduce serotonin synthesis, and alter neurotransmitter function, contributing to negative symptoms and suicidal ideation.[10] These associations make NLR a biologically plausible and clinically relevant marker to explore in suicide risk assessment.

The study from DR Sardjito Hospital in Yogyakarta adds to this growing body of evidence, demonstrating a strong association between elevated NLR and suicidal ideatioin patients with affective disorders. The cross-sectional retrospective study analyzed data from 80 patients with affective disorder (40 with suicidal ideation and 40 without) admitted from January to December 2023. The main findings were:

- **Higher NLR in suicide ideation**

Patient with suicidal ideation had significantly higher mean NLR values (3.55) compared to those without (2.46, $p<0.001$).

- **Predictive performance**

The receiver operating characteristic (ROC) analysis yielded an area under curve (AUC) of 0.783 for NLR, indicating good predictive ability. The optimal cut-off value was 2.77, with 72.5% sensitivity, 72.5% specificity, and an odds ratio (OR) of 6.95.

- **PLR not significant**

Although platelet lymphocyte ratio (PLR) was higher in the suicidal ideation group, it was not statistically significant predictor after adjusting for other factors.

These result highlights NLR's potential as clinically useful biomarker to identify patients at elevated suicide risk within the context of affective disorder. This study offers a significant contribution to both psychiatric clinical practice and to the wider psychiatric field by highlighting the potential usefulness of NLR as an accessible biomarker for suicide risk assessment in patients with affective disorders.

From the clinical practice perspective, the findings provide psychiatrists with an objective, low-cost, and widely accessible tool to complement traditional suicide risk evaluation, which often rely on subjective patient reports and clinician interpretation. In settings where patients may withhold suicidal thoughts due to stigma or fear, an elevated NLR could serve as an early warning signal prompting more detailed psychosocial assessments, where advanced neuroimaging or cytokine assays are impractical. In addition, integrating NLR measurement into standard admission laboratory work could help stratify patients according to suicide risk, allowing for targeted interventions and optimizing resource allocation. In high-risk settings, such as psychiatric patient units, NLR could be integrated into routine admission labs to identify individuals for more intensive suicide risk assessment.

This result reinforces the role of systemic inflammation in the pathophysiology of suicidal ideation and affective disorders. It strengthens the biological framework linking neuroinflammation, immune dysregulation, and mood disturbance, opens the door to translational research into novel therapeutic targets. The identification of a statistically significant cut-off for NLR (2.77) with reasonable sensitivity and specificity also provides a foundation for multicenter validation studies and for incorporating NLR into predictive models that combine biological, psychological, and social variables. The research bridging a critical gap between laboratory findings and psychiatric care, supporting the integration of biological markers into suicide prevention strategies. It highlights how a simple, inexpensive test can have substantial clinical value in advancing neurobiological understanding of mood disorders and social behavior.

Although the study provides compelling evidence of an association between elevated NLR and suicidal ideation in affective disorders, several limitations and critical considerations must be addressed before translating these finding into routine psychiatric practice or into broader psychiatric research. From a clinical perspective, NLR is a non-specific biomarker influenced by numerous physiological and pathological factors, including acute infections, chronic inflammatory diseases, autoimmune conditions, malignancies, medication effects, and lifestyle factors such as smoking or poor diet. Without careful clinical correlation, elevated NLR values may lead to false positives in suicide risk screening, potentially resulting in unnecessary interventions or patient anxiety. The identified cut-off value is population-specific and may vary across different ethnicities, healthcare settings, and laboratory standards.

Single-timepoint NLR measurement during acute hospitalization limits the understanding of temporal dynamics and the potential for NLR as a longitudinal monitoring tool. The relatively small and single-centered sample also reduces generalizability, highlighting the need for multicenter, prospective studies with larger and more diverse populations. In addition, the study did not control for all possible confoundersthat may influence both inflammation markers and psychiatric symptoms. For future research, combining NLR with other inflammatory and clinical variables, applying standardized laboratory protocols, and exploring mechanistic relation

between inflammation and suicide could strengthen its predictive validity.

This study from DR Sardjito Hospital highlights NLR's potential utility as a pragmatic screening adjunct in psychiatric setting-particularly in low resource environment where advanced diagnostic modalities are not available. However, the real significance of this work lies not only in its immediate clinical implications but also in its potential to reshape how psychiatry approaches risk assessment. It reinforces the notion that biological and psychosocial dimensions of suicide risk are not mutually exclusive but rather complementary, and that integrating objective biomarker into standard care could enhance early detection, facilitate targeted interventions, and ultimate save lives. In the evolving landscape of precision psychiatry, this study points to a future in which suicide prevention strategies are informed by both human narratives and biological signals. If pursued with scientific rigor and clinical prudence, the integration of markers like NLR could mark a pivotal shift from reactive crisis management to proactive, evidence-based suicide prevention.

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