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Neutrophil-related inflammatory activation during medication-overdose suicide attempts in depressive patients: a case-control study with within-subject pre-attempt comparison

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Abstract

Background

Inflammatory activation has been implicated in suicidal behavior in major depressive disorder, but whether these alterations reflect stable vulnerability or acute state-related changes occurring around the suicidal crisis remains unclear. This study compared inflammatory laboratory parameters between depressive patients presenting after medication-overdose suicide attempt and depressive controls without a current suicide attempt, and examined within-subject change using pre-attempt laboratory measurements.

Methods

This case-control study included 74 depressive patients admitted to the emergency department after medication-overdose suicide attempt and 75 depressive outpatients without a current suicide attempt. Diagnoses were confirmed using the Structured Clinical Interview for DSM-5, Clinician Version (SCID-5-CV). White blood cell count, neutrophil count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio, systemic immune-inflammation index, and C-reactive protein were compared between groups, and multivariable logistic regression models were fitted. In a subgroup of suicide attempters (n = 38), laboratory measurements obtained within the preceding 3 months were compared with admission measurements.

Results

The suicide attempt group had higher white blood cell, neutrophil, and monocyte counts and higher NLR values, and lower PLR values, than depressive controls. Neutrophil count remained independently associated with suicide attempt in multivariable analyses. Within-subject analyses showed significantly higher neutrophil counts during the suicide attempt period than at previous measurements, whereas NLR did not differ significantly.

Conclusions

Neutrophil-related inflammatory activation was associated with suicide attempt in depressive patients and was higher during the acute post-attempt presentation than at previous measurements. Routinely available blood count parameters may provide adjunctive information about the acute physiological state accompanying suicidal crises, although the contribution of the ingested substances themselves cannot be excluded.

Introduction

Major depressive disorder (MDD) is one of the leading contributors to disability worldwide and is strongly associated with suicidal behavior. Although suicidal ideation and suicide attempts occur across a wide range of psychiatric disorders, MDD remains among the diagnoses most closely linked to suicide-related morbidity and mortality. Despite advances in clinical assessment, the prediction of suicidal behavior in daily practice is still largely based on subjective reporting and clinical observation, and reliable biological markers have not yet been established [1, 2]. In recent years, growing evidence has suggested that inflammatory processes may contribute to both the pathophysiology of depression and the emergence of suicidal behavior. Several studies have demonstrated elevated levels of peripheral inflammatory markers, including C-reactive protein (CRP), interleukin (IL)-1β, IL-6, tumor necrosis factor-α, and hematological inflammatory indices in patients with suicidality [2, 3]. Meta-analytic findings indicate that suicide attempts are associated with activation of immune-inflammatory and neurotoxic pathways, supporting the view that suicidality may be accompanied by a measurable biological stress response [4]. Among peripheral inflammatory markers, complete blood count-derived indices such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR) and systemic immune-inflammation index (SII) have attracted increasing attention because they are inexpensive, rapidly available, and routinely measured in clinical settings. Previous studies reported elevations in several of these indices among patients with suicidal ideation and suicide attempts, particularly in depressive disorders and adolescent populations. NLR has been one of the most consistently associated markers, while recent studies also suggested potential roles for MLR and SII in distinguishing suicidal from non-suicidal depressive patients [5–7]. Growing evidence suggests that the association between inflammation and suicidality may not be explained solely by depressive symptom severity. Elevated inflammatory activity has been observed even after controlling for depression severity, supporting the possibility that suicidality may represent a partially distinct biological state within depressive disorders [8]. In addition, neuroimmune-endocrine models propose that chronic stress, hypothalamic-pituitary-adrenal axis dysregulation, inflammatory activation, and altered neurotransmitter metabolism may interact in the development of suicidal behavior [1, 9].

Despite the growing literature, several important limitations remain. Most available studies have used cross-sectional designs and evaluated inflammatory markers only during or shortly after a suicide attempt. As a result, it is still unclear whether the observed inflammatory alterations reflect a pre-existing vulnerability, an acute stress response associated with the suicidal crisis, or both. Meta-analytic findings further suggest that inflammatory activation may be more pronounced in current suicide attempts than in lifetime suicidal behavior, raising the possibility that at least some inflammatory alterations may reflect an acute biological state associated with the suicidal crisis [4]. Similarly, studies evaluating laboratory parameters during the acute post-attempt period have reported reductions in inflammatory indices such as NLR and PLR after clinical stabilization and discharge [10]. Therefore, the present study aimed to compare inflammatory hemogram and biochemical parameters between patients with depressive disorder who presented with suicide attempts and patients with depressive disorder without a current suicide attempt. In addition, in a subgroup of suicide attempters with available previous laboratory data, inflammatory markers obtained before the suicide attempt were compared with

admission measurements during the acute suicidal presentation in order to explore whether inflammatory alterations reflected a pre-existing vulnerability or an acute state-related biological response. To our knowledge, studies incorporating pre-attempt inflammatory measurements within the same individuals remain very limited in the current literature. By examining both between-group differences and within-subject changes, we aimed to contribute to the ongoing discussion regarding whether inflammatory alterations in suicidality represent trait-related vulnerability markers or acute state-related biological responses.

Methods

Study Design and Population

The study was performed in accordance with the Declaration of Helsinki and approved by the Ümraniye Training and Research Hospital Ethics Committee (Approval No: 69, Date: 10 April 2025). Written informed consent was obtained from all participants prior to data collection. This case-control study included patients admitted to the emergency department following suicide attempt by medication overdose and depressive psychiatric outpatients evaluated between 1 May 2025, and 1 November 2025. Psychiatric diagnoses were confirmed using the Structured Clinical Interview for DSM-5, Clinician Version (SCID-5-CV), a previously published structured diagnostic interview, using its validated Turkish version [11, 12]. Previous laboratory measurements obtained within the preceding 3 months were retrieved from electronic medical records for longitudinal analyses. Patient records were anonymized before analysis to ensure confidentiality. The study population consisted of individuals aged 18 years or older who had available complete blood count and biochemical measurements at admission.

The suicide attempt group included patients presenting after intentional medication overdose, while the control group consisted of depressive psychiatric outpatients without current suicide attempt. Depressive diagnoses in both groups were established using structured psychiatric evaluation conducted by psychiatrists trained in the administration of the SCID-5-CV. Only individuals meeting SCID-5-CV criteria for a depressive episode were included in both the suicide attempt and control groups. By selecting a depressed control population rather than psychiatrically healthy controls, the study aimed to minimize the confounding effect of depressive symptomatology on inflammatory parameters.

Exclusion criteria included active inflammatory or autoimmune disease, chronic kidney disease, chronic liver disease, cerebrovascular disease, hematological disorders, use of anti-inflammatory medications, and heavy smoking (> 1 pack/day). Individuals with missing laboratory or clinical data were excluded from the final analyses.

Sociodemographic variables included age, sex, educational status, marital status, occupational status, living arrangement, previous suicide attempt history, psychiatric history, and current psychiatric treatment status. These variables were recorded using a structured data collection form developed by the authors for this study; an English translation of the form is provided as Supplementary Material 1.

Laboratory Assessments

Laboratory parameters obtained at admission included white blood cell count (WBC), neutrophil count, lymphocyte count, monocyte count, platelet count, C-reactive protein, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, and systemic immune-inflammation index. For a subgroup of suicide attempters, previous laboratory measurements obtained within the preceding 3 months were retrospectively retrieved from hospital electronic medical records for longitudinal comparison analyses.

NLR, PLR, and MLR were calculated using standard hematological formulas. SII was calculated as: SII = platelet count × neutrophil count / lymphocyte count.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages.

Normality assumptions were evaluated visually and analytically. Group comparisons for continuous variables were performed using independent samples t-test or Mann–Whitney U test, as appropriate. Categorical variables were compared using chi-square test or Fisher's exact test.

Multivariable logistic regression analyses were performed to identify independent factors associated with suicide attempt. Two separate regression models were constructed to avoid multicollinearity between neutrophil count and derived inflammatory indices. Variables were selected for the multivariable models based on clinical relevance, observed between-group differences, and the need to limit model complexity relative to the sample size. Because several hematological variables were biologically or mathematically interrelated, overlapping markers were not entered simultaneously. Neutrophil count was retained as the principal cell-based inflammatory marker because it showed the most consistent pattern across the between-group and within-subject analyses, while CRP and PLR were included as complementary inflammatory measures. In the sociodemographic-clinical model, age and sex were retained as basic covariates, together with living arrangement and previous suicide attempt history as clinically relevant suicide-related variables. No automated stepwise variable-selection procedure was used. Model 1 included laboratory variables (age, sex, CRP, PLR, and neutrophil count), while Model 2 included sociodemographic and clinical variables (age, sex, living arrangement, previous suicide attempt history, and neutrophil count). Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test.

In a subgroup of suicide attempters with available previous laboratory measurements obtained within the preceding 3 months, within-subject longitudinal analyses were performed to compare inflammatory markers prior to the suicide attempt period with admission measurements during the acute suicide

attempt presentation. Due to non-normal distribution, paired comparisons were conducted using Wilcoxon signed-rank tests.

No formal adjustment for multiple comparisons was applied. Given the correlation among the inflammatory parameters examined, interpretation emphasized the consistency of findings across between-group, within-subject, and multivariable analyses rather than isolated p values.

A two-tailed p-value < 0.05 was considered statistically significant for all tests.

Results

Participant Characteristics

A total of 149 individuals were included in the final analyses, comprising 75 controls and 74 patients presenting after suicide attempt by medication overdose. The mean age of the participants was comparable between groups (33.58 ± 7.96 years in controls vs. 31.06 ± 10.02 years in the suicide attempt group, p = 0.052). The suicide attempt group had a significantly higher proportion of males (33.8% vs. 17.3%, p = 0.021), individuals living alone (17.6% vs. 4.0%, p = 0.007), and participants with previous suicide attempt history (28.4% vs. 5.3%, p < 0.001). Marital status also differed significantly between groups, with a higher proportion of unmarried individuals in the suicide attempt group (p = 0.043). Educational level, occupational status, psychiatric history, and current psychiatric treatment status did not significantly differ between groups. Detailed sociodemographic characteristics of the study groups are presented in Table 1.

Table 1
Comparison of Sociodemographic Characteristics Between Groups

Variable	Suicide Attempt (n = 74)	Control (n = 75)	p-value
Age (years)	31.06 ± 10.02	33.58 ± 7.96	0.052
Sex			
Female	49 (66.2%)	62 (82.7%)	**0.021**
Male	25 (33.8%)	13 (17.3%)	
Education level			
Primary/Middle school	23 (31.1%)	26 (34.7%)	0.641
High school/University	51 (68.9%)	49 (65.3%)	
Marital status			
Married	33 (44.6%)	48 (64.0%)	**0.043**
Single/Divorced	41 (55.4%)	27 (36.0%)	
Occupation			
Not working	39 (52.7%)	47 (62.7%)	0.218
Working	35 (47.3%)	28 (37.3%)	
Living arrangement			
Alone	13 (17.6%)	3 (4.0%)	**0.007**
With family	61 (82.4%)	72 (96.0%)	
History of suicide attempt			
Absent	53 (71.6%)	71 (94.7%)	**< 0.001**
Present	21 (28.4%)	4 (5.3%)	
Psychiatric history			
Absent	38 (51.4%)	50 (66.7%)	0.057
Present	36 (48.6%)	25 (33.3%)	
Current psychiatric treatment			
Not receiving	62 (83.8%)	68 (90.7%)	0.208
Receiving	12 (16.2%)	7 (9.3%)	

Laboratory Findings

The suicide attempt group demonstrated significantly higher WBC counts (9.68 ± 3.07 vs. 7.54 ± 2.13 ×10³/μL, p < 0.001), neutrophil counts (6.39 ± 2.73 vs. 4.71 ± 1.71 ×10³/μL, p < 0.001), monocyte counts (0.56 ± 0.21 vs. 0.45 ± 0.13 ×10³/μL, p = 0.002), and NLR values (2.87 ± 2.02 vs. 2.16 ± 0.76, p = 0.017) compared with controls. PLR values were significantly lower in the suicide attempt group (118.63 ± 40.26 vs. 135.50 ± 39.20, p = 0.020). No significant differences were observed regarding CRP, platelet count, MLR, or SII levels between groups. Laboratory findings of the study groups are summarized in Table 2.

Table 2
Comparison of Laboratory Parameters Between Groups

Variable	Suicide Attempt (n = 74)	Control (n = 75)	p-value
CRP (mg/L)	3.03 ± 4.15	1.90 ± 1.99	0.315
WBC (×10³/μL)	9.68 ± 3.07	7.54 ± 2.13	**< 0.001**
Neutrophil (×10³/μL)	6.39 ± 2.73	4.71 ± 1.71	**< 0.001**
Monocyte (×10³/μL)	0.56 ± 0.21	0.45 ± 0.13	**0.002**
Lymphocyte (×10³/μL)	2.55 ± 1.04	2.19 ± 0.64	0.052
Platelet (×10³/μL)	274.19 ± 63.93	280.10 ± 55.42	0.584
NLR	2.87 ± 2.02	2.16 ± 0.76	**0.017**
PLR	118.63 ± 40.26	135.50 ± 39.20	**0.020**
MLR	0.24 ± 0.12	0.22 ± 0.07	0.484
SII	784.72 ± 515.01	634.73 ± 270.15	0.185

CRP: C-reactive protein, **WBC**: white blood cell count, **NLR**: neutrophil-to-lymphocyte ratio, **PLR**: platelet-to-lymphocyte ratio, **MLR**: monocyte-to-lymphocyte ratio, **SII**: systemic immune-inflammation index.

Longitudinal Comparison of Previous and Admission Laboratory Measurements

Previous laboratory measurements obtained prior to the suicide attempt period were available for a subgroup of suicide attempters. In this subgroup (n = 38), neutrophil counts were significantly higher during the suicide attempt period compared with previous measurements (6.32 ± 1.97 vs. 5.60 ± 3.14 ×10³/μL, Wilcoxon signed-rank test, p = 0.027). In contrast, no significant differences were observed for WBC (p = 0.101), CRP (p = 0.370), NLR (p = 0.207), PLR (p = 0.960), or SII (p = 0.097). Detailed longitudinal comparisons of previous and admission laboratory parameters are presented in Table 3.

Table 3
Longitudinal Comparison of Previous and Admission Laboratory Parameters in Suicide Attempters

Variable	Previous Measurement	Admission Measurement	p-value
WBC (×10³/μL)	8.89 ± 3.43	9.63 ± 2.40	0.101
Neutrophil (×10³/μL)	5.60 ± 3.14	6.32 ± 1.97	**0.027**
Monocyte (×10³/μL)	0.67 ± 0.87	0.56 ± 0.21	0.839
CRP (mg/L)	4.40 ± 10.62	3.19 ± 4.40	0.370
NLR	3.04 ± 3.70	2.75 ± 1.34	0.207
PLR	144.19 ± 167.20	119.27 ± 37.16	0.960
SII	794.75 ± 901.56	771.14 ± 402.90	0.097

WBC: white blood cell count, **CRP**: C-reactive protein, **NLR**: neutrophil-to-lymphocyte ratio, **PLR**: platelet-to-lymphocyte ratio, **SII**: systemic immune-inflammation index.

Multivariable Logistic Regression Analyses

Model 1: Laboratory Model

In the laboratory-based multivariable logistic regression model, neutrophil count remained independently associated with suicide attempt (OR = 1.54, 95% CI: 1.23–1.93, p < 0.001) after adjustment for age, sex, CRP, and PLR. Male sex (OR = 2.52, 95% CI: 1.05–6.07, p = 0.039) and lower PLR values (OR = 0.99, 95% CI: 0.98–0.999, p = 0.039) were also independently associated with suicide attempt. The model demonstrated acceptable calibration (Hosmer–Lemeshow p = 0.221) and explained 30.9% of the variance (Nagelkerke R^2 = 0.309).

Model 2: Sociodemographic and Clinical Model

In the parsimonious sociodemographic-clinical model, neutrophil count remained independently associated with suicide attempt (OR = 1.56, 95% CI: 1.24–1.98, p < 0.001) after adjustment for age, sex, living arrangement, and previous suicide attempt history. Male sex (OR = 2.45, 95% CI: 1.00–5.96, p = 0.049) and living alone (OR = 4.31, 95% CI: 1.05–17.54, p = 0.042) were also independently associated with suicide attempt. Previous suicide attempt history demonstrated a trend toward significance (OR = 1.89, 95% CI: 0.92–3.85, p = 0.082). The model demonstrated good calibration (Hosmer–Lemeshow p = 0.358) and explained 34.6% of the variance (Nagelkerke R^2 = 0.346). Multivariable logistic regression analyses are presented in Table 4.

Table 4
Multivariable Logistic Regression Analyses for Suicide Attempt

Model 1.				
Variable	**B**	**SE**	**OR (95% CI)**	**p-value**
Age	-0.034	0.020	0.97 (0.928–1.006)	0.092
Sex (male)	0.924	0.449	2.52 (1.046–6.072)	**0.039**
CRP	0.094	0.065	1.10 (0.966–1.248)	0.152
Neutrophil	0.431	0.115	1.54 (1.227–1.929)	**< 0.001**
PLR	-0.011	0.005	0.99 (0.979–0.999)	**0.039**
Model 2.				
Variable	**B**	**SE**	**OR (95% CI)**	**p-value**
Age	-0.016	0.020	0.98 (0.946–1.023)	0.410
Sex (male)	0.895	0.455	2.45 (1.003–5.964)	**0.049**
Living alone	1.460	0.719	4.31 (1.05–17.54)	**0.042**
History of suicide attempt	0.634	0.364	1.89 (0.923–3.852)	0.082
Neutrophil	0.447	0.119	1.56 (1.238–1.975)	**< 0.001**
CRP: C-reactive protein, **PLR**: platelet-to-lymphocyte ratio				

Discussion

Our study examined peripheral inflammatory markers in depressive patients presenting after suicide attempts by intentional medication overdose and compared them with depressed outpatients without a current suicide attempt. The suicide attempt group demonstrated significantly higher WBC, neutrophil, monocyte, and NLR values, whereas PLR values were lower than those observed in the control group. More importantly, neutrophil count remained independently associated with suicide attempts after adjustment for potential confounding variables. In the subgroup analysis including previous laboratory measurements obtained before the index suicide attempt, neutrophil levels were significantly higher during emergency presentation than during earlier outpatient assessments. The persistence of neutrophil elevation despite the use of a depressive control group suggests that neutrophil-related inflammatory activation may be associated more specifically with acute suicidal behavior than with depressive symptoms alone. Although WBC levels were also significantly higher in the suicide attempt group, neutrophil count was emphasized because it showed consistent associations across longitudinal and multivariable analyses and may represent a biologically more specific indicator of innate immune activation than total leukocyte count.

The relationship between inflammation and suicidal behavior has increasingly attracted attention in recent years. Meta-analytic evidence has consistently demonstrated elevated inflammatory activity in suicidal patients, including increases in IL-1β, IL-6, CRP, and blood count–derived inflammatory indices [2–4]. Studies specifically focusing on depressive disorders similarly reported elevations in NLR, PLR, MLR, and SII among patients with suicidal ideation or suicide attempts [6, 7, 13, 14]. O'Donovan et al. showed that inflammatory activation may remain associated with suicidal ideation even after controlling for depression severity, suggesting that suicidality itself may represent a partially distinct biological dimension within depressive disorders [8]. In the present study, the use of a depressive control group allowed a more specific evaluation of suicide-related inflammatory alterations, beyond the inflammatory changes attributable to depression alone.

Our findings are consistent with previous studies reporting elevated neutrophil-related inflammatory markers in suicidal populations, as well as with meta-analytic evidence of altered NLR, PLR, and MLR in depressive and mood disorders [15, 16]. Velasco et al. reported increased NLR and PLR values in patients with major depressive disorder and suicide attempt history, with NLR remaining independently associated with suicidal behavior after multivariable adjustment [5]. Similar observations have also been reported in adolescent and young adult cohorts, although the pattern appears to vary according to clinical subtype. Cui et al. reported elevated neutrophil and platelet counts and SII values in adolescents with first-episode, drug-naïve depression and suicide attempts, with SII independently associated with suicide attempts after adjustment. In contrast, Liu et al. observed the strongest inflammatory alterations in adolescents with comorbid non-suicidal self-injury and suicide attempts, whereas the suicide-attempt-only group did not show a distinct inflammatory profile relative to depression alone [7, 13]. Together with the present findings, these studies support the growing evidence that neutrophil-related inflammatory activation may be associated with suicidal behavior across different age groups and clinical settings.

One of the most notable findings of the present study was that neutrophil count itself remained independently associated with suicide attempts after adjustment analyses. This observation may be clinically and biologically relevant because neutrophils represent a central component of innate immune activation during acute physiological stress. Previous studies have generally focused on derived inflammatory indices such as NLR; however, our findings suggest that absolute neutrophil count itself may carry important information regarding suicidal crises. Interestingly, although NLR was significantly elevated in the suicide attempt group compared with controls, it did not differ significantly between emergency presentation and previous outpatient measurements in the within-subject analysis, whereas neutrophil count increased significantly during the acute episode. This pattern raises the possibility that absolute neutrophil count may be more sensitive to acute state-related changes than NLR in this sample. Prospective studies with repeated measurements are needed to determine whether these markers differ in their temporal dynamics. This interpretation is partly supported by previous literature. Lovig et al. observed stronger inflammatory alterations in patients with recent rather than past suicide attempts, suggesting temporal sensitivity of inflammatory activation [17]. Vasupanrajit et al. also reported that inflammatory activation appears more pronounced in current suicide attempts than in lifetime suicidal behavior [4]. Although our historical laboratory measurements cannot be considered definitive euthymic

baseline values, the availability of pre-attempt data within the same individuals offers a perspective that remains rare in the current literature, where most studies have relied on cross-sectional comparisons or post-attempt follow-up, and may help distinguish trait-related vulnerability from acute state-dependent activation.

The biological mechanisms underlying the association between neutrophil-related inflammatory markers and suicidal behavior are not yet fully understood, but accumulating evidence suggests that innate immune activation may play an important role. Previous meta-analyses demonstrated elevated proinflammatory cytokines, particularly IL-1β and IL-6, in suicidal patients across peripheral blood and central nervous system samples [3]. These cytokines are closely involved in neutrophil activation, survival, and migration, providing a possible biological explanation for the neutrophil elevation observed in suicidal patients. Supporting this hypothesis, transcriptomic studies in major depressive disorder have demonstrated upregulation of innate immune and neutrophil-related gene networks in peripheral blood, while genetic studies have implicated inflammatory pathway genes in suicidal ideation and suicidal behavior [18, 19]. Experimental studies further support this relationship. Aguilar-Valles et al. demonstrated that brain-infiltrating neutrophils contribute to depression-like behaviors during systemic inflammation, whereas Kim et al. showed that activated neutrophils interact directly with microglial pathways during neuroinflammatory states [20, 21]. Consistent with this state-dependent framework, a recent study showed that neuroinflammatory activity, indexed by translocator protein binding, was associated with greater suicidal ideation during real-world stress exposure in individuals with depression [22]. Together, these findings suggest that elevated neutrophil counts in suicidal patients may reflect more than a nonspecific stress response and could represent part of a broader innate immune dysregulation associated with suicidal crises.

Another important issue concerns the potential effect of medication overdose itself on inflammatory parameters. Acute toxic exposure, physiological stress, autonomic activation, and direct pharmacological effects of ingested substances may contribute to leukocyte and platelet alterations; indeed, Lionte et al. reported that inflammation-related indexes such as NLR and MLR are elevated upon emergency admission in acute poisoning and predict intensive care hospitalization and mortality, indicating that acute intoxication can itself activate these markers [23]. Ideally, the inclusion of a non-suicidal overdose comparison group would therefore have helped disentangle the contribution of intoxication from that of suicidal behavior. Nevertheless, evidence from trauma-related suicidal behavior studies suggests that the inflammatory activation associated with suicidal behavior may not be attributable solely to physical injury or acute medical stress. Zellner et al. demonstrated significantly greater inflammatory responses in suicidal compared with non-suicidal falls from height despite adjustment for injury severity [24]. Similarly, Miyazaki et al. reported that NLR remained independently associated with suicidal trauma after controlling for trauma-related variables [25]. These findings support the possibility that suicidal behavior itself may be accompanied by a distinct inflammatory response beyond the direct somatic consequences of injury or intoxication.

The lower PLR values and the absence of a significant CRP difference observed in our cohort should also be interpreted cautiously. The literature remains inconsistent regarding platelet-related indices [6, 14], and acute stress-related lymphocyte redistribution together with potential pharmacological effects of ingested substances on platelet dynamics may partly explain the lower PLR values in overdose-related suicide attempts [26]. With respect to CRP, findings across studies are heterogeneous, with elevated levels reported in some cohorts of suicidal patients assessed in adolescent or emergency settings and in direct overdose comparison studies [27–29], whereas other studies have failed to demonstrate significant CRP differences despite clear neutrophil-related alterations [22, 26], which in turn appear more consistently associated with suicidal behavior across settings [5, 14, 15]. This dissociation may be biologically meaningful: unlike neutrophil count, which can rise rapidly through acute stress-related sympathetic and neuroendocrine activation, CRP is a slower hepatic acute-phase reactant driven by sustained, IL-6-mediated systemic inflammation. The observed profile may therefore reflect a rapid neutrophil-predominant innate immune response during acute suicidal crises rather than a generalized systemic inflammatory state.

Sociodemographic and clinical differences between groups should also be considered when interpreting the findings. Male sex, living alone, and previous suicide attempt history were more frequent among suicide attempters, while male sex and living arrangement remained significant in adjusted analyses. These observations are broadly consistent with previous evidence identifying prior suicide attempt as an important clinical risk factor for future suicidal behavior and linking social isolation-related factors, including living alone, with increased suicide risk [30, 31]. While previous suicide attempt history did not remain independently significant in the adjusted model, its higher frequency among suicide attempters may still reflect underlying psychological vulnerability, impaired stress regulation, and recurrent suicidal cognition. In contrast, living alone remained independently associated with suicide attempt and may contribute to reduced social support, loneliness, and diminished access to emotional buffering during periods of crisis. Importantly, neutrophil count remained independently associated with suicide attempt even after adjustment for these variables, suggesting that the observed inflammatory alterations were not solely attributable to sociodemographic differences between groups.

Several limitations should be acknowledged. The observational case-control design limits causal interpretation. Historical laboratory values were retrospectively retrieved from routine records, and the clinical context of those earlier measurements could not be fully determined. Standardized measures of depression severity, suicide intent, and attempt lethality were not available; therefore, residual confounding related to clinical severity cannot be excluded. Importantly, because the substances ingested during the suicide attempt were not documented and may have differed from patients' previously prescribed medications, the acute increase in neutrophil count relative to earlier measurements may partly reflect the direct pharmacological or toxic effects of the ingested agents rather than a biological state specific to the suicidal crisis itself, as acute intoxication alone can elevate inflammatory indices. This possibility cannot be excluded with the available data. Finally, inflammatory evaluation was limited to routine hematological and biochemical parameters, while cytokine and kynurenine pathway measurements were unavailable.

Despite these limitations, the present study has several important strengths. The use of a depressive control group reduced confounding related to depression-associated inflammation, routinely available hematological markers increased clinical applicability, and the inclusion of pre-attempt laboratory measurements provided a rarely studied within-subject perspective. Overall, our findings support the growing evidence that neutrophil-related inflammatory activation may be associated with suicidal behavior in depressive disorders. In particular, the increase in neutrophil levels during the suicidal episode raises the possibility that neutrophil activation may partly reflect an acute biological state accompanying suicidal crises. Prospective longitudinal studies incorporating repeated inflammatory measurements, cytokine profiles, and toxicological characterization are needed to clarify the temporal and mechanistic significance of these findings.

Conclusion

Patients presenting after suicide attempt by medication overdose demonstrated significantly elevated neutrophil-related inflammatory markers compared with depressed controls without a current suicide attempt. Neutrophil count remained independently associated with suicide attempt across multivariable models and increased significantly during the acute suicidal episode compared with previous measurements obtained within the preceding months. These findings suggest that neutrophil-related inflammatory activation may accompany acute suicidal crises beyond depression-related inflammation alone. Given its low cost, rapid availability, and routine use in emergency settings, neutrophil count may provide adjunctive laboratory information about the acute physiological state accompanying suicidal presentations in depressive patients. Further prospective longitudinal studies are needed to clarify the temporal and mechanistic relationship between inflammation and suicidal behavior.

Abbreviations

CI: confidence interval

CRP: C-reactive protein

DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

IL: interleukin

MDD: major depressive disorder

MLR: monocyte-to-lymphocyte ratio

NLR: neutrophil-to-lymphocyte ratio

OR: odds ratio

PLR: platelet-to-lymphocyte ratio

SCID-5-CV: Structured Clinical Interview for DSM-5, Clinician Version

SII: systemic immune-inflammation index

WBC: white blood cell

Declarations

Ethics approval and consent to participate

The study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Ümraniye Training and Research Hospital, University of Health Sciences, İstanbul, Türkiye (Approval No: 69; date of approval: 10 April 2025). Written informed consent was obtained from all participants for the use of their clinical data in research.

Consent for publication

Not applicable. No individually identifiable participant data are included in this manuscript.

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available because of institutional data protection requirements, but are available from the corresponding author on reasonable request. To protect participant privacy, only de-identified and anonymized data will be shared.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SCH conceptualized and designed the study, performed the statistical analysis, and drafted the manuscript. UTD contributed to data acquisition, data curation, and interpretation of the results, and critically revised the manuscript. Both authors read and approved the final manuscript.

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