Journal of Epidemiology and Public Health (2026), 11(03): 337-352
Master's Program in Public Health, Universitas Sebelas Maret

Review

Open Access

Association between Systemic Immune-Inflammation Index and Self-Harm Behavior: A Scoping Review

Ronny Tri Wirasto[1)], Windhy Monica[1)]

[1)]Department of Psychiatry, Universitas Gadjah Mada, Indonesia

Received: June 02, 2026; Accepted: July 03, 2026; Available online: July 16, 2026

ABSTRACT

Background: Emerging evidence suggests that systemic inflammation may contribute to the pathophysiology of depression and self-harm. This study aims to map the scientific evidence regarding the relationship between Systemic Immune-Inflammation Index (SII) as a readily available biomarker and self-harm behavior across various populations and clinical contexts, while identifying patterns of findings, methodological variations, and existing research gaps.
Subjects and Method: This research employs a scoping review methodology based on the Arksey and O'Malley framework and reported in accordance with the PRISMA Extension for Scoping Review. Literature was sourced from databases such as PubMed and ScienceDirect. Seven studies were included in the final synthesis and the critical appraisal of the selected papers followed the Joanna Briggs Institute (JBI) guidelines.
Results: Higher SII levels were consistently associated with increased suicide risk, particularly in treatment-naïve and first-episode Major Depressive Disorder (MDD) populations. Adolescents with co-occurring NSSI and SA demonstrated the most pronounced inflammatory profiles, whereas findings were less consistent in isolated NSSI or SA groups.
Conclusion: Current evidence suggests that SII may have potential utility as an adjunctive biomarker for self-harm risk stratification and its clinical utility remains limited by moderate predictive accuracy and methodological heterogeneity.

Keywords: biomarker, Systemic Immune-Inflammation Index, self-harm, suicide attempt

Correspondence:
Ronny Tri Wirasto. Department of Psychiatry, Universitas Gadjah Mada. Jl. Farmako, Sleman, Yogyakarta, Indonesia. Email: ronny3w@ugm.ac.id.

Cite this as:
Wirasto RT, Monica W (2026). Association between Systemic Immune-Inflammation Index and Self-Harm Behavior: A Scoping Review. *J Epidemiol Public Health*. 11(3): 337-352. https://doi.org/10.26911/-jepublichealth.2026.11.03.10.

BACKGROUND

Self-harm is a serious mental health problem as it commonly begins in adolescence, is associated with impaired emotional regulation, and may progress to suicidal behavior in some individuals (Duarte et al., 2020). In populations with major depressive disorder (MDD), self-harm behaviors have substantial clinical relevance because non-suicidal self-injury (NSSI) and suicide attempt (SA) are common, often comorbid, and associated with varying degrees of clinical risks (Peng et al., 2024). However, assessment of self-harm and suicidal behavior remains largely dependent on subjective reports, underscoring the need for more objective biological markers for early identification and

risk stratification (Cheng et al., 2022; Fu et al., 2025).

In recent years, low grade inflammation has increasingly been recognized as a potential biological mechanism that contributes to depression and suicidal behavior (Lovig et al., 2026; Osimo et al., 2019). Studies have shown that elevated peripheral inflammation markers are associated with greater depressive symptoms, impulsivity, and increased prevalence of suicidal behavior, although findings across studies remain inconsistent (Cheng et al., 2022; Lewandowska et al., 2026; Schumacher et al., 2025). Among existing biomarkers, the Systemic Immune-Inflammation Index (SII), computed using neutrophil, lymphocyte, and platelet counts, has received increasing attention because it can be derived from routine blood tests, is affordable and accessible, and has been investigated in various psychiatric disorders, including MDD with suicidal risk (Bai et al., 2025; Cui et al., 2023; Moriarity et al., 2023; Qiao et al., 2025).

Nevertheless, evidence regarding the relationship between SII and self-harm behavior remain limited and fragmented. Furthermore, considerable heterogeneity exists across studies regarding participant characteristics, clinical settings, definitions of self-harm, inflammatory indices evaluated, and outcome measures, making direct comparison of findings difficult and precluding a comprehensive understanding of the current evidence. Therefore, this scoping review aims to map the scientific evidence regarding the relationship between SII and self-harm behaviors, including NSSI and suicide attempt, across various populations and clinical contexts, while identifying patterns of findings, methodological variations, and existing research gaps.

SUBJECTS AND METHOD

1. Study Design

This study reviewed the literature on the association between Systemic Immune-Inflammation Index (SII) and self-harm behavior using a scoping review approach. Scoping review allows researchers to explore key concepts, map evidence, and identify research gaps. This approach follows the framework developed by Arksey and O'Malley (2005), which outlines structured stages for conducting scoping reviews, including defining the review focus using the PCC (Population, Concept, Context) framework, identifying relevant articles, and documenting the study selection process using PRISMA flow diagram to identify literature, extract data, and conduct mapping or analysis of the findings.

This scoping review aimed to address the following question: "How has the association between SII and self-harm behavior been characterized across different populations and clinical settings?" The population included individuals across all age groups and with a history of or current showing self-harm behaviors, including documented suicide attempts (SA), non-suicidal self-injury (NSSI), and deliberate self-harm (DSH). This review focused on SII as a biomarker and its association with the presence, degree of severity, frequency, or clinical outcomes of self-harm behaviors. This review covered various clinical settings, including emergency departments, inpatient wards, and outpatient clinics, as well as community-based and epidemiological studies across diverse geographical and cultural contexts.

Literature search was conducted between January and March 2026 using PubMed and ScienceDirect databases, and Boolean and truncation operators were applied to combine search terms related to

SII and self-harm. The search included the following keywords and search strings: ("systemic immune-inflammation index" OR "systemic immune inflammation index" OR SII) AND (self-harm OR "self harm" OR "self-injury" OR "self injury" OR "non-suicidal self-injury" OR NSSI OR "suicide attempt*" OR "deliberate self-harm" OR parasuicide) AND (neutrophil* OR lymphocyte* OR platelet*).

Two reviewers independently evaluated all retrieved records using title and abstract screening before determining full-text eligibility based on predetermined inclusion and exclusion criteria. Using a uniform data-charting form, the same two reviewers independently extracted the data. Discussion and consensus were used to settle any disputes pertaining to study eligibility or extracted data.

2. Inclusion Criteria

The inclusion criteria for this scoping review comprised scientific publications published in English or Indonesian, primary studies or literature reviews relevant to the review topic, and studies published within the past five years to ensure the relevance and currency of the information.

3. Exclusion Criteria

The exclusion criteria included editorials, comments, letters to the editor, conference abstracts without sufficient data, non-peer-reviewed literature, and general narrative reviews without empirical data related to SII and self-harm behavior. Articles without accessible full texts were also excluded.

4. Operational Definition of Variables

Operational definitions for inflammation and self-harm behavior biomarkers are as follows:

Systemic Immune-Inflammation Index (SII): A composite hematological inflammatory index calculated from routine peripheral blood counts using the following formula: SII = (platelet count × neutrophil count) / lymphocyte count. SII is used as an indicator of systemic inflammatory and immune status.

Self-Harm Behavior: Every intentional self-harming behavior performed with or without suicidal intent, including suicide attempts (SA), non-suicidal self-injury (NSSI), and deliberate self-harm (DSH), as identified in each study (through clinical interviews, medical records, or standardized questionnaires).

Suicidal Behavior: A subcategory of self-harm behavior involving suicide attempts or preparatory acts associated with self-injury performed with suicidal intent, as defined in the included articles.

Psychiatric Diagnosis: Mental disorders diagnosed based on standard diagnostic criteria (DSM-5 or ICD-10) or clinical assessments in the included studies, such as major depressive disorder, bipolar disorder, schizophrenia, and borderline personality disorder.

5. Study Instruments

PRISMA Extension for Scoping Reviews (PRISMA-ScR) was used to describe the article selection process in this scoping review. PRISMA is an evidence-based reporting tool designed to improve transparency and consistency in the reporting of systematic and scoping reviews by documenting the number of records identified, screened, excluded, and ultimately included at each stage of the process(Tricco et al., 2018). PRISMA is considered appropriate for this study because it enhances the clarity of the literature identification and selection process in scientific publication.

Following the article selection process, the methodological quality of the included studies was assessed using the Critical Appraisal instrument developed by Joanna Briggs Institute (JBI), tailored to the study design (Barker et al., 2025;

Barker et al., 2026). The JBI appraisal tools evaluate internal validity, risk of bias, and the overall relevance aspects, thereby allowing researchers to identify the strengths and limitations of studies available. This appraisal was conducted to support the interpretation of findings rather than to serve as the primary basis for study exclusion, except in cases of severe methodological limitations (Porritt et al., 2023).

6. Data Analysis

The final stage involved integrating the scoping review findings into a structured report. Data charting was conducted for each selected article to identify key elements. The findings were then synthesized descriptively through numerical summaries and thematic mapping to identify patterns in the association between SII and self-harm behaviors across clinical settings, highlight research gaps, and formulate recommendations for future studies and potential clinical implications.

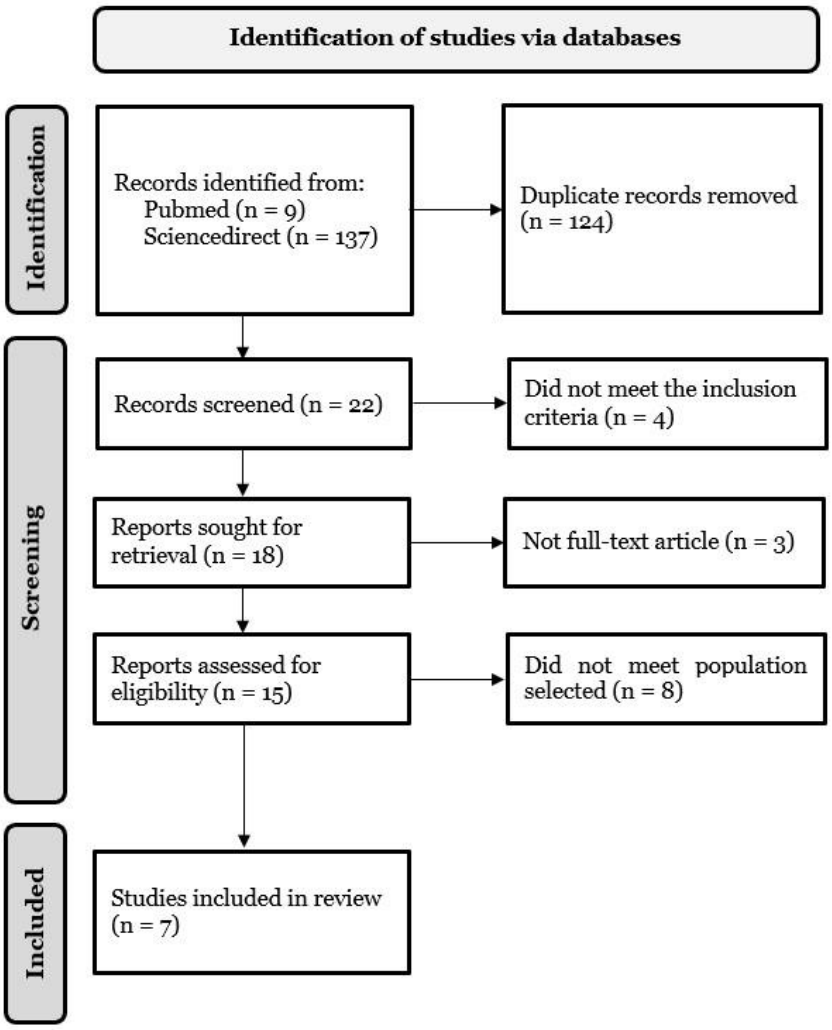

Figure 1. Prisma-ScR Flow Diagram

RESULTS

Seven articles that met the inclusion criteria were charted to identify key characteristics of each study, including study objectives, design, sample characteristics, inflammatory biomarkers assessed, and principal findings (Table 1). The included studies

comprised five cross-sectional studies and two retrospective cohort studies were involved. Each research design was evaluated using distinct critical appraisal criteria based on Joanna Briggs Institute (JBI) critical appraisal tool scores (Table 2 and 3).

Two studies were conducted in a developed country (China) while the remaining studies were in developing countries. The study populations included adolescents and adults with various severe mental disorders (schizophrenia, MDD, and bipolar disorder) across diverse clinical settings. Following article selection, key elements were mapped out as part of the scoping review process.

Based on the critical appraisal results, six included articles were classified as good category, indicating strong methodological quality and high validity, whereas one study was classified as moderate quality due to its use of secondary data from retrospective medical records, which limited the availability of standardized information. Retrospective cohort studies received higher appraisal scores than cross-sectional studies due to aspects such as follow-up, control of confounding variable, and stronger temporal inference.

Table 1. Critical Appraisal of Included Studies

Author (Year)	Study Design	Inclusion Criteria	Exposure Measurement	Outcome Measurement	Confounding Factors	Statistical Analysis
Cui et al. (2023)	Cross-sectional study	✓	✓	✓	Adequately addressed	Appropiate
Ninla-Aesong et al. (2024)	Retrospective cohort study	✓	✓	✓	Adequately addressed	Appropiate
Fu et al. (2025)	Cross-sectional study	✓	✓	✓	Adequately addressed	Appropiate
Gökçay et al. (2025)	Cross-sectional study	✓	✓	✓	Adequately addressed	Appropiate
Wu et al. (2025)	Retrospective cohort study	✓	✓	✓	Adequately addressed	Appropiate
Bakay & Bakay (2026)	Cross-sectional study	✓	✓	✓	Adequately addressed	Appropiate
Liu et al. (2026)	Cross-sectional study	✓	✓	✓	Adequately addressed	Appropiate

Table 2. Joanna Briggs Institute (JBI) Critical Appraisal Tool Scores for Cohort Studies

Retrospective cohort study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Overall
Ninla-Aesong et al. (2024)	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	No	Yes	Good (9.5/11)
Wu et al. (2025)	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	NA	NA	Yes	Moderate (7/11)

Yes = 1 point; Unclear = 0.5 point; No and NA (Not applicable) = 0 point. Overall methodological quality was classified as Good (>70% of the maximum score), Moderate (50–70%), or Poor (<50%).

Table 3. Joanna Briggs Institute (JBI) critical appraisal tool scores for cross sectional studies

Cross Sectional Studies	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Overall
Cui et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good (8/8)
Fu et al. (2025)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good (8/8)
Gökçay et al. (2025)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Good (7/8)
Bakay and Bakay (2026)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good (8/8)
Liu et al. (2026)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good (8/8)

Yes = 1 point; Unclear = 0.5 point; No and NA (Not applicable) = 0 point. Overall methodological quality was classified as Good (>70% of the maximum score), Moderate (50–70%), or Poor (<50%).

As shown in Table 4, the most commonly studied populations were adolescents, young adults, or first-episode patients diagnosed with MDD. Several studies specifically differentiated participants with NSSI, SA, or co-occurring NSSI and SA. The included studies primarily focused on inflammatory biomarkers derived from routine blood counts to assess the association between inflammation and self-harm behavior. Most studies were conducted in hospital or psychiatric service settings, including both inpatient and outpatient care, and predominantly employed retrospective or cross-sectional study designs. Overall, the findings suggest that elevated systemic inflammatory markers are associated with an increased risk of suicidal behaviors, although the observed pattern is not always consistent across subgroups.

Table 4. Summary of Included Studies in the Scoping Review

Author (Year)	Country	Study Design	P (Population)	C (Concept)	C (Context)	Key Notes
Cui et al. (2023)	China	Cross-sectional study	Children and adolescents with first-episode, drug-naïve MDD (n = 263)	SII and suicide attempt	Inpatient psychiatric hospital during COVID-19 pandemic	Patients with SA had higher HDRS, neutrophils, platelets, and SII; SII cut-off 548.15 with AUC 0.661; high SII independently predicted total SA and recent SA, but not past SA.
Ninlaaesong et al. (2024)	Thailand	Retrospective cohort study	Young adults with MDD and matched healthy controls (139 MDD, 54 HC)	Novel and classical inflammatory indices (SII, SIRI, NLR, MLR, PLR)	University hospital psychiatry clinic/ outpatient setting	MDD with SA showed significantly higher MLR and SIRI; NLR had the best ROC performance for distinguishing SA (AUC 0.71, cutoff 1.82); SII and NLR were stronger for MDD diagnosis than for SA classification.
Fu et al. (2025)	China	Cross-sectional study	357 DSM-V diagnosed MDD patients	Inflammatory indices including SII	Hospital-based psychiatric ward	MDD patients with suicidal tendencies showed higher logSII.

Author (Year)	Country	Study Design	P (Population)	C (Concept)	C (Context)	Key Notes
Gökçay et al. (2025)	Turkey	Cross-sectional study	100 patients hospitalized for a recent suicide attempt, 74 individuals with psychiatric disorders without a recent suicide attempt, and 85 healthy controls	Inflammatory indices derived from routine complete blood count (NLR, PLR, SII, SIRI, PIV) and serum metabolic indices	Hospital-based psychiatric ward	Suicide-attempt group showed higher leukocyte and neutrophil counts, lower lymphocytes, and higher NLR, SII, SIRI, and PIV than non-attempt group.
Wu et al. (2025)	China	Retrospective cohort study	338 treatment-naïve patients experiencing a first-episode of MDD and 76 healthy individuals	Association between SII, suicide attempts and clinical risk factors	Hospital-based clinical setting	Patients with MDD exhibited elevated neutrophil and platelet counts as well as higher SII values compared with the control group; the SA group demonstrated higher HDRS scores, neutrophil counts, platelet counts and SII values; an SII cut-off values of 515.3 yielded an AUC of 0.69; an elevated SII value was significantly associated with recent SA.
Bakay and Bakay (2026)	Türkiye	Cross-sectional study	Adult patients with MDD with or without a history of SA (n = 204)	The roles of inflammatory indices (SII, SIRI, PIV)	Psychiatric clinics in tertiary hospitals	The SA group was younger and exhibited with higher WBC, neutrophil count, NLR, SII, SIRI, and PIV values, as well as lower lymphocyte counts; these findings suggest a greater systemic inflammatory burden among patients with MDD and a history of SA.
Liu et al. (2026)	China	Cross-sectional study	Adolescent hospitalized patients with MDD categorized into pure MDD, NSSI-only, SA-only, and co-occurring NSSI and SA (n = 618)	Association between CBC-derived inflammatory indices and NSSI and SA	Adolescent psychiatric wards in general hospitals	The NSSI+SA group exhibited the most pronounced inflammatory profile, characterized by higher neutrophil counts and elevated NLR, MLR, PLR, and SII values, as well as lower lymphocyte counts; NLR was identified as an independent risk factor for the NSSI+SA group; SA-

Author (Year)	Country	Study Design	P (Population)	C (Concept)	C (Context)	Key Notes
						only group did not exhibit specific inflammatory profiles.

SII, Systemic Inflammation Response Index; NLR, neutrophil-to-lymphocyte ratio, MLR, monocyte-to-lymphocyte ratio; SIRI, systemic inflammation response index; PIV, pan-immune-inflammation value; CBC, complete blood count; MDD, major depressive disorder; HC, Healthy Control; NSSI, non-suicidal self-injury; SA, suicide attempts; ROC, Receiver Operating Characteristic; AUC, Area Under the Curve; HDRS, Hamilton Depression Rating Scale

According to the thematic mapping presented in Table 5, the included studies in this scoping review were categorized into five main themes (See Table 5).

Table 5. Thematic Mapping in The Scoping Review

Theme	Sub-theme	Article(s)
Inflammatory biomarkers in MDD and suicidality	a. Classical CBC-derived indices (NLR, PLR, MLR, platelet count)	Liu et al., 2026; Bakai et al., 2025; Ninla-aesong et al., 2024; Wu et al., 2025; Cui et al., 2023; Gökçay et al., 2025
	b. Novel composite indices (SII, SIRI, PIV)	Bakai et al., 2025; Ninla-aesong et al., 2024; Fu et al., 2025; Wu et al., 2025; Cui et al., 2023
	c. Erythroid and metabolic markers (RBC, Hb, TyG, lipid profile)	Gökçay et al., 2025
Clinical phenotypes of suicidal and self-harm behavior in MDD	a. Distinction between NSSI, SA, and co-occurring NSSI and SA in adolescents	Liu et al., 2026
	b. Suicide attempts vs non-attempts in adult with MDD	Bakai et al., 2025; Ninla-aesong et al., 2024; Wu et al., 2025; Gökçay et al., 2025
	c. Suicidal ideation, suicidal tendency, and risk gradients	Fu et al., 2025; Wu et al., 2025
Inflammatory profiles associated with suicidal/ self-harm risk	a. Robust inflammatory signature in high-risk phenotypes (e.g. NSSI+SA, SA with high SII/PIV)	Liu et al., 2026; Bakai et al., 2025; Wu et al., 2025
	b. Restricted or absent inflammatory changes in specific subgroups (e.g. SA-only, NSSI-only)	Liu et al., 2026; Ninla-aesong et al., 2024
	c. Sex, age, and comorbidity influences on inflammatory indices	Liu et al., 2026; Bakai et al., 2025
Methodological aspects and measurement issues	a. Design characteristics (cross-sectional, retrospective, single-center inpatient/outpatient samples)	Bakai et al., 2025; Liu et al., 2026; Fu et al., 2025; Wu et al., 2025; Ninla-aesong et al., 2024
	b. Control of confounding factors (infection, autoimmune disease, medication, BMI, comorbidities)	Bakai et al., 2025; Liu et al., 2026; Cui et al., 2023; Ninla-aesong et al., 2024; Wu et al., 2025

Theme	Sub-theme	Article(s)
	c. Statistical modelling and cut-off determination (logistic regression, ROC/AUC analysis)	Bakai et al., 2025; Liu et al., 2026; Ninla-aesong et al., 2024; Fu et al., 2025; Wu et al., 2025
Clinical implications and future research directions	a. Use of inflammatory indices for risk stratification and screening in MDD	Bakai et al., 2025; Liu et al., 2026; Ninla-aesong et al., 2024; Wu et al., 2025; Fu et al., 2025
	b. Relationship between inflammatory markers and treatment outcomes (e.g. SSRI response, platelet-based predictors)	Ninla-aesong et al., 2024; Cui et al., 2023
	c. Identified knowledge gaps and need for longitudinal, multimodal biomarker studies	Bakai et al., 2025; Liu et al., 2026; Fu et al., 2025; Ninla-aesong et al., 2024; Wu et al., 2025

BMI, body mass index; SII, Systemic Inflammation Response Index; NLR, neutrophil-to-lymphocyte ratio, MLR, monocyte-to-lymphocyte ratio; SIRI, systemic inflammation response index; PIV, pan-immune-inflammation value; CBC, complete blood count; RBC, red blood cell; Hb, haemoglobin; TyG, triglyceride-glucose index; MDD, major depressive disorder; HC, Healthy Control; NSSI, non-suicidal self-injury; SA, suicide attempts; ROC, Receiver Operating Characteristic; AUC, Area Under the Curve; SSRI, selective serotonin reuptake inhibitor

The first theme, inflammatory biomarkers in MDD and suicidality, suggests that existing evidence consistently identifies inflammatory index derived from routine blood counts as important markers in understanding the association between MDD and suicidal behavior. While classical indices such as NLR, PLR, MLR and platelet count were widely used to reflect systemic inflammatory activity, newer composite indices such as SII, may provide a more comprehensive assessment of cumulative immune–inflammatory burden (Bakay and Bakay, 2026; Liu et al., 2026; Ninla-aesong et al., 2024; Wu et al., 2025). Several studies further included hematological and metabolic markers to examine the relationship between inflammation and metabolic dysfunction associated with depression (Fu et al., 2025; Gokcay et al., 2025). This theme emphasizes that the role of inflammation in suicidal behavior among patients with MDD is multidimensional and cannot be explained by a single marker.

The second theme, clinical phenotypes of suicidal and self-harm behavior in MDD, emphasizes the importance of distinguishing between various clinical manifestations of self-harm and suicidal behaviors in the context of MDD. In adolescents, the separation of NSSI, SA, and co-occurring NSSI and SA allows for the identification of high-risk phenotypes that are clinically distinct from pure MDD (Liu et al., 2026). In adults, distinguishing MDD patients with or without a history of SA, as well as assessing risk escalation from suicidal ideation to suicidal behavior suggest that symptom burden and risk profiles are not homogenous, and that phenotypic variations are associated with observed differences in inflammatory patterns (Cui et al., 2023; Ninla-aesong et al., 2024; Wu et al., 2025).

The third theme, inflammatory profiles associated with suicidal/self-harm risk, highlights distinct inflammatory patterns across high-risk phenotypes compared with other subgroups. A study

identify pronounced inflammatory "signature" in groups with co-occurring NSSI and SA, or in patients with SA and elevated SII values, characterized by increased composite indices and reduced lymphocyte counts, suggesting broader innate immune activation (Liu et al., 2026). In contrast, certain subgroups, such as SA-only or NSSI-only, demonstrated limited or less pronounced inflammatory changes, and variations in indices were also influenced by age, sex, and comorbidities (Cui et al., 2023; Gokcay et al., 2025; Wu et al., 2025). This theme underscores the biological heterogeneity underlying clinical categories of self-harm clinical behaviors that may otherwise appear similar.

The fourth theme, methodological aspects and measurement issues, highlights that the strengths and consistency of findings are strongly influenced by study design, measurement methods, and control of confounding factors. Most studies employed cross-sectional or retrospective designs and were conducted in single-center settings with specific inpatient or outpatient samples, thereby limiting the temporal inference and generalizability of the findings (Bakay and Bakay, 2026; Cui et al., 2023; Fu et al., 2025; Liu et al., 2026; Ninla-aesong et al., 2024). Control for infections, autoimmune diseases, medication use, BMI, and other comorbidities, as well as the application of advanced statistical models plays a critical role not only in isolating biomarker signals, but also in demonstrating that interpretation of inflammatory indices depends heavily on the methodological context of each study.

The fifth theme, clinical implications and future research directions, summarizes the potential integration of inflammatory indices into clinical practice while also highlighting substantial existing knowledge gaps. All studies have proposed the use of NLR, SII, SIRI, PIV and other relevant indices as tools for risk stratification and supplementary screening in patients with MDD, as well as for predicting self-harm risk, treatment response, and other clinical outcomes. However, the absence of validated cut-off values across populations, the reliance on non-longitudinal study designs, and the lack of multimodal studies have led researchers to recommend prospective multi-center studies that integrate hematological biomarkers, other inflammatory markers, and clinical data to evaluate the utility of these biomarkers more robustly and with greater translational relevance.

DISCUSSION

The findings of this scoping review suggest that inflammatory biomarkers based on routine blood tests show a relatively consistent association with suicidal and self-harm behaviors among patients with MDD, particularly in adolescents and young adults. Overall, studies indicate that patients with MDD and a history of SA tend to exhibit elevated neutrophil, platelet, and composite inflammatory indices such as SII, NLR, MLR, SIRI, and PIV, compared with patients without SA. These patterns support the hypothesis that low-grade systemic inflammation may contribute to the biological vulnerability underlying suicidal behavior, beyond the psychosocial factors that have historically dominated the literature.

Among markers reported in the literature, SII appears to be the marker most consistently associated with SA, particularly among patients experiencing a first-episode of MDD who have not yet received treatment. Cui et al. (2023) and Wu et al. (2025) reported that patients with SA exhibited higher SII scores than those without SA, and that elevated SII scores

were associated with an increased recent risk of SA, even after adjustment for important clinical factors, including age, sex, body mass index, disease duration, and depression severity (Wu et al., 2025). This finding is important, as SII may represent more than a passive marker for inflammation and can serve as an additional indicator for stratifying suicide risk among patients with MDD. Nevertheless, the AUC values reported in both studies were moderate, suggesting that SII may be more suitable as a supportive marker than a standalone diagnostic instrument.

Other than SII, NLR also presented notable relevance across various clinical contexts. Ninla-aesong et al. (2024) reported that NLR exhibited the highest performance in ROC analysis among MLR, PLR, SII, and SIRI for identifying MDD patients with or without SA. Meanwhile, Liu et al. (2026) who focused on adolescents with MDD, identified NLR as the strongest independent risk factor associated with the comorbid NSSI and SA group. These findings indicate that NLR may be more sensitive in reflecting innate immune activation associated with impulsivity, emotional distress, and a tendency toward more severe self-harm behaviors (Dionisie et al., 2021; Gokcay et al., 2025; Moriarity et al., 2023; Zhang et al., 2026). Biologically, neutrophil predominance relative to lymphocytes may also indicate the presence of systemic proinflammatory activity that could affect serotoninergic neurotransmission, glutamate receptors, neuroplasticity, and stress regulation, all of which are relevant to the pathophysiology of depression and suicidal behavior (Kindler et al., 2022; Lewandowska et al., 2026; Qiao et al., 2025).

One of the most important findings of this synthesis is the difference in inflammatory profiles among clinical subgroups characterized by self-harm and suicidal behaviors. Liu et al. (2026) found that adolescents with comorbid NSSI and SA exhibited the strongest inflammatory profiles, marked with elevated neutrophil counts, NLR, MLR, PLR, and SII levels, as well as reduced lymphocyte counts, compared with patients with pure MDD, NSSI-only, or SA-only. In contrast, SA-alone group did not display specific inflammatory patterns, suggesting that suicidal behavior in MDD is not a homogenous biological phenomenon. Comorbid NSSI and SA may represent a high-risk clinical phenotype characterized by more pronounce immune activation, whereas SA-only may be more strongly influenced by acute situational factors, temporal impulsivity, or other non-inflammatory determinants. Therefore, distinguishing among NSSI-alone, SA-alone, and comorbid NSSI and SA subgroups may play an important role in future biomarker research to prevent bias arising from clinical heterogeneity.

Methodologically, inconsistencies across studies may also be attributable to differences in research design, sample characteristics, and the inflammatory indices evaluated. As majority of studies employed retrospective or cross-sectional designs, the causal relationship between inflammation and suicidal behavior remains uncertain. In addition, several studies included more homogeneous populations, such as drug-naïve patients experiencing a first-episode of MDD or hospitalized adolescents, whereas others included adults with a broader age range. Such variation may influence inflammatory marker levels, considering that age, sex, nutritional status, medical comorbidities, medication exposure, smoking habits, and lifestyle factors are known to affect peripheral inflammatory profiles. Therefore, inconsistencies observed in certain

markers, such as elevated SII levels in several studies without consistent superiority over NLR, may reflect biological and methodological heterogeneity rather than weaknesses of the markers themselves.

From a clinical perspective, this suggests that inflammatory indices derived from complete blood count (CBC) tests offer advantages due to their affordability, accessibility and availability through routine laboratory examinations (Moriarity et al., 2023; Paniagua et al., 2024). These characteristics make them attractive objective tools for risk assessment, particularly in settings where resources are limited, or when more complex biomarkers, such as cytokine and C-Reactive Protein (CRP), are unavailable (Kindler et al., 2022; Qiao et al., 2025). However, it is important to note that these markers have not demonstrated sufficient specificity to be used as standalone diagnostic tools or predictors of suicidal behavior. The generally moderate AUC values, lack of validated cut-off values across populations, and influence of numerous confounding factors indicate that these biomarkers should be interpreted alongside comprehensive clinical assessment, including evaluation of depressive symptoms, impulsivity, history of NSSI, history of SA, family background, and psychosocial stressors.

From biology perspective, association between elevated SII and self-harm behavior may be partially explained by pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) (Lewandowska et al., 2026). Increased peripheral inflammatory activity reflected by elevated neutrophil and platelet counts has been linked to higher circulating levels of IL-6 and CRP (Bai et al., 2024; Han et al., 2025). Peripheral inflammatory cytokines may activate microglia and release additional pro-inflammatory mediators contributing to neuroinflammation and impaired synaptic plasticity within frontolimbic circuits involved in emotional regulation and impulse control (Qiao et al., 2025). IL-6 and TNF-α may activate indoleamine 2,3-dioxygenase (IDO), shifting tryptophan metabolism away from serotonin synthesis toward the kynurenine pathway. This process reduces serotonin availability while increasing neuroactive metabolites such as quinolinic acid, which may promote glutamatergic excitotoxicity and increase vulnerability to suicidal behaviors (Cheng et al., 2022).

Although most studies reported a positive association between elevated inflammatory biomarkers and suicidal behavior, the strength and consistency of these associations varied across studies. These inconsistencies are likely attributable to several methodological and clinical differences. First, the included studies involved heterogeneous populations, ranging from adolescents to adults, and from treatment-naïve first-episode MDD to chronic or mixed psychiatric populations. Since inflammatory responses may vary according to age, illness duration, medication exposure, and psychiatric comorbidities, direct comparison across studies is challenging. Second, the definition of self-harm differed considerably. While several studies focused exclusively on suicide attempts, others included non-suicidal self-injury (NSSI), suicidal ideation, or combined NSSI and suicide attempt groups. These behaviors may represent distinct clinical phenotypes with different underlying biological mechanisms and inflammatory profiles. Third, variations in the inflammatory biomarkers evaluated may also contribute to inconsistent findings. Although SII integrates neutrophil, platelet, and lymphocyte counts into a composite index, some studies reported

stronger predictive performance for other biomarkers, such as NLR or SIRI, suggesting that no single inflammatory marker consistently captures the complex pathophysiology of self-harm. Finally, differences in study design, sample size, control of confounding factors, and statistical modelling may have further influenced the observed associations. Therefore, the current evidence should be interpreted cautiously, as the observed inconsistencies likely reflect both biological heterogeneity and methodological variation rather than contradictory findings.

Overall, this scoping review demonstrates that elevated SII is consistently associated with increased suicidal risk, particularly among individuals with major depressive disorder, although the strength of this association varies across clinical populations and study designs. The current evidence supports the potential role of SII as an accessible inflammatory biomarker that may complement existing suicide risk assessment strategies. Nevertheless, methodological heterogeneity and the predominance of observational studies indicate that the current evidence remains insufficient to support its use as a standalone predictive biomarker.

Several limitations across the included studies should also be taken into consideration. First, predominance of retrospective and cross-sectional designs limits temporal assessment, making it difficult to determine whether inflammation precedes suicidal behavior or instead arises as a consequence of accompanying acute conditions. Second, most studies were conducted in single-cew nter settings, limiting the generalizability of results to the broader population. Third, definitions of suicidal behavior varied across studies. For instance, several studies distinguished recent AS from past SA, whereas other studies assessed only a general history of SA. Fourth, not all studies employed structured and standardized instruments for suicidal behavior assessment, leaving room for classification bias. Fifth, the majority of the studies assessed only hematology biomarkers without integrating other inflammatory markers, such as IL-6, TNF-α, CRP, or other oxidative stress parameters, resulting in only partial understanding of biological mechanisms.

An additional limitation of this scoping review is the restricted database coverage. The literature search was conducted exclusively in PubMed and ScienceDirect. Although these databases index a substantial proportion of biomedical and psychiatric research, relevant studies indexed in other databases, such as Embase, PsycINFO, Web of Science, or Scopus, may not have been captured. Consequently, the evidence synthesized in this review may not represent the entire body of available literature on the association between the SII and self-harm behavior. In addition, future investigations should prioritize prospective longitudinal and multicenter studies with larger and more diverse populations to clarify the temporal relationship between systemic inflammation and self-harm behavior and integrate SII with other biological, psychological, and social risk factors to develop multimodal prediction models that may provide greater clinical accuracy than inflammatory markers alone.

FINANCIAL SUPPORT AND SPONSORSHIP

Nill or none.

ACKNOWLEDGEMENT

The authors would like to express their sincere gratitude to all who contributed to the completion of this study.

CONFLICT OF INTEREST

The authors declare that the study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

REFERENCES

Bai S, Asarnow JR, Babeva KN, Irwin MR (2024). IL-6 predicts non-suicidal self-injury over 3 months in high-risk adolescents. BJPsych Open. 10: e51. https://doi.org/10.1192/bjo.2023.656

Bai Y, Fang Z, Dai H, Zhang Q, You P (2025). The correlation between systemic immune-inflammation index and major depression in patients with depression. Front Psychiatry. 16. https://doi.org/10.3389/fpsyt.2025.1580151.

Bakay H, Bakay B (2026). Composite Inflammatory Burden and Suicide Risk: The Predictive Role of SII, SIRI, and PIV in Patients with Major Depressive Disorder. Bratislava Med J. https://doi.org/10.1007/s44411-026-00496-3

Barker TH, Hasanoff S, Aromataris E, Stone JC, Leonardi-Bee J, Sears K, et al. (2026). The revised JBI critical appraisal tool for the assessment of risk of bias for analytical cross-sectional studies. JBI Evid Synth. 24(3): 401-8. https://doi.org/10.1124/jbies-24-00523.

Barker TH, Hasanoff S, Aromataris E, Stone JC, Leonardi-Bee J, Sears K, et al. (2025). The revised JBI critical appraisal tool for the assessment of risk of bias for cohort studies. JBI Evid Synth. 23(3)1. https://doi.org/-10.11124/JBIES-24-00103.

Cheng Y, Wang Y, Wang X, Jiang Z, Zhu L, Fang S (2022). Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Monocyte-to-Lymphocyte Ratio in Depression: An Updated Systematic Review and Meta-Analysis. Front Psychiatry. https://doi.org-/10.3389/fpsyt.2022.893097

Cui S, Liu Z, Liu Y, Yao G, Wu Y, Li J, Sun F, et al. (2023). Correlation between systemic immune-inflammation index and suicide attempts in children and adolescents with first-episode, drug-naïve major depressive disorder during the COVID-19 Pandemic. J Inflamm Res. 16: 4451–4460. https:-//doi.org/10.2147/JIR.S433397.

Dionisie V, Filip GA, Manea MC, Movileanu RC, Moisa E, Manea M, Riga S, et al. (2021). Neutrophil-to-lymphocyte ratio, a novel inflammatory marker, as a predictor of bipolar type in depressed patients: A quest for biological markers. J Clin Med. 10. https://doi.org/10.3390/jcm1009192.

Duarte TA, Paulino S, Almeida C, Gomes HS, Santos N, Gouveia-Pereira M (2020). Self-harm as a predisposition for suicide attempts: A study of adolescents' deliberate self-harm, suicidal ideation, and suicide attempts. Psychiatry Res. 287. https://doi.org/10.-1016/j.psychres.2019.112553.

Fu Z, Jiang J, Gao L, Zheng Y, Zhu Q (2025). Multi-system biomarkers of suicide risk in major depressive disorder: integrating erythroid parameters, composite inflammatory indices, and metabolic dysregulation. BMC Psychiatry. 25. https://doi.org/-10.1186/s12888-025-07616-3.

Gokcay H, Takim U, Acikgoz MG, Namli MN, Balcioglu YH (2025). Exploring the role of impulsivity, aggression, lipid profiles, and inflammatory markers in suicide attempts: a cross-diagnostic study. Braz J Psychiatry. 47. https://doi.org/10.47626/1516-4446-2024-4026.

Han Y, Huang X, Du Y, Yao Z (2025). Inflammation and impulsivity pathways in non-suicidal self-injury among bipolar disorder: A 24-week longitudinal cohort study. J Affect Disord. 391: 120015. https://doi.org-/10.1016/j.jad.2025.120015.

Kindler J, Koenig J, Lerch S, van der Venne P, Resch F, Kaess M (2022). Increased immunological markers in female adolescents with non-suicidal self-injury. J Affect Disord. 318: 191–195. https://doi.org/10.1016/j.jad.20-22.08.125.

Lewandowska M, Leszczyński-Czeczatka J, Siemiński M (2026). Inflammatory Biomarkers in Acute Suicidal Behaviors. Int J Mol Sci. https://doi.org/-10.3390/ijms27041691.

Liu J, Zhai X, Gao C, Zhang S, Fei D, Zhang X, Jin M, et al. (2026). Analysis of complete blood counts and derived inflammatory indices with non-suicidal self-injury and suicide attempt in adolescents with major depressive disorder. Front Psychiatry 17. https://doi.org/10.3389/fpsyt.20-26.1781733.

Lovig C, Osvath P, Saghy E, Molnar C, Kovacs MA, Petho B, Simon D, et al. (2026). Low-grade inflammatory parameters may be associated with recent suicide attempts – a naturalistic study among psychiatric inpatients with depressive disorders. Front Psychiatry 17. https://doi.org/-10.3389/fpsyt.2026.1707768.

Moriarity DP, Grehl MM, Walsh RFL, Roos LG, Slavich GM, Alloy LB (2023). A systematic review of associations between emotion regulation characteristics and inflammation. Neurosci Biobehav Rev. https://doi.org/10.101-6/j.neubiorev.2023.105162.

Ninla-aesong P, Kietdumrongwong P, Neupane SP, Puangsri P, Jongkrijak H, Chotipong P, et al. (2024). Relative value of novel systemic immune-inflammatory indices and classical hematological parameters in predicting depression, suicide attempts and treatment response. Sci Rep. 14. https://doi.org/10.1038/s41598-024-70097-z.

Osimo EF, Baxter LJ, Lewis G, Jones PB, Khandaker GM (2019). Prevalence of low-grade inflammation in depression: A systematic review and meta-Analysis of CRP levels. Psychol. Med. https://doi.org/10.1017/S0033291719001454.

Paniagua G, González-Blanco L, Sáiz PA, Moya-Lacasa C, Gutiérrez L, Martínez-Botía P, et al. (2024). Platelet and white blood-cell-based ratios: Differential inflammatory markers of severe mental disorders?. Span J Psychiatry Mental Health. https://doi.-org/10.1016/j.sjpmh.2023.03.002.

Peng B, Wang R, Zuo W, Liu H, Deng C, Jing X, Hu H, et al. (2024). Distinct correlation network of clinical characteristics in suicide attempters having adolescent major depressive disorder with non-suicidal self-injury. Transl Psychiatry. 14. https://doi.org/10.10-38/s41398-024-02843-w.

Porritt K, McArthur A, Lockwood C, Munn Z (2023). JBI's approach to evidence implementation: a 7-phase process model to support and guide getting evidence into practice. JBI Evid Implement. 21: 3–13. https://doi.org-/10.1097/XEB.0000000000000361.

Qiao D, Qi Y, Zhang X, Wen Y, Huang Y, Li Y, Liu P, et al. (2025). The possible effect of inflammation on non-suicidal self-injury in adolescents with depression: a mediator of connectivity

within corticostriatal reward circuitry. Eur Child Adolesc Psychiatry. 34: 2871–2885. https://doi.org/10.1007-/s00787-025-02709-6.

Schumacher A, Tu E, Albaum C, Korczak DJ (2025). The systemic immune-inflammation index (SII) as a biomarker for depression in a community sample of adolescents. Compr Psychoneuroendocrinol. 23. https://-doi.org/10.1016/j.cpnec.2025.100302

Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, Moher D, et al. (2018). PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med. 169: 467–473. https://doi.org/-10.7326/M18-0850.

Wu Y, Jiang W, Chen M, Jiang Q, Huang H, Guo W, Yuan Y (2025). Correlation between systemic immune inflammatory index and suicidal attempt in patients with first-episode untreated depression and its risk factors. Neuropsychiatr Dis Treat. 21: 827–839. https://doi.org/10.2147/NDT.S-512964.

Zhang W, Zhang Y, Xu T, Wang Y, Yu E, Yue J (2026). Inflammatory indices are associated with non-suicidal self-injury in adolescents with major depressive disorder. BMC Psychiatry 26. https://doi.org/10.1186/s12888-025-07705-3.