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Review

Hematological Inflammatory Markers and Chronic Diseases: Current Evidence and Future Perspectives

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Abstract

Background/Objectives: Complete blood count (CBC)-derived markers such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) have gained increasing attention as accessible indicators of systemic inflammation. These parameters, calculated from routine blood tests, are widely available in clinical settings and are potentially relevant for a variety of chronic diseases. This review aims to explore current evidence and highlight potential future directions regarding the use of hematologic inflammatory biomarkers in chronic disease. **Methods**: We performed an extensive literature search on PubMed to identify full-text original studies published in the past five years, focused on investigating the clinical applications of hematologic inflammatory markers in chronic conditions. **Results**: CBC-derived inflammatory markers have been studied in a wide range of chronic diseases, including autoimmune diseases, metabolic disorders, chronic kidney disease, chronic infections, psychiatric diseases, and other conditions. These markers have been evaluated for multiple clinical purposes, such as aiding diagnosis, monitoring disease status, assessing disease activity, disease subtype characterization, predicting prognosis, and evaluating associations with disease outcomes. **Conclusions**: As chronic diseases affect millions of individuals globally, placing a burden for the healthcare system, patients, and their families, simple and cost-efficient tools like CBC-derived inflammatory markers have the potential to improve clinical case management.

Keywords: chronic diseases; hematological inflammatory markers; disease monitoring; systemic inflammation

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1. Introduction

Chronic diseases, the leading cause of death worldwide, are associated with substantial morbidity and represent a persistent burden on healthcare systems, including significant financial strain. By 2030, the costs related to chronic conditions are projected to reach 47 billion dollars worldwide. Given the vast number of individuals requiring ongoing diagnosis, monitoring, and treatment, there is an urgent need for innovative, accessible, and cost-effective biomarkers to improve clinical management and reduce healthcare costs [1,2].

Probably the most widely available, inexpensive, and rapid laboratory investigation is the automated complete blood count (CBC), which provides a large number of calculated

parameters [3]. CBC-derived ratios emerged as biomarkers associated with inflammatory status and can be applied in the diagnosis, monitoring, prognosis, and assessment of therapeutic response in various diseases, as inflammation is associated with a broad spectrum of conditions and their progress [4–8].

CBC-derived hematological inflammatory biomarkers are ratios usually involving absolute count of CBC parameters, including AISI—aggregate index of systemic inflammation (Neutrophils × Monocytes × Platelets ÷ Lymphocytes); BLR—basophil-to-lymphocyte ratio (Basophils ÷ Lymphocytes); dNLR—derived neutrophil-to-lymphocyte ratio (Neutrophils ÷ [White blood cells—Neutrophils]); ELR—eosinophil-to-lymphocyte ratio (Eosinophils ÷ Lymphocytes); IIC—cumulative inflammatory index ((mean corpuscular volume × width of erythrocyte distribution × neutrophils)/(lymphocytes × 1000)); LMR—lymphocyte-to-monocyte ratio (Lymphocytes ÷ Monocytes); MLR—monocyte-to-lymphocyte ratio (Monocytes ÷ Lymphocytes); MPR—monocyte-to-platelet ratio (Monocytes ÷ Platelets); NLR—neutrophil-to-lymphocyte ratio (Neutrophils ÷ Lymphocytes); NMR—neutrophil-to-monocyte ratio (Neutrophils ÷ Monocytes); PIV—pan-immune-inflammation value (Neutrophils × Monocytes × Platelets ÷ Lymphocytes); PLR—platelet-to-lymphocyte ratio (Platelets ÷ Lymphocytes); PMR—platelet-to-monocyte ratio (Platelets ÷ Monocytes); PWR—platelet-to-white blood cell ratio (Platelets ÷ White blood cells); RLR—red cell distribution width-to-lymphocyte ratio (RDW ÷ Lymphocytes); RPR—red cell distribution width-to-platelet ratio (RDW ÷ Platelets); SII—systemic immune-inflammation index (Platelets × Neutrophils ÷ Lymphocytes); and SIRI—systemic inflammation response index (Neutrophils × Monocytes ÷ Lymphocytes) [9–15].

These biomarkers reflect the balance between innate and adaptive immune responses, coagulation, and oxidative stress, providing insight into both acute and chronic inflammatory states. Recent studies have shown that these markers correlate with disease severity, organ involvement, treatment response, and prognosis across multiple medical disciplines, including cardiovascular, neurological, psychiatric, dermatological, metabolic, autoimmune, infectious, and other chronic diseases. Given their non-invasive nature, widespread availability and prognostic potential, hematological inflammatory markers have become increasingly attractive tools for risk stratification, early detection, and monitoring of disease activity in clinical practice [4–8].

This review synthesizes current evidence on the clinical utility of hematological inflammatory markers in non-malignant chronic conditions, highlighting their diagnostic, prognostic and therapeutic relevance across diverse disease contexts.

The objective of this comprehensive, non-systematic review is to summarize and discuss the current evidence on the role of hematological inflammatory markers in chronic non-oncologic diseases. The review aims to highlight their clinical relevance across various chronic conditions, while identifying gaps in the existing literature and proposing directions for future research.

Oncologic disorders were not included in the present review. The scientific literature on hematological inflammatory markers in cancer is vast and highly specific, warranting a dedicated analysis to adequately address the complex mechanisms and diverse clinical implications involved. Therefore, to maintain focus and ensure a more coherent discussion, this review was restricted to non-oncologic chronic diseases.

The data analysis was purely qualitative. The studies were grouped based on conditions and presented in tables including study, disease, number of participants and controls, and reported results for the investigated biomarkers.

2. Materials and Methods

For this comprehensive, non-systematic review, a thorough literature search was performed on PubMed using the keywords 'hematological inflammatory markers NOT review' in July and August 2025. The applied filters included publications from the past five years, English-language literature, and free full text. Additionally, reviews, case reports, editorials, and letters to the editor were excluded. Retracted articles were not included. Only original studies involving humans that investigated hematological inflammatory parameters as ratio derived solely from complete blood count, in the context of chronic conditions were included. Neoplasia, acute conditions, and studies focused on procedures, investigation, or therapies rather than chronic conditions and studies, which investigated exposures in apparently healthy individuals, were excluded. The articles were filtered based on title, abstract, and full text. The main findings and study details from the primary sources were presented in tables, after grouping the available research on disease categories.

Studies were not excluded based on design, population, or outcomes, as the aim of this review was to provide a comprehensive and integrative overview rather than conduct a systematic review or meta-analysis. Consequently, no formal risk-of-bias assessment tool was applied, and a reproducible methods section or PRISMA flowchart was not included.

3. Results

After the above-described selection methodology, 72 articles were included in this literature review, covering various chronic conditions that were grouped in seven categories: cardiovascular disorders and associated conditions, psychiatric and neurological disorders, chronic infections, dermatological conditions, diabetes mellitus, autoimmune and inflammatory conditions, and other chronic conditions, as presented below. The research examined various ratios obtained from the total blood count in diverse quantities (Figure 1).

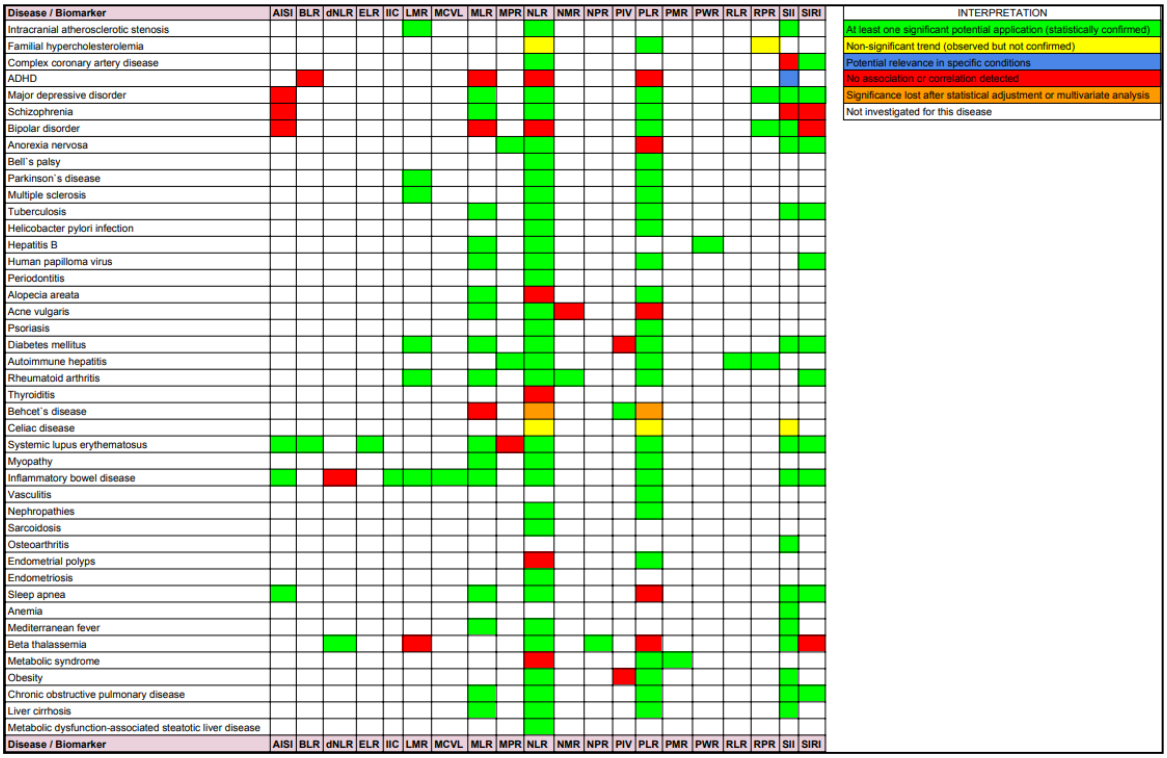


Figure 1. Overview of the evaluation status of hematological inflammatory indices in chronic conditions based on the results of the included studies.

3.1. Cardiovascular Disorders and Associated Conditions

Hematological inflammatory markers have shown relevance in cardiovascular and related conditions. The studies published within the past five years demonstrated relationships of different parameters in patients with hypercholesterolemia, atherosclerosis, and coronary artery disease, as shown in Table 1 and Figure 2 [16–18]. In intracranial atherosclerotic stenosis, LMR independently predicted symptomatic plaques [16]. In familial hypercholesterolemia (FH), PLR was elevated in probable and definite FH [17]. In angina patients, SIRI helped identify those with coronary disease [18].

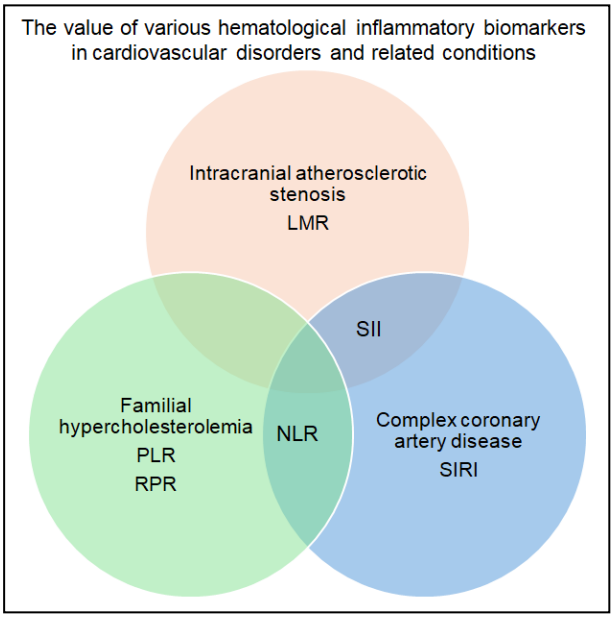


Figure 2. Hematological inflammatory markers in cardiovascular disorders and related conditions.

Different odds ratios obtained for hematological inflammatory indices in chronic conditions are presented in Figure 3.

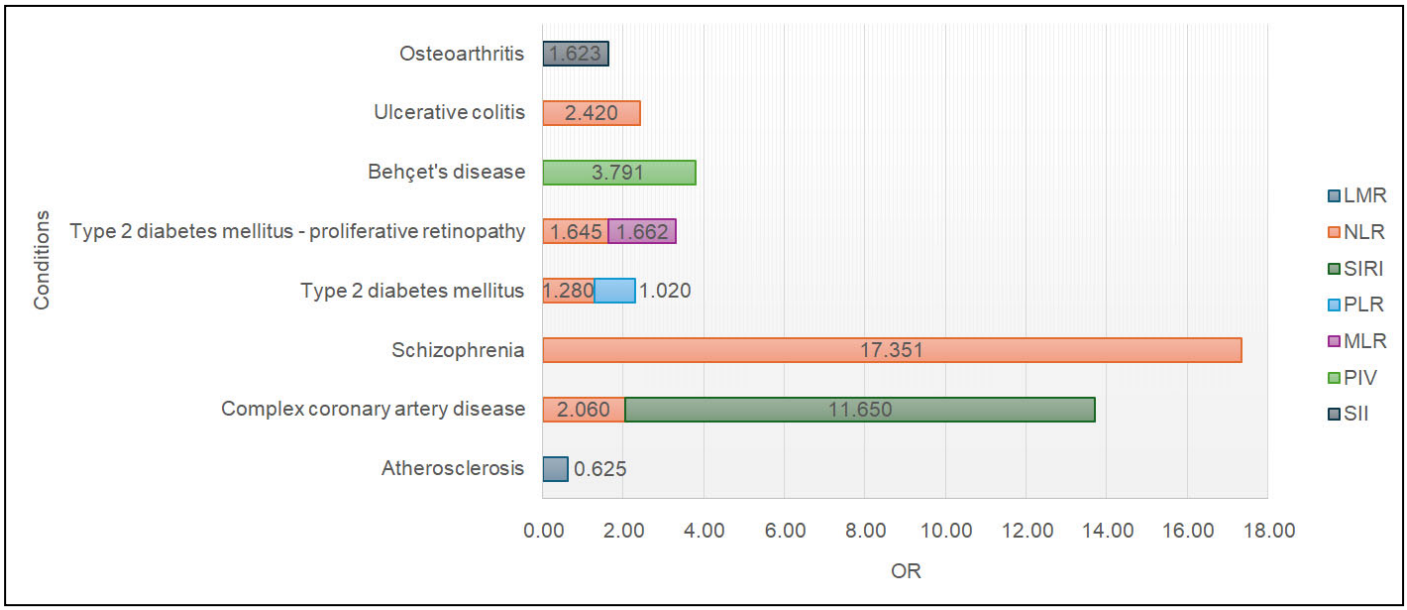


Figure 3. Odds ratios obtained for hematological inflammatory biomarkers in different chronic conditions.

Table 1. Hematological inflammatory markers in cardiovascular disorders and related conditions.

Study	Condition	Study Details	Main Findings
Wu et al., 2022 [16]	Atherosclerosis	• 59 patients with intracranial atherosclerotic stenosis • Investigated biomarkers: LMR, NLR, and SII	LMR (p = 0.005), NLR (p = 0.001), and SII (p = 0.002) associated significantly with plaque enhancement, but only LMR showed a strong negative linear correlation with the contrast ratio (r = 0.716, $p < 0.001$). A statistically significant association with symptomatic disease was observed for NLR (p = 0.011) and LMR (p = 0.001). LMR was independently associated with symptomatic disease (OR - 0.625, 95% CI 0.421–0.928, p = 0.02). For predicting symptomatic plaque, LMR yielded sensitivity of 80.0%, specificity of 70.6%, and AUC of 0.765 (cut-off: LMR $\leq$ 4.0).
Vaseghi et al., 2022 [17]	FH	• 1074 patients with clinically confirmed FH and 473 hyperlipidemic controls without FH • Investigated biomarkers: NLR, PLR, RPR	PLR was significantly elevated (p = 0.003) in FH patients compared to controls and higher in probable/definite FH than in possible FH ($p < 0.001$). The associations remained statistically significant after applying three models of adjustment for confounding variables (comparison with non-FH - p = 0.026, p = 0.032, p = 0.013, for comparison with possible FH - p = 0.002, p = 0.007, p = 0.029). Without being statistically significant, NLR was higher in the FH group, and RPR was lower among FH patients. Linear regression showed a non-significant independent association between RPR and total cholesterol in patients with FH ($p < 0.001$).
Urbanowicz et al., 2024 [18]	Coronary artery disease	• 256 patients with symptoms compatible with angina pectoris • Investigated biomarkers: SIRI, NLR, and SII	NLR (OR = 2.06, $p < 0.001$, CI 95% = 1.39–3.05) and SIRI (OR = 11.65, $p < 0.001$, CI 95%= 4.22–32.16) associated with complex coronary artery disease. After logistic multiple regression analysis, SIRI associated with coronary artery disease (OR = 5.52, p = 0.02, CI 95% = 1.89–16.15). A SIRI above 1.21 indicated the patients that had coronary disease (AUC - 0.725, $p < 0.001$, sensitivity - 49.19%, specificity - 85%).

FH—familial hypercholesterolemia, AUC—area under the curve, NLR—neutrophil-to-lymphocyte ratio, PLR—platelet-to-lymphocyte ratio, RPR—red cell distribution width to platelet count ratio, LMR—lymphocyte-to-monocyte ratio, SII—systemic immune-inflammation index, and SIRI—systemic inflammation response index.

3.2. Psychiatric and Neurological Disorders

Multiple recent studies evaluated the implications of complete blood count-derived ratios in psychiatric and neurological disorders, covering a wide range of conditions, including major psychiatric disorders, affective conditions, Parkinson's disease, ADHD, and others, as presented in Table 2 and Figure 4 [19–29]. NLR, PLR, LMR, MLR, SII, SIRI, and composite indices show altered profiles across psychiatric and neurological disorders. Elevated NLR, SII, SIRI, and AISI are commonly observed in schizophrenia [21,23], bipolar disorder [22,23], depression [22,23,25], Parkinson's disease [27,28], multiple sclerosis [29], and anorexia nervosa [24], often correlating with disease severity, symptom scores, or treatment response. PLR and MLR are frequently increased in major depressive disorder, bipolar mania, and non-responders to antidepressants [21,22,25]. LMR tends to decrease in Parkinson's disease and correlates negatively with symptom severity [27]. In ADHD, SII relates to hyperactivity scores [20], while in Bell's palsy and multiple sclerosis, NLR and PLR are generally higher than in controls [26,29]. Genetic risk for psychiatric disorders shows weak, but sometimes significant, associations with NLR, PLR, and MLR, modulated by lifestyle factors [21].

Table 2. Hematological inflammatory markers in psychiatric and neurological disorders.

Study	Condition	Study Details	Main Findings
Kamrani et al., 2025 [19]	Depression	• 3226 healthy individuals and 429 with depression • Investigated biomarkers: PLR, RLR, RPR, and GLR	In depressed patients, no significant associations were observed among DII higher scores and hematologic ratios.
Ceyhun et al., 2022 [20]	Adult ADHD	• 74 adult ADHD patients and 70 healthy controls • Investigated biomarkers: NLR, PLR, MLR, BLR, and SII	There were no significant results for these markers in ADHD patients compared to controls. Hyperactivity scores correlated positively with SII (r = 0.247, p = 0.034).
Sewell et al., 2021 [21]	Major psychiatric disorders	• Data from UK Biobank for 367,329 individuals with MDD, 366,465 with SCZ, and 366,383 with BD • Investigated biomarkers: NLR, PLR, and MLR (associations with disorder PRSs)	For MDD PRS, initial associations of NLR and PLR with genetic risk disappeared after controlling lifestyle covariates. For SCZ PRS, significant negative associations were identified with NLR, PLR, and MLR. For BD PRS, the only significant result after full adjustment was a negative association with PLR.
Wei et al., 2022 [22]	Affective disorders	• 14,007 patients with affective disorders and 6847 healthy individuals • Investigated biomarkers: SII, PLR, and RPR	Among the whole group of patients with affective disorders, only RPR was statistically significant ($p < 0.001$). Even after corrections, PLR, SII, and RPR values were significantly different between patients with MDD and controls ($p < 0.001$ for PLR, $p = 0.04$ for SII and $p < 0.001$ for RPR) and patients with BD and controls ($p < 0.001$ for PLR, $p < 0.001$ for SII and $p < 0.001$ for RPR). Patients with manic episodes of BD had the highest SII values. Patients with major depressive disorder had the highest PLR. PLR ($p < 0.001$) and SII ($p < 0.001$) had a statistically significant difference between patients with BD and those with MDD.

Table 2. *Cont.*

Study	Condition	Study Details	Main Findings
Qiu et al., 2024 [23]	Schizophrenia, bipolar disorder, and depression	• 335 patients with schizophrenia, 68 patients with bipolar disorder, 202 patients with depression, and 282 healthy individuals • Investigated biomarkers: NLR, AISI, SII, and SIRI	OR was 17.351 ($p = 0.007$) for the association of NLR with schizophrenia. NLR was a predictive factor for schizophrenia (AUC-0.625, $p < 0.001$, critical value 2.123, sensitivity-89.7%, and specificity-35.8%).
Rog et al., 2025 [24]	Anorexia nervosa	• 50 hospitalized female patients with anorexia nervosa • Investigated biomarkers: NLR, MLR, PLR, SII, and SIRI	NLR (AUC-0.745), MLR (AUC-0.785), SII (AUC-0.736), and SIRI (AUC-0.803) differed significantly among the responders and non-responders to treatment among this group of patients.
Ninla-Aesong et al., 2024 [25]	Major depressive disorder	• 139 patients with major depressive disorders and 54 healthy individuals • Investigated biomarkers: SII, SIRI, NLR, MLR, and PLR	NLR, PLR, SII, and SIRI had higher values in patients with MDD, compared to healthy controls ($p < 0.0001$ for each biomarker). MLR was also higher in MDD, without being statistically significant ($p = 0.162$). All investigated biomarkers were higher in patients with suicide attempts, but only MLR ($p = 0.005$) and SIRI ($p = 0.012$) were statistically significant. A cut-off value of 1.645 for NLR (AUC = 0.73, p-value < 0.0001, sensitivity = 71.2%, specificity = 67.2%) and a cut-off value of 428.67 for SII (AUC = 0.74, p-value < 0.0001, sensitivity = 75.5%, specificity = 62.5%) had diagnostic relevance for MDD. A cut-off of 1.82 for NLR could differentiate patients with MDD with suicide attempts (AUC = 0.71, p-value < 0.0001, sensitivity = 72.1%, specificity = 65.6%). For PLR, a cut-off value of 135.77 could differentiate non-responders to treatment with selective serotonin reuptake inhibitors (AUC = 0.74, $p = 0.033$, sensitivity = 83.8%, specificity = 62.5%).
Kim et al., 2021 [26]	Bell's palsy	• 54 patients with Bell's palsy and 39 healthy individuals • Investigated biomarkers: NLR and PLR	Patients had significantly higher values of NLR ($p = 0.007$) and PLR ($p = 0.012$). NLR positively correlated with the grade of facial paralysis (r = 0.661, $p < 0.0001$).
Li et al., 2024 [27]	Parkinson's disease	• 186 patients with Parkinson's disease and 201 healthy individuals • Investigated biomarkers: NLR and LMR	Patients had higher levels of NLR and lower levels of LMR, both being significantly associated with the disease ($p < 0.001$). NLR had an AUC of 0.6200, a sensitivity of 50.54%, and a specificity of 71.5%, while for LMR, AUC was 0.6253, with a sensitivity of 48.39% and a specificity of 73%.

Table 2. *Cont.*

Study	Condition	Study Details	Main Findings
Stanca et al., 2022 [28]	Parkinson's disease	• 45 patients with Parkinson's disease and 46 healthy individuals • Investigated biomarkers: NLR and PLR	NLR ($p = 0.04$) and PLR ($p < 0.001$) had significant differences between the patients and the control group. PLR was correlated with disease stage ($p = 0.027$) and disease duration ($p = 0.001$).
Dezayee et al., 2024 [29]	Multiple sclerosis	• 40 patients with relapsing-remitting multiple sclerosis and 30 healthy individuals • Investigated biomarkers: NLR, LMR, and PLR	Each of the investigated biomarkers had statistically significant elevated levels ($p < 0.001$) in patients with multiple sclerosis.

LMR—lymphocyte-to-monocyte ratio, NLR—neutrophil-to-lymphocyte ratio, SII—systemic immune-inflammation index, PLR—platelet-to-lymphocyte ratio, RPR—red cell distribution width-to-platelet ratio, GLR—granulocyte-to-lymphocyte ratio, SIRI—systemic inflammation response index, RLR—red cell distribution width-to-lymphocyte ratio, MLR—monocyte-to-lymphocyte ratio, PAR—platelet-to-albumin ratio, AISI—aggregate index of systemic inflammation, DII—dietary inflammatory index, ADHD—attention deficit hyperactivity disorder, SII—systemic immune-inflammation index, MLR—monocyte-to-lymphocyte ratio, MDD—major depressive disorder, SCZ—schizophrenia, BD—bipolar disorder, PRS—polygenic risk score, and AUC—area under curve.

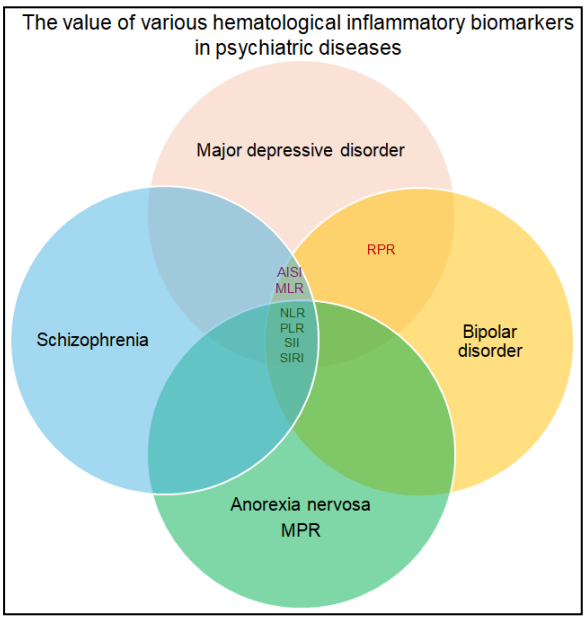


Figure 4. Hematological inflammatory markers in psychiatric diseases.

3.3. Chronic Infections

NLR, PLR, MLR, SII, SIRI, and PWR show consistent alterations in chronic infections, reflecting disease severity, persistence, and prognosis, as presented in Table 3 [30–37]. In latent tuberculosis (TB), diabetes-associated TB, and severe TB, NLR, PLR, MLR, SII, and SIRI levels vary, with lower values often linked to comorbidities or mortality risk, while higher MLR may indicate more severe disease [30–32]. In *Helicobacter pylori* infection, PLR is elevated and NLR decreased [33], whereas in chronic periodontitis, NLR is higher than in controls [37]. In HBV-related decompensated cirrhosis, low PWR, NLR, and MLR predict poorer outcomes, with combined indices improving prognostic accuracy [34,35]. Persistent HPV infection is associated with higher NLR, PLR, MLR, and SIRI [36].

Table 3. Hematological inflammatory markers in chronic infections.

Study	Condition	Study Details	Main Findings
Liu et al., 2025 [30]	Tuberculosis	• 7042 individuals without an active TB diagnosis, out of which 523 had a positive LTBI result • Investigated biomarkers: SII, NLR, PLR, and MLR	The LTBI group had significantly lower values of the SII ($p = 0.038$) and PLR ($p = 0.003$) and non-statistically significant lower values of MLR ($p = 0.562$) and NLR ($p = 0.352$) ratios. After applying models for adjustments for confounding variables, all the investigated biomarkers correlated statistically with LTBI status (SII: $p < 0.001$ and $p = 0.013$; NLR: $p < 0.001$ and $p < 0.008$; PLR: $p < 0.001$ and $p = 0.023$; MLR: $p < 0.001$ and $p = 0.002$).
He et al., 2025 [31]	Tuberculosis	• 1106 patients with confirmed pulmonary tuberculosis, including 326 patients who had confirmed diabetes mellitus • Investigated biomarkers: MLR, PLR, NLR, SII, and SIRI	The patients with TB and diabetes mellitus had significantly lower MLR ($p < 0.001$), PLR ($p < 0.001$), NLR ($p < 0.001$), SII ($p < 0.001$), and SIRI ($p < 0.001$) values. Low MLR ($p = 0.021$) and PLR ($p = 0.003$) were classified as independent risk factors for developing diabetes mellitus. For the diagnosis of diabetes mellitus in patients with pulmonary tuberculosis, the AUC for MLR was 0.600, and for PLR, it was 0.584.
Buttle et al., 2021 [32]	Tuberculosis	• 264 patients with tuberculosis • Investigated biomarkers: MLR	MLR was higher in male patients.
Saglam et al., 2023 [33]	*Helicobacter pylori* infection	• 522 pediatric patients with complaints of chronic dyspeptic symptoms were divided via gastroduodenoscopy and gastric biopsy into independent categories: *Helicobacter pylori* positive and *Helicobacter pylori* negative, respectively, in esophagitis positive and esophagitis negative cases • Investigated biomarkers: PLR and NLR	Patients positive for *Helicobacter pylori* had significantly higher PLR values ($p = 0.023$) and significantly lower NLR values ($p = 0.023$). Among patients with and without esophagitis, no significant differences were observed.
Zhang et al., 2020 [34]	Hepatitis B	• 131 participants admitted for decompensated cirrhosis in the context of HBV infection • Investigated biomarkers: PWR	PWR was significantly lower among non-survivors ($p = 0.037$). There was also a negative correlation between the PWR and MELD scores ($r = -0.277$, $p = 0.001$). For mortality in the context of HBV decompensated cirrhosis, the AUC was 0.721 for PWR, with a sensitivity of 73.3% and a specificity of 63.8%, for a cut-off value of 14.2.
Li et al., 2020 [35]	Hepatitis B virus-related decompensated cirrhosis	• 174 patients with hepatitis B virus-related decompensated cirrhosis • Investigated biomarkers: MLR, NLR	NLR ($p < 0.001$) and MLR ($p = 0.004$) were significantly lower in patients who survived. AUC for NLR was 0.804 ($p < 0.001$, cut-off = 3.78), with a sensitivity of 70.8% and a specificity of 82%. AUC for MLR was 0.681, ($p = 0.003$, cut-off = 0.59), with a sensitivity of 75% and a specificity of 60.7%.

Table 3. *Cont.*

Study	Condition	Study Details	Main Findings
Bilir et al., 2022 [36]	Persistent human papilloma virus infection	• 114 HPV positive patients, 41 of them with persistent infection • Investigated biomarkers: NLR, PLR, MLR, SIRI	All the parameters were higher in the patients with persistent infection (NLR - $p = 0.0001$, PLR - $p = 0.005$, MLR - $p = 0.0001$, SIRI - $p = 0.0001$). For the detection of persistent infection, the AUC of SIRI was 0.71 (cut-off 0.65), with a sensitivity of 95% and a specificity of 79%.
Bhattacharya et al., 2022 [37]	Periodontitis	• 40 patients with chronic periodontitis and a control group of 40 healthy individuals • Investigated biomarkers: NLR	Higher NLR values were observed in patients with periodontitis ($p = 0.013$).

NLR—neutrophil-to-lymphocyte ratio, SII—systemic immune-inflammation index, PLR—platelet-to-lymphocyte ratio, SIRI—systemic inflammation response index, MLR—monocyte-to-lymphocyte ratio, TB—tuberculosis, LTBI—latent tuberculosis infection, HBV—hepatitis B virus, PWR—platelet-to-white blood cell ratio, MELD—Model For End-Stage Liver Disease, HPV—human papilloma virus, and AUC—area under curve.

3.4. Dermatological Conditions

NLR, MLR, and PLR are altered in chronic dermatological conditions and often reflect disease activity or treatment response, as detailed in Table 4 [38–42]. In alopecia areata, MLR and PLR are elevated, correlating with disease severity and duration, with MLR showing high diagnostic accuracy [38]. In acne vulgaris, MLR is generally higher than in controls, while NLR and PLR show variable associations, and both NLR and MLR decrease with isotretinoin therapy [39]. In psoriatic arthritis, NLR and PLR correlate with disease activity scores, though some studies report no significant differences versus controls [41,42].

Table 4. Hematological inflammatory markers in dermatological conditions.

Study	Condition	Study Details	Main Findings
Aksoy Sarac et al., 2023 [38]	Alopecia areata	• 70 patients diagnosed with alopecia areata (AA) and 70 healthy controls • Investigated biomarkers: MLR, PLR, and NLR	MLR and PLR were significantly higher in AA patients compared with controls ($p < 0.001$). PLR correlated positively with disease duration (r = 0.297, $p = 0.013$) and severity (r = 0.315, $p = 0.008$). Diagnostic utility: MLR (cut-off = 0.216; AUC = 0.873) demonstrated high sensitivity (85.7%) and specificity (70%), while PLR (cut-off 111.715; AUC = 0.727) showed moderate usefulness, with 75.7% sensitivity and 58.6% specificity. Logistic regression indicated that elevated MLR ($p < 0.001$) and PLR ($p = 0.037$) values increased the risk of AA by 6.30- and 2.76-fold, respectively, supporting their role as good and moderately useful diagnostic tests for AA.
Demirbas et al., 2025 [39]	Acne vulgaris	• 450 patients aged 16 to 45 years with acne vulgaris were included. All participants had been treated with isotretinoin. • Investigated biomarkers: NLR and MLR	NLR and MLR decreased overtime with isotretinoin therapy ($p < 0.001$).

Table 4. *Cont.*

Study	Condition	Study Details	Main Findings
Pala et al., 2023 [40]	Acne vulgaris	• 61 individuals diagnosed with acne vulgaris and 35 healthy controls • Investigated biomarkers: MLR, NLR, NMR, and PLR	MLR was significantly higher in the acne group compared to controls ($p = 0.044$).
Rostamian et al., 2024 [41]	Psoriasis	• 74 patients diagnosed with psoriatic arthritis • Investigated biomarkers: NLR and PLR	DAPSA scores exhibited statistically significant associations with both NLR ($p = 0.005$) and PLR ($p = 0.048$).
Amer et al., 2024 [42]	Psoriasis	• 30 patients with psoriatic arthritis and 20 controls • Investigated parameters: NLR	There were no significant variations in NLR between the groups.

NLR—neutrophil-to-lymphocyte ratio, MLR—monocyte-to-lymphocyte ratio, PLR—platelet-to-lymphocyte ratio, NMR—neutrophil-to-monocyte ratio, A—alopecia areata, DAPSA—disease activity in psoriatic arthritis, and AUC—area under curve.

3.5. Diabetes Mellitus

The implications of hematological inflammatory markers have been widely evaluated in diabetes mellitus, as presented in Table 5 [43–53]. Hematological inflammatory markers, including NLR, PLR, MLR, SII, and SIRI, are generally elevated in Type 2 diabetes and associated complications [45–53]. Multiple studies showed that especially NLR and PLR rise in diabetic patients and are related to various clinical manifestations or complications. They are elevated in children with insulin resistance, together with SII [43], and their values associate with HbA1c in patients with Type 2 diabetes mellitus, reflecting poor glycemic control [45,46,52]. Common complications, such as nephropathy (reflected by microalbuminuria and proteinuria), neuropathy, retinopathy, or deep vein thrombosis, often associate higher values of the hematological inflammatory biomarkers [46,48,50,51,53].

Table 5. Hematological inflammatory markers in diabetes mellitus.

Study	Condition	Study Details	Main Findings
Okuyan et al., 2024 [43]	Insulin resistance in children	• 210 children aged 6 to 18 years, divided into two groups: 96 with insulin resistance and 114 without • Investigated parameters: SII, NLR, PLR	Patients with insulin resistance had elevated values of NLR ($p < 0.001$), PLR ($p = 0.001$), and SII ($p < 0.001$) compared with those without. Patients with vitamin D within normal range had lower NLR ($p < 0.001$), PLR ($p = 0.002$) and SII ($p < 0.001$).
Zhu et al., 2022 [44]	Type 2 diabetes mellitus	• 42 patients diagnosed with severe diabetic retinopathy, 18 patients with diabetic macular edema among them, and 24 patients without • Investigated biomarkers: NLR, PLR, MLR.	In this patient cohort, NLR, PLR, and MLR were not significantly associated with the development of diabetic macular edema.

Table 5. *Cont.*

Study	Condition	Study Details	Main Findings
Taban et al., 2025 [45]	Type 2 diabetes mellitus	• 300 patients with Type 2 diabetes mellitus and 300 healthy controls • Investigated biomarkers: NLR, PLR	Diabetic patients had higher NLR and PLR, with mean values of 3.12 versus 1.66 for NLR ($p = 0.001$) and 249.05 versus 131.41 for PLR ($p = 0.001$). Obese diabetic patients exhibited even more pronounced elevations in these markers (NLR - $p = 0.001$, PLR - $p = 0.001$). Both NLR (OR = 1.28, $p < 0.001$) and PLR (OR = 1.02, $p = 0.004$) showed significant positive associations with HbA1c levels.
Chollangi et al., 2023 [46]	Type 2 diabetes mellitus	• 90 adults with uncontrolled Type 2 diabetes (HbA1c 7%), 45 with microalbuminuria and the other 45 without • Investigated parameters: NLR	NLR value was significantly higher in diabetic patients with microalbuminuria compared to those without ($p < 0.001$). NLR correlated significantly and positively with HbA1c in patients with microalbuminuria (r = 0.662, $p < 0.001$). To detect microalbuminuria in diabetic patients, AUC for NLR was 0.859, with an optimal cut-off value of 2.13, yielding a sensitivity of 88.9% and a specificity of 77.3%.
Amaeshi et al., 2024 [47]	Type 2 diabetes mellitus	• 109 patients with Type 2 diabetes mellitus, divided into a group with optimal glycemic control and a group with suboptimal glycemic control • Investigated biomarkers: NLR, PLR	The mean NLR was similar between both groups of T2DM patients. The PLR values were slightly higher among patients, but it was not statistically significant. Neither NLR nor PLR were correlated with HbA1c levels.
Shyam V et al., 2023 [48]	Diabetes mellitus	• 218 patients, half of them with diabetes mellitus, and half of the total with deep vein thrombosis (overlapping groups) • Investigated biomarkers: NLR, PLR	Both NLR ($p = 0.0001$) and PLR ($p = 0.038$) were significantly elevated in diabetic patients with DVT compared to those without. NLR correlated with HbA1c (r = 0.7361, $p = 0.001$). An NLR cut-off of 2.83 achieved 67% sensitivity and 92% specificity for detecting DVT in diabetic patients. (AUC = 0.833) For PLR, the optimal threshold was 131.46, yielding 56% sensitivity and 90% specificity (AUC = 0.762).
Uslu et al., 2025 [49]	Diabetes mellitus	• 62 non-diabetic individuals, 97 prediabetic patients, and 327 diabetic patients • Investigated biomarkers: NLR, PLR, LMR, SIRI, SII, PIV	PLR was significantly lower in the diabetic patients ($p = 0.011$). In the diabetic group, severity of PNP showed positive correlations with NLR ($p = 0.001$) and SIRI ($p = 0.005$) and negative correlations with LMR ($p = 0.037$).
AlShareef et al., 2024 [50]	Type 2 diabetes mellitus	• 768 adult patients with Type 2 diabetes mellitus, categorized into two groups: those with diabetic neuropathy and those without • Investigated biomarkers: NLR, PLR	HbA1c was positively correlated with NLR (r = 0.193, $p = 0.007$). The study found that patients with diabetic neuropathy exhibited significantly higher NLR ($p = 0.011$).

Table 5. *Cont.*

Study	Condition	Study Details	Main Findings
Dascalu et al., 2023 [51]	Type 2 diabetes mellitus	• 129 patients with Type 2 diabetes mellitus, categorized into three groups: those without retinopathy, those with non-proliferative diabetic retinopathy, and those with proliferative diabetic retinopathy • Investigated biomarkers: NLR, PLR, SII, MLR	Significantly elevated NLR (p = 0.005), MLR (p = 0.001) and SII (p = 0.013) were identified in the proliferative diabetic retinopathy patients, compared to the other two groups. For predicting proliferative diabetic retinopathy, NLR achieved a sensitivity of 40% and a specificity of 86.9%, AUC = 0.662, for a cut-off value of 3.18 (p = 0.001), MLR had sensitivity of 35.6% and a specificity of 92.9%, AUC = 0.643, for a cut-off value of 0.364 (p = 0.006), and SII had a sensitivity of 35.6% and a specificity of 85.7%, AUC = 0.627, for a cut-off value of 763.8 (p = 0.015). NLR (OR = 1.645, p = 0.002) and MLRx10 (OR = 1.662, p = 0.0017) were identified as potential risk factors.
Aygun et al., 2024 [52]	Type 2 diabetes mellitus	• 1790 participants: 1300 non-diabetic, 327 prediabetic, and 163 diabetic • Investigated biomarkers: NLR	HbA1c positively correlated with NLR (r = 0.18, p < 0.01).
Patro et al., 2025 [53]	Type 2 diabetes mellitus	• 160 patients with Type 2 diabetes mellitus • Investigated biomarkers: PLR, SII	PLR and SII were significantly higher in patients with proteinuria (p < 0.001).

NLR—neutrophil-to-lymphocyte ratio, SII—systemic immune-inflammation index, PLR—platelet-to-lymphocyte ratio, SIRI—systemic inflammation response index, MLR—monocyte-to-lymphocyte ratio, PIV—pan-immune-inflammation value, DVT—deep vein thrombosis, and PNP—polyneuropathy.

3.6. Autoimmune and Inflammatory Conditions

NLR, PLR, MLR, MPR, SII, SIRI, NMR, PIV, ELR, BLR, dNLR, AISI, and IIC are altered across autoimmune and inflammatory diseases, reflecting disease activity, severity, organ involvement, and prognosis, as detailed in Table 6 and Figure 5 [54–75]. In rheumatoid arthritis, NLR, PLR, MLR, and SIRI correlate with disease activity, synovitis, bone erosion, and cardiovascular risk [55–61]. In autoimmune hepatitis, PLR, RLR, MPR, and RPR effectively indicate inflammation and fibrosis [54]. In systemic lupus erythematosus, MLR, ELR, NLR, and PLR are elevated, with higher values associated with organ involvement, anemia, and active disease [65–67]. Dermatomyositis and immune-mediated necrotizing myopathy show increased NLR, MLR, and PLR, with MLR distinguishing the two myopathies [68]. NLR is generally elevated in Behçet's disease [63], Crohn's disease [69], ulcerative colitis [71,72], sarcoidosis [74], and osteoarthritis [75], often correlating with disease severity or chronicity.

Table 6. Hematological inflammatory markers in autoimmune and inflammatory conditions.

Study	Condition	Study Details	Main Findings
Domerecka et al., 2022 [54]	Autoimmune hepatitis	• 30 adult patients diagnosed with autoimmune hepatitis and a matching control group of 30 healthy volunteers without signs of inflammation • Investigated biomarkers: NLR, RPR, RLR, MPR, PLR	Patients with autoimmune hepatitis had elevated MPR ($p = 0.0004$), RPR ($p = 0.0007$), NLR ($p < 0.0001$). PLR and RLR achieved perfect discrimination for detecting autoimmune hepatitis, with AUC = 1.00 (sensitivity 100%, specificity 100%, $p < 0.0001$). For the other biomarkers, the following performances were obtained: RPR – AUC = 0.75 (sensitivity 56.67%, specificity 90%, $p = 0.0001$), NLR – AUC = 0.84 (sensitivity 70%, specificity 96.67%, $p < 0.0001$), and MPR – AUC = 0.77 (sensitivity 66.67%, specificity 76.67%, $p < 0.0001$). Additionally, MPR (AUC = 0.93), PLR (AUC = 0.86), and RPR (AUC = 0.91) markers demonstrated strong utility in detecting liver fibrosis in patients with autoimmune hepatitis.
Gonzales-Sierra et al., 2023 [55]	Rheumatoid arthritis	• 430 adult patients with rheumatoid arthritis • Investigated biomarkers: NLR, MLR, PLR, SIRI	NLR, MLR, PLR, and SIRI were elevated in rheumatoid arthritis patients. These markers were correlated with traditional cardiovascular risk factors.
Masoumi et al., 2024 [56]	Rheumatoid arthritis	• 305 adult patients with rheumatoid arthritis, stratified into four groups: remission, low, moderate, and high activity • Investigated biomarkers: NLR, PLR, LMR	NLR (r = 0.21, $p = 0.0003$) and PLR (r = 0.23, $p = 0.0001$) correlated with activity scores. NLR (AUC = 0.66, cut-off = 1.85, sensitivity = 81%, specificity = 49%, $p < 0.001$) and PLR (AUC = 0.64, cut-off = 10.9, sensitivity = 61%, specificity = 68%, $p = 0.001$) could distinguish between active and remission states of rheumatoid arthritis.
Targonska-Stepniak et al., 2021 [57]	Rheumatoid arthritis	• 113 patients with rheumatoid arthritis • Investigated biomarkers: NLR and PLR	PLR ($p = 0.03$) was significantly lower in patients with elderly onset, compared with patients with disease onset at a younger age. Both markers associated with various parameters of disease activity.
Obaid et al., 2023 [58]	Rheumatoid arthritis	• 62 patients with rheumatoid arthritis and 20 healthy individuals • Investigated biomarkers: NMR, NLR, LMR	NMR ($p = 0.0001$), LMR ($p = 0.001$), and NLR ($p = 0.001$) were significantly higher in the patients, compared to the control group and correlated with classic inflammatory markers for rheumatoid arthritis. For diagnosis, NMR had an AUC of 0.861 (cut-off = 4.7, sensitivity = 87%, specificity= 80%, $p = 0.0001$). LMR had an AUC of 0.807 (cut-off = 4.35, sensitivity = 62.3%, specificity = 90%, $p = 0.0001$) and NLR (cut-off = 1.35, sensitivity = 57.4%, specificity = 80%, $p = 0.008$).
Cheng et al., 2024 [59]	Rheumatoid arthritis	• 135 patients with rheumatoid arthritis and normal acute phase reactants • Investigated biomarkers: NLR, PLR, LMR	Only PLR was positively correlated with synovitis (r = 0.419, $p = 0.001$) and bone erosion (r = 0.252, $p = 0.015$) at ultrasound. A cut-off value of at least 159.6 associated with an AUC of 0.7868, a sensitivity of 80.95%, and a specificity of 74.24% for synovitis with a GS grade of at least 2. The AUC was 0.7690, with a sensitivity of 68% and a specificity of 83.87%, for a cut-off value of at least 166.1 in identifying synovitis PD Grade 2 and more.

Table 6. *Cont.*

Study	Condition	Study Details	Main Findings
Targonska-Stepniak et al., 2020 [60]	Rheumatoid arthritis	• 126 patients with rheumatoid arthritis • Investigated biomarkers: NLR, PLR, LMR	NLR (r = 0.21, 0.25 and 0.24; p = 0.02, p = 0.004, p = 0.008) and PLR (r = 0.25, 0.24 and 0.26; p = 0.004, p = 0.007, p = 0.003) demonstrated positive correlations with all the scores of disease activity indicated by ultrasound, but also with diverse activity parameters.
Sahin et al., 2022 [61]	Rheumatoid arthritis	• 324 children with arthritis and 324 healthy children • Investigated biomarkers: NLR, MLR	NLR was significantly higher in patients with arthritis (p = 0.001). NLR and MLR did not differ significantly between patients with juvenile rheumatoid arthritis and those with other arthritis.
Sharma et al., 2025 [62]	Thyroiditis	• 25 cases of Hashimoto's thyroiditis and 111 cases with thyroid enlargement as controls • Investigated biomarkers: NLR	No relevant associations were identified.
Okak et al., 2024 [63]	Behçet's disease	• 177 patients with Behçet's disease, 85 with vascular disease, and 92 without • Investigated biomarkers: NLR, MLR, PLR, PIV	For detection of vascular Behçet's disease, PIV had an AUR of 0.654 (cut-off = 261.6, sensitivity = 75.3%, specificity = 55.4%, p < 0.001). PIV was also a significant risk factor in both univariate and multivariate analysis (OR = 3.791, p < 0.001; OR = 2.758, p = 0.007). NLR and PLR were highlighted as potential risk factors only in univariate analysis and not after multivariate analysis.
Kivrakoglu et al., 2025 [64]	Celiac disease	• 115 patients with celiac disease • Investigated parameters: NLR, PLR, SII	SII, NLR, and PLR did not differ statistically significantly among histological stages, but higher values were observed in patients with Marsh Grade 3a and 3b compared with Grade 1 and 2. Lower values of these indices were observed in Grade 3c.
Baykal et al., 2024 [65]	Systemic lupus erythematosus	• 44 patients with systemic lupus erythematosus and 26 controls • Investigated biomarkers: NLR, PLR, MLR, MPR, AISI, SII, and SIRI	NLR (p = 0.01), SII (p = 0.048), and SIRI (p = 0.025) were significantly higher in patients compared to controls. Patients with elevated disease activity scores had significantly higher NLR (p = 0.01) and SII (p = 0.048). For predicting disease activity, NLR had an AUC of 0.699 (cut-off = 2.8, sensitivity = 61.2%, specificity = 71.3%, p = 0.031), SII had an AUC of 0.695 (cut-off = 415, sensitivity = 85%, specificity = 76.1%, p = 0.021), SIRI had an AUC of 0.681 (cut-off = 2.56, sensitivity = 83%, specificity = 69.7%, p = 0.004), and AISI had an AUC of 0.782 (cut-off = 328, sensitivity = 78%, specificity = 58.1%, p = 0.006). MLR associated with antibody positivity at disease onset (p = 0.012).
Suszec et al., 2020 [66]	Systemic lupus erythematosus	• 136 patients with systemic lupus erythematosus • Investigated biomarkers: NLR, BLR, PLR, ELR, MLR	NLR values were higher in patients with cutaneous and/or mucosal (p = 0.05) and kidney involvement (p < 0.001), and in patients with antibodies against double stranded DNA (p = 0.03). BLR (p < 0.001 and p = 0.01) and MLR (p < 0.001 and p = 0.01) were higher in patients with vasculitis, arthritis, and myositis. ELR (p < 0.001) was higher in patients with vasculitis. PLR was higher in patients with hematological disorders (p = 0.01) and nephritis (p = 0.03).

Table 6. *Cont.*

Study	Condition	Study Details	Main Findings
Moreno-Torres et al., 2022 [67]	Systemic lupus erythematosus	• 77 patients with systemic lupus erythematosus and 80 healthy individuals • Investigated parameters: NLR and PLR	NLR and PLR had higher values in patients than in controls ($p < 0.001$), but also in patients with anemia, compared to systemic lupus erythematosus patients without anemia ($p < 0.0001$). Both markers had various associations and correlations with parameters of clinical activity.
Ma et al., 2025 [68]	Myopathy	• 27 patients with immune-mediated necrotizing myopathy, 14 patients with dermatomyositis, and 85 healthy controls • Investigated biomarkers: NLR, MLR, and PLR	Patients with immune-mediated necrotizing myopathy had statistically significant higher MLR than healthy controls ($p = 0.0084$) and lower than patients with dermatomyositis ($p = 0.0089$). Patients with dermatomyositis had significantly higher NLR compared to patients with immune-mediated necrotizing-myopathy ($p = 0.0395$). Compared to healthy controls, patients with dermatomyositis had higher PLR ($p = 0.0042$). For differentiating the two conditions, NLR had an AUC of 0.6984, and MLR had an AUC of 0.7487.
Omer et al., 2025 [69]	Inflammatory bowel disease	• 34 patients with Crohn's disease, 34 patients with ulcerative colitis, and 52 healthy controls • Investigated parameters: NLR	NLR ($p < 0.0001$) was significantly higher in patients with inflammatory bowel disease. To differentiate between Crohn's disease and ulcerative colitis, an AUC of 0.733 was obtained for NLR (cut-off = 2.11, sensitivity = 67.16%, specificity = 76.92%, $p < 0.0001$).
Huang et al., 2022 [70]	Vasculitis	• 190 patients with vasculitis (myeloperoxidase-anti-neutrophil cytoplasmic antibody) • Investigated biomarkers: PLR	PLR did not correlate with the activity score. PLR was associated with lower risk of end-stage kidney disease ($p = 0.038$, HR = 0.518).
Poenariu et al., 2023 [71]	Ulcerative colitis	• 46 patients with ulcerative colitis and 23 controls • Investigated biomarkers: NLR, dNLR, AISI, SII, SIRI, MLR, PLR, IIC, MCVL	Various significant associations were identified for all of the markers (except for dNLR) and disease activity and extent. MCVL had an AUC of 0.709 (cut-off = 45.63, sensitivity = 73.33%, specificity = 58.7%, $p = 0.025$), and PLR had an AUC of 0.704 (cut-off = 129.4, sensitivity = 73.33%, specificity = 54.35%, $p = 0.047$).
Cui et al., 2022 [72]	Ulcerative colitis	• 386 patients with ulcerative colitis • Investigated biomarkers: NLR, PLR, LMR	NLR, PLR and LMR varied significantly among subgroups of patients ($p < 0.001$) and correlated with endoscopic activity (NLR and PLR positively, LMR negatively). For disease activity, NLR had an OR of 2.42 and 2.38, depending on the scoring system. All the markers had good diagnostic performance to differentiate activity from remission, with AUC ranging from 0.739 to 0.796.
Pana et al., 2024 [73]	Nephropathies	• 196 patients with IgA nephropathy and 138 patients with membranous nephropathy • Investigated biomarkers: NLR, PLR	PLR was significantly higher in patients with membranous nephropathy ($p = 0.01$). Higher NLR was associated with mortality in patients with membranous nephropathy.

Table 6. *Cont.*

Study	Condition	Study Details	Main Findings
Bekir et al., 2021 [74]	Sarcoidosis	• 348 patients with sarcoidosis • Investigated parameters: NLR	NLR was higher in patients with chronic disease, compared to those with remission ($p = 0.006$).
Yilmaz et al., 2025 [75]	Osteoarthritis	• 946 patients with osteoarthritis • Investigated biomarkers: SII	Values of SII of 627.9 can differentiate severe forms of osteoarthritis with limited performances (sensitivity - 42.5% and specificity - 70.6%, AUC = 0.596, $p < 0.001$). OR for SII was 1.623 in multivariate analysis, $p = 0.003$.

LMR—lymphocyte-to-monocyte ratio, NLR—neutrophil-to-lymphocyte ratio, SII—systemic immune-inflammation index, PLR—platelet-to-lymphocyte ratio, RPR—red cell distribution width-to-platelet ratio, SIRI—systemic inflammation response index, RLR—red cell distribution width-to-lymphocyte ratio, MLR—monocyte-to-lymphocyte ratio, NMR—neutrophil-to-monocyte ratio, PIV—pan-immune-inflammation value, AISI—aggregate index of systemic inflammation, MPR—monocyte-to-platelet ratio, ELR—eosinophil-to-lymphocyte ratio, dNLR—derived neutrophil-to-lymphocyte ratio, IIC—cumulative inflammatory index, and AUC—area under curve.

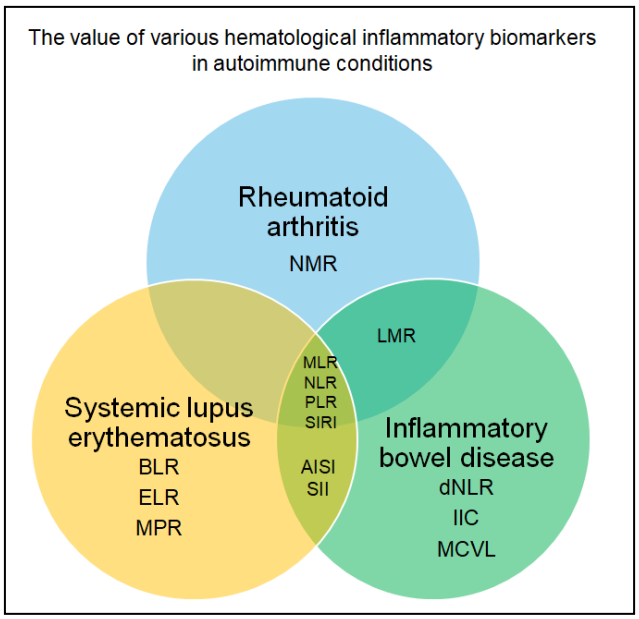


Figure 5. Hematological inflammatory markers in autoimmune conditions.

3.7. Other Chronic Conditions

NLR, PLR, MLR, SII, SIRI, AISI, NPR, PMR, and PIV are relevant in a variety of other chronic conditions, reflecting inflammation, disease severity, and prognosis, as detailed in Table 7 [76–87]. NLR and PLR are elevated in gynecological conditions such as endometrial polyps and endometriosis, with NLR combined with CA-125 showing strong diagnostic performance [76,77]. In obstructive sleep apnea, SII, NLR, SIRI, AISI, and MLR correlate with disease severity and oxygen desaturation [78]. SII and NLR predict anemia risk and complications in Mediterranean fever [80], thalassemia minor [81], and metabolic dysfunction-associated steatotic liver disease [87]. In obesity and metabolic syndrome, PLR, PMR, and SII show variable associations with sex and body mass [82–84]. In chronic obstructive pulmonary disease and liver cirrhosis, NLR, PLR, MLR, and SII indicate disease severity, acute exacerbations, and pro-inflammatory status, with combined biomarker models improving predictive accuracy [85,86].

Table 7. Hematological inflammatory markers in other conditions.

Study	Condition	Study Details	Main Findings
Keyif et al., 2025 [76]	Endometrial polyps	• 60 patients with endometrial polyps, 60 patients with chronic endometritis, and 60 healthy individuals • Investigated biomarkers: NLR, PLR	PLR (p = 0.015) was significantly higher in patients with endometrial polyps and was an independent predictor for this condition (p = 0.045).
Nouri et al., 2025 [77]	Endometriosis	• 346 females, including 230 with endometriosis, and the other participants were females with benign conditions • Investigated biomarkers: NLR	Females with endometriosis had significantly higher NLR ($p < 0.001$). NLR had a sensitivity of 83.4% and a specificity of 52.5% for a cut-off of 1.5 (AUC - 0.699).
Pau et al., 2023 [78]	Sleep apnea	• 295 patients with obstructive sleep apnea • Investigated biomarkers: NLR, PLR, MLR, SII, SIRI, and AISI	NLR (r = 0.12, p = 0.05) and SII (r = 0.115, 0.006) were positively correlated with apnea hypopnea index. NLR (r = 0.16, p = 0.0075), SII (r = 0.16, p = 0.009), SIRI (r = 0.15, p = 0.013), and AISI (r = 0.15, p = 0.015) were positively correlated with the oxygen desaturation index. Oxygen saturation was correlated with NLR (r = −0.21, p = 0.0002), SII (r = −0.21, p = 0.0006), SIRI (r = 0.24, p = 0.0001), AISI (r = −0.23, p = 0.0002), and MLR (r = −0.153, p = 0.014). SIRI was independently associated with lower oxygen saturation (r = −0.1935, p = 0.0087).
Chen et al., 2024 [79]	Anemia	• 19,851 adults, out of which 1501 had anemia • Investigated biomarkers: SII	A significantly positive correlation between the individuals' risk of anemia and the value of SII was identified (OR = 1.51, $p < 0.001$).
Atik et al., 2024 [80]	Mediterranean fever	• 168 patients with Mediterranean fever • Investigated biomarkers: NLR, MLR, SII	MLR (AUC: 0.700), NLR (AUC: 0.801), and SII (AUC: 0.858) were defined as very sensitive parameters in determining sacroiliitis in patients with Mediterranean fever.
Ciceri et al., 2025 [81]	Beta thalassemia	• 50 patients with thalassemia minor and 100 healthy individuals • Investigated biomarkers: NPR, NLR, dNLR, LMR, PLR, SII and SIRI	Patients with beta thalassemia had significantly increased NPR (p = 0.001), dNLR (p = 0.001), NLR (p = 0.010), and SII (p = 0.038).
Najafzadeh et al., 2023 [82]	Metabolic syndrome	• 1033 individuals - 279 with metabolic syndrome and 754 without • Investigated biomarkers: PLR, PMR, NLR	PMR was significantly lower in participants with metabolic syndrome. PLR and PMR were significantly higher in females than in males with metabolic syndrome ($p < 0.001$).
Thavaraputta el al., 2020 [83]	Obesity	• Healthy individuals • Investigated biomarkers: NLR, PLR, SII	The investigated biomarkers were significantly associated with higher body mass index, with variations depending on the gender.
Bas Aksu et al., 2025 [84]	Obesity	• 315 patients with obesity • Investigated biomarkers: SII, PIV and NLR	No meaningful association observed for these parameters in patients grouped by HBA1c levels.

Table 7. *Cont.*

Study	Condition	Study Details	Main Findings
Li et al., 2025 [85]	Chronic obstructive pulmonary disease	• 254 patients with chronic obstructive pulmonary disease • Investigated biomarkers: SII, SIRI, NLR, PLR, MLR	The investigated biomarkers can be used to identify patients with moderate-to-severe diseases. Higher levels associated with acute exacerbations and readmission to hospital. Highest diagnostic accuracy for moderate-to-severe disease was obtained from combining the 5 biomarkers, with a cut-off value of 0.38, obtaining an AUC of 0.837.
Pomacu et al., 2021 [86]	Liver cirrhosis	• 35 patients with liver cirrhosis and 10 healthy controls • Investigated biomarkers: NLR, MLR, PLR, SII	NLR, MLR, and PLR had significantly higher values in patients who had cirrhosis related to hepatitis B or hepatitis C. Patients with toxic hepatitis had high PLR values compared to controls. NLR and MLR can indicate pro-inflammatory hepatic status.
Zhang et al., 2024 [87]	Metabolic dysfunction-associated steatotic liver disease	• 16,859 patients with metabolic dysfunction-associated steatotic liver disease • Investigated biomarkers: NLR	NLR had positive linear associations with all-cause mortality and cardiovascular mortality, predicting mortality in these patients.

NLR—neutrophil-to-lymphocyte ratio, SII—systemic immune-inflammation index, PLR—platelet-to-lymphocyte ratio, SIRI—systemic inflammation response index, MLR—monocyte-to-lymphocyte ratio, AISI—aggregate index of systemic inflammation, PIV—pan-immune-inflammation value, PMR—platelet-to-monocyte ratio, and AUC—area under curve.

4. Discussion

Hematological inflammatory biomarkers are modified in a broad range of diseases—cardiovascular, neuropsychiatric, autoimmune and inflammatory disorders, infections, skin disorders, and many others—their variation being related to diagnosis, disease severity, activity, prognosis, treatment outcome, etc. While their investigation is important in any health condition, their implications in chronic conditions are of particular interest due to their high prevalence and long period of healthcare required [1,2,4–8,88–90].

While it was not the topic of the current review, hematological inflammatory biomarkers can be combined in ratios with other routine laboratory tests, such as C-reactive protein, glucose, cholesterol fractions, etc., and provide a wide spectrum of biomarkers with various applications [90–94]. Furthermore, hematological inflammatory biomarkers can be included in more complex predictive models based on integrating more types of accessible data for patients, for example, age and other clinical details or more routine investigations results, thus increasing their precision and value [23,51,95].

While hematological inflammatory biomarkers are widely available in the majority of healthcare settings and extensive research has been conducted to investigate these biomarkers in chronic conditions, the majority of studies involve a modest number of patients, and the results require validation. Furthermore, there is a high diversity among study designs on this topic, covering various diseases with participants that had different characteristics. With these biomarkers being associated with a wide spectrum of conditions and inflammatory-associated status, specific clinical uses need to be filtered. Therefore, the generalizability of the results is limited, and including these biomarkers in guidelines requires more evidence.

While hematologic inflammatory indices provide valuable insight into systemic inflammation, many chronic diseases share overlapping alterations in these ratios. This overlap reflects common immune-inflammatory mechanisms rather than disease-specific

processes. Therefore, diagnostic discrimination among various chronic disease states may be enhanced through the use of additional, more specific biomarkers. Markers such as C-reactive protein, erythrocyte sedimentation rate, and pro-inflammatory cytokines can refine the assessment of systemic inflammation [96]. Furthermore, organ- or pathway-specific parameters, such as lipid and glucose metabolism markers [97,98], autoantibodies [99], liver, and renal function tests [100], may help distinguish the inflammatory profiles of different disease categories. Combining hematologic indices with these targeted biomarkers, and potentially with imaging or molecular data, could therefore enhance both the specificity and the clinical interpretability of inflammatory patterns across chronic diseases [101].

Apart from pathological variations, there are also physiological variations in hematological inflammatory indices. Studies that stratified participants by age or gender have shown that these biomarkers exhibit statistically significant differences, which may affect their relevance for evaluating specific conditions. For example, a study on pediatric patients revealed that the discriminative power of hematological inflammatory indices in the context of COVID-19 varies with age, suggesting that clinical decision limits should be defined for distinct age groups [102]. Differences between sexes are also relevant [22,32,50]; for instance, the MLR is higher in male patients with tuberculosis compared to females [32]. Furthermore, hematological inflammatory biomarkers vary with lifestyle factors—for example, smoking influences inflammatory status [103]—and, therefore, smokers may present altered levels of these indices. Considering all these aspects, the interpretation of hematological inflammatory biomarkers across different conditions and disease states should be approached with caution.

The current review was limited by a series of factors. Due to a wide variety of scientific papers, assessing different hematological inflammatory biomarkers, and different chronic conditions, no quantitative analysis was feasible, and the review is limited to providing an overview of the topic. The literature search was restricted to a single database, PubMed, which may have resulted in the omission of relevant studies indexed in other databases. Second, only English-language, free full-text articles published within the last five years were included, which could have introduced language bias, potentially overlooking significant contributions published in other languages.

Another limitation of this review is that the search was restricted to "free full text" articles. While this approach ensured the accessibility and transparency of the reviewed sources, it may have inadvertently excluded a substantial portion of relevant studies available only through subscription-based databases, thereby introducing selection bias and limiting the comprehensiveness of the evidence base. Future reviews may benefit from including both open-access and subscription-based studies to provide a more complete and balanced synthesis of the evidence.

As a comprehensive, non-systematic review, studies were not excluded based on study design, population, or outcomes. While this allowed for a broad and integrative perspective, it also introduced heterogeneity in the included studies, which could limit the comparability and generalizability of findings. Under these limitations, no formal risk-of-bias assessment and no reproducible methods section or PRISMA flowchart were feasible, reflecting the non-systematic nature of this work. These factors collectively limit the ability to make definitive, evidence-based conclusions and preclude quantitative synthesis or meta-analysis.

While many studies report statistically significant associations of hematological inflammatory biomarkers with various outcomes, these measures vary widely between diseases and individual studies, limiting direct clinical applicability.

Heterogeneity arises from differences in patient populations, disease stages, comorbidities, and analytical factors, depending on laboratory equipment, reagents, and result

reporting. As no universally accepted thresholds exist for most hematological inflammatory indices, there is considerable cut-off variability. Furthermore, the majority of the primary studies is retrospective and may not adequately control for key confounders, even though most of the included studies accounted for key confounding variables such as age, sex, body mass index, smoking status, and the presence of comorbidities. Temporal variability of testing for complete blood count can affect results. Collectively, these factors contribute to the observed heterogeneity, do not allow direct comparison and generalization of findings, and limit the direct clinical translation of these biomarkers.

Because of this marked heterogeneity in study designs, populations, disease stages, and statistical methodologies, we did not attempt to calculate pooled effect sizes or summary diagnostic/prognostic performance metrics. Likewise, it was not methodologically appropriate to aggregate the results to derive overall ranges for performance indices or other statistics reported in the original studies, nor to merge them into unified or synthetic visual representations.

Instead, we opted for a comprehensive, qualitative synthesis, summarizing each study in tables with the study population, condition, number of participants and controls, and key findings for the investigated biomarkers. This approach allows readers to appreciate broad trends across multiple chronic, non-oncologic conditions while acknowledging the variability in the underlying evidence.

However, the current review provides a structured and comprehensive literature review of the latest impactful discoveries, covering the most prevalent chronic conditions that affect millions of individuals worldwide. Future research should focus on conducting systematic reviews and meta-analyses targeting specific disease categories or groups of related chronic conditions, where sufficient primary research exists. Such studies should employ standardized search strategies across multiple databases, include formal risk-of-bias assessments, and consider both English and non-English publications to ensure comprehensive coverage.

Furthermore, separate reviews focusing specifically on oncologic conditions are warranted, given the vast literature on this topic, to allow detailed and condition-specific insights, enabling quantitative synthesis, standardized cut-offs, and more robust assessment of diagnostic or prognostic utility.

5. Conclusions

Complete blood count-derived ratios have potential applications across various chronic diseases, including diagnosis, monitoring, assessment of disease activity and stage, evaluation of treatment response, detection of complications, and identification of subclinical forms. These indices are promising and widely accessible; however, they are not yet replacements for established biomarkers or clinical decision rules without further validation. Current evidence is primarily derived from small studies, and considerable heterogeneity exists in study populations, cut-offs, and methodologies. Therefore, further research and rigorous validation are required before these inexpensive and readily available biomarkers can be integrated into routine clinical practice.

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Abbreviations

The following abbreviations are used in this manuscript:

AA	alopecia areata
ADHD	attention deficit hyperactivity disorder
AISI	aggregate index of systemic inflammation
AUC	area under the curve
BD	bipolar disorder
BLR	basophil-to-lymphocyte ratio
CI	confidence interval
DAPSA	disease activity in psoriatic arthritis
DII	dietary inflammatory index
dNLR	derived neutrophil-to-lymphocyte ratio
DVT	deep vein thrombosis
ELR	eosinophil-to-lymphocyte ratio
HR	hazard ratio
IIC	cumulative inflammatory index
FH	familial hypercholesterolemia
LMR	lymphocyte-to-monocyte ratio
LTBI	latent tuberculosis infection
MCVL	mean corpuscular volume - lymphocytes ratio
MDD	major depressive disorder
MLR	monocyte-to-lymphocyte ratio
MPR	monocyte-to-platelet ratio
NLR	neutrophil-to-lymphocyte ratio
NMR	neutrophil-to-monocyte ratio
NPR	neutrophil-platelet ratio
OR	odds ratio
PIV	pan-immune-inflammation value
PLR	platelet-to-lymphocyte ratio
PMR	platelet-to-monocyte ratio
PNP	polyneuropathy
PRS	polygenic risk score
PWR	platelet-to-white blood cell ratio
RLR	red cell distribution width-to-lymphocyte ratio
RPR	red cell distribution width-to-platelet ratio
SCZ	schizophrenia
SII	systemic immune-inflammation index
SIRI	systemic inflammation response index

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