IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 24, Issue 4 Ser. 5 (April. 2025), PP 12-21
www.iosrjournals.org

The Association Of Systemic Inflammatory Response Index In All Stages Of Periodontitis: A Systematic Review

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Abstract
Background:
Periodontitis is a chronic inflammatory disease that affects the tissues supporting the teeth and has been linked to systemic inflammation and a range of chronic conditions. The Systemic Inflammatory Response Index (SIRI), which combines neutrophil, monocyte, and lymphocyte counts, is emerging as a promising marker for assessing systemic inflammatory status.
Objective:
This systematic review aimed to evaluate the relationship between SIRI and periodontitis, examining its potential as a diagnostic and prognostic biomarker for periodontal disease severity and progression.
Methods:
A comprehensive literature search was conducted across multiple databases, including PubMed, Web of Science, Scopus, and Google Scholar, to identify relevant studies published up to 2024. The review followed PRISMA guidelines and included original research examining the relationship between SIRI, periodontal disease severity, and systemic inflammatory conditions. Inclusion criteria encompassed observational and clinical studies with quantitative data on SIRI measurements.
Results:
The evidence indicates that elevated SIRI levels are significantly associated with more severe periodontal destruction, including greater probing depth, clinical attachment loss, and bone loss. Subgroup analyses also suggest that factors such as age, sex, and ethnicity may influence these associations. Furthermore, SIRI correlated with other inflammatory markers, supporting its potential as a composite measure of systemic inflammation
Conclusion:
Our findings support the use of SIRI as a promising biomarker for periodontitis. However, standardization of measurement methods and further prospective studies are needed to validate its clinical utility. Integrating SIRI into periodontal diagnostics could enhance early detection, risk stratification, and interdisciplinary management of both oral and systemic inflammatory conditions.
Keywords: *Systemic Inflammatory Response Index, Periodontitis, Inflammatory Markers, Systemic disease, Neutrophils, Lymphocytes, Monocytes.*

Date of Submission: 16-04-2025 Date of Acceptance: 26-04-2025

I. Introduction

Periodontitis is a chronic inflammatory illness that affects the tooth's supporting components and is one of the most common oral health problems in the globe (Kassebaum et al. 2014; Peres et al. 2019). According to contemporary estimates, periodontitis affects almost half of the world's population, with severe cases affecting over 743 million people. This disorder is caused by a dysregulated host immunological response to a dysbiotic oral microbiota, which results in gradual degradation of the periodontal ligament and alveolar bone, eventually leading to tooth loss (Kwon, Lamster, and Levin 2021). Beyond its oral manifestations, periodontitis is becoming recognized as a cause of systemic inflammation and is linked to chronic disorders such as

cardiovascular disease, diabetes, hypertension, and poor pregnancy outcomes. Given the considerable impact of periodontitis on global health, there is an urgent need for reliable biomarkers that can measure affected persons inflammatory status and aid in early detection and disease management (Genco and Borgnakke 2013).

Inflammation is central to the development of periodontitis. Neutrophils, monocytes, and lymphocytes have a role in the immunological response to microbial dysbiosis, releasing pro-inflammatory cytokines such IL-1β, TNF-α, and IL-6. Traditional inflammatory indicators such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and fibrinogen have long been used to detect systemic inflammation. However, these indicators lack specificity and do not provide a complete picture of the immune-inflammatory balance in periodontitis (Cekici et al. 2014).

Single-molecule indicators also fail to represent the complex interplay of immune cells that contribute to disease progression (Paraskevas, Huizinga, and Loos 2008; Acharya et al. 2019; Magán-Fernández et al. 2020). Traditional diagnostic methods, such as clinical examinations and radiographs, often detect the disease only after significant tissue damage has occurred. This limitation has driven the search for new biomarkers that can enable earlier detection, more accurate assessment of disease severity, and better monitoring of treatment responses.

The Systemic Inflammatory Response Index (SIRI) is an emerging biomarker that combines neutrophil, monocyte, and lymphocyte counts into one formula (SIRI = neutrophils × monocytes / lymphocytes). SIRI, which was originally created as a prognostic indicator in oncology, has been useful in predicting unfavorable outcomes in a variety of malignancies, including pancreatic, colorectal, bladder and lung carcinomas (Qi et al. 2016; Hayama et al. 2025; Ye et al. 2023; Jiang et al. 2021; Zhou et al. 2021). SIRI has lately been investigated as a marker of systemic inflammation in cardiovascular illnesses, metabolic disorders, and chronic inflammatory conditions (Zhao et al. 2022; Wei et al. 2023). SIRI has the potential to be a useful biomarker for periodontitis due to its capacity to represent the dynamic interactions between pro-inflammatory and regulatory immune cells. Despite accumulating data indicating its function in systemic disorders, the link between SIRI and periodontitis is still poorly understood.

Furthermore, some studies have suggested that SIRI may be preferable to standard inflammatory markers because of its capacity to combine multiple immunological components into a single result (C.-H. Yang et al. 2025). Unlike CRP and ESR, which are generic measures of inflammation, SIRI reflects a more complex balance of immune activation and control (Harrison 2015). . As a result, an increased SIRI score may indicate an excessive inflammatory response, as seen in other chronic illnesses like metabolic syndrome and rheumatoid arthritis (Urbanowicz et al. 2022; Xu et al. 2022). This shows that SIRI could have a broader role in monitoring systemic inflammation beyond cancer and cardiovascular disease. However, more research is needed to confirm its clinical significance in periodontology and assess its potential utility in diagnosing and tracking periodontal disease progression.

While SIRI is a novel approach to measuring systemic inflammation, various limitations must be addressed before its clinical implementation in periodontitis. One of the main problems is the absence of established reference ranges for SIRI in periodontal patients. Unlike its known predictive significance in oncology and cardiology, there is no agreement on the best SIRI levels for periodontitis diagnosis and severity assessment. This heterogeneity makes it difficult to compare data across studies, limiting SIRI's clinical value in routine periodontal examination.

Also, SIRI is a static measurement that offers a snapshot of immune state at a certain time point. Periodontitis is a chronic disease with phases of exacerbation and remission, therefore a single SIRI measurement may not adequately reflect disease progression (Abdulkareem et al. 2023). Longitudinal studies are needed to assess SIRI's stability over time and possible function in monitoring therapy response. Furthermore, whereas SIRI integrates different immune cell types, it does not account for other major inflammatory mediators such as cytokines, chemokines, and oxidative stress markers, all of which play important roles in periodontal pathogenesis (Ramadan et al. 2020).

Another significant issue is the variability in the methodology employed to measure SIRI among research. Variability in laboratory procedures, variances in blood sample processing, and a lack of established protocols for immune cell counting can all contribute to contradictory results (Mangoni and Zinellu 2024; W. Wang et al. 2024). This methodological variety makes it challenging to determine universal SIRI cutoff values in periodontal research. Furthermore, because the majority of existing research are observational, it is unclear that increasing SIRI levels are the cause or result of periodontitis (Y. Hu et al. 2024). SIRI may fail to capture the complexities of periodontal disease progression if these aspects are not taken into account. Furthermore, the feasibility of employing SIRI in clinical settings is unknown, as access to differential blood counts and the necessity for precise calculations may limit its broad use in dental practice (S. Luo et al. 2024).

While the SIRI has been extensively studied and validated as a prognostic marker in various medical fields, including oncology, cardiology, and immunology, its application in dentistry remains limited (Qi et al. 2016; Zhao et al. 2022; C.-H. Yang et al. 2025). Although some studies have begun to explore the association

between SIRI and periodontal diseases, the body of research is still relatively small compared to other medical disciplines. This disparity highlights the need for more focused investigations to establish SIRI's clinical utility in dental settings.

The oral cavity, which was once seen in isolation, is now acknowledged as a window into general health. New research reveals that periodontitis contributes significantly to systemic inflammation, and its chronic nature may have consequences for the progression of other inflammatory and metabolic illnesses (Genco and Sanz 2020; Hajishengallis 2015; Sedghi, Bacino, and Kapila 2021). However, typical periodontal assessments focus on clinical markers like as probing depth (PD), clinical attachment loss (CAL), and radiographic bone loss, which indicate previous structural damage rather than ongoing inflammatory activity. This retroactive method frequently causes a delay in identification and treatment until considerable and permanent harm has occurred (Mariotti and Hefti 2015; Soheili et al. 2024).

SIRI provides a dynamic measure of systemic inflammatory burden, which could help with this diagnostic difficulty. In the context of periodontitis, a chronic microbial assault can activate monocytes, which ultimately develop into osteoclasts and contribute to alveolar bone loss.

This systematic review aims to overcome these gaps by compiling data on the relationship between SIRI and periodontitis. The review is governed by three main objectives. First, it aims to assess the strength and consistency of the link between SIRI levels and periodontitis in various populations. Second, it seeks to determine how changes in SIRI relate to the severity of periodontal disease, as defined by clinical attachment loss, probing depth, and radiographic bone loss. Third, the study seeks to highlight major methodological constraints and gaps in current research that may inform future investigations.

The Systemic Inflammation Response Index (SIRI) is calculated using three types of white blood cells: neutrophils, monocytes, and lymphocytes. The formula is: SIRI = (neutrophil count × monocyte count) / lymphocyte count. In a typical blood sample, neutrophils make up about 70% of total white blood cells, lymphocytes account for 20–40%, and monocytes comprise 2–8%. Elevated neutrophil counts often indicate an acute inflammatory response, while increased monocyte levels can reflect chronic inflammation or immune system activation. Conversely, a low lymphocyte count, known as lymphopenia, is often associated with severe inflammation or stress (Ding et al. 2024).

II. Methodology

This search strategy was tailored to 4 databases, including PubMed, ResearchGate, BMC Oral Health and Google Scholar, to identify studies published from 2009 to 2024. The potential search keywords included "Systemic Inflammatory Response Index," "Inflammatory Markers," and "Periodontal Disease." The review followed PRISMA guidelines (Moher et al. 2009) and included original research examining the relationship between SIRI, periodontal disease severity, and systemic inflammatory conditions. The referenced articles concluded that monitoring the systemic inflammatory response is crucial for assessing disease activity, prognosis, and treatment efficacy in systemic diseases and periodontitis.

The studies were grouped based on the severity of periodontitis: (Caton et al. 2018)

- Stage 1: Initial Periodontitis
- Stage II: Moderate Periodontitis
- Stage III: Severe Periodontitis with potential for additional tooth loss
- Stage IV: Severe Periodontitis with potential for loss of the dentition

Eligibility Criteria

Inclusion Criteria:

- Studies involving adult participants (aged 18 years and older) diagnosed with periodontitis and other systemic inflammatory diseases.
- Studies must report on the calculation and assessment of the Systemic Inflammatory Response Index (SIRI) based on complete blood count parameters (e.g., platelet count, neutrophil count, lymphocyte count).
- Studies must use established clinical criteria for diagnosing periodontitis (e.g., clinical attachment loss, probing depth, radiographic evidence of bone loss).
- Types of study like cross-sectional, retrospective, and cohort studies.

Exclusion Criteria:

- Populations under 18 years of age.
- Studies that do not use established clinical criteria for diagnosing periodontitis (e.g., clinical attachment loss, probing depth, radiographic evidence).

- Studies that do not report on the calculation or assessment of the Systemic Inflammatory Response Index (SIRI).
- Studies focusing on pregnant women, as hormonal changes can significantly affect periodontal health.

Figure 1: Identification of studies via

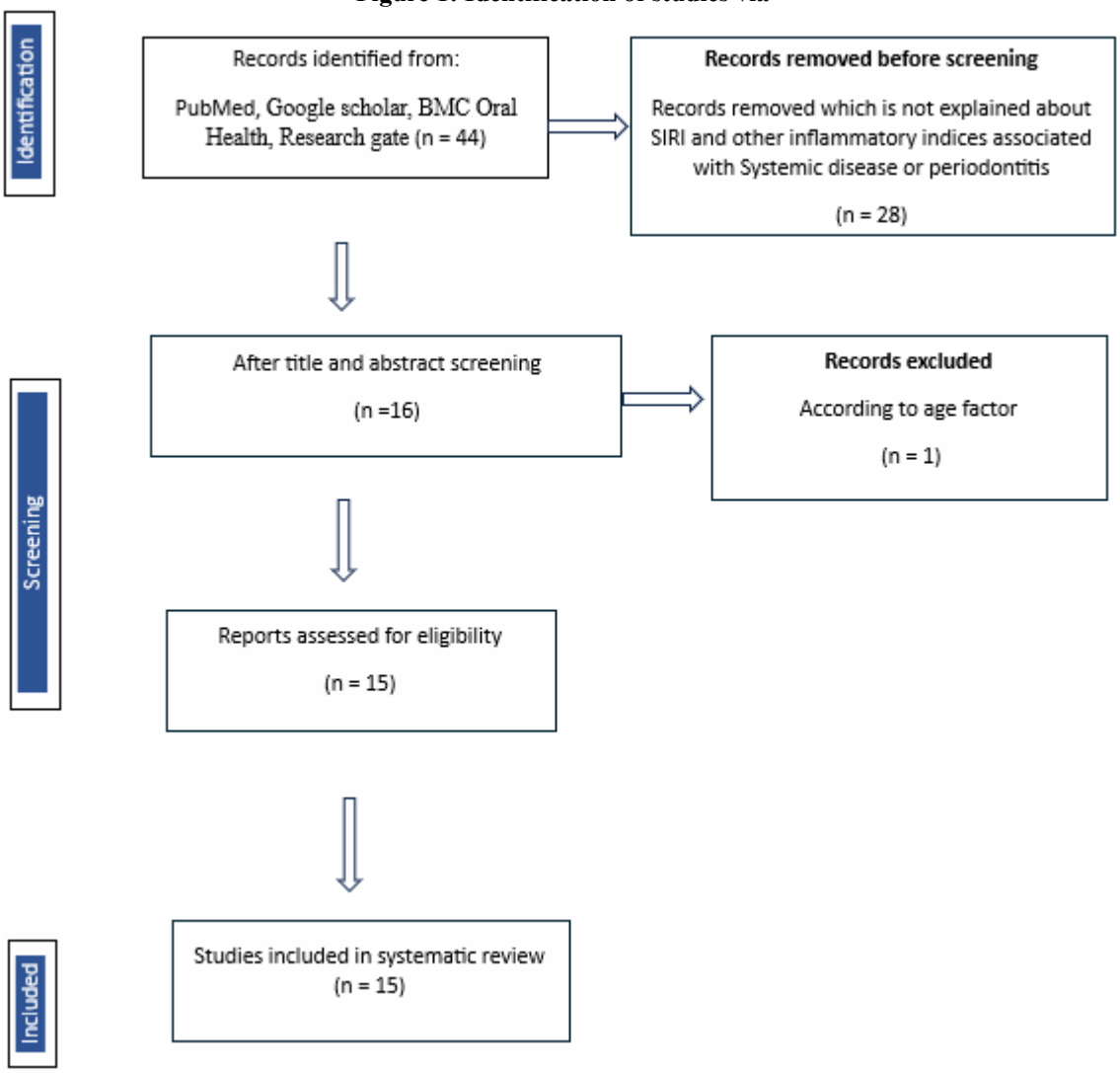

Table 1- Characteristics included in this study

No.	Author	Year	Country	Study Design	Sample size	Mean Age	SIRI (OR-Odds Ratio)	P-values	Duration	Follow-up
1.	Yuan chen et al.	2019	China	Cohort	285	22-80	≤0.84	<0.001	2005-2010	5 years
2.	Shangling hu et al.	2024	China	Cross sectional	737	40-70	0.668	<0.001	2014-2022	7 years
3.	Tomasz urbanowioz et al.	2024	Poland	Retrospective	256	67	6.06	0.001	Jan – Oct 2022	10 months

4.	Ding et al.	2024	China	Cohort	207	60	2.53	0.003	2015-2020	5 years
5.	K Han et al.	2022	China	Retrospective	1770	50-70	1.127	0.007	June 2016-Nov 2017	18 months
6.	Wang et al.	2024	China	Cross sectional	55,081	>20	1.31	<0.001	NHANES (1999 & 2018)	20 years
7.	Shiyi Luo and colleagues et al.	2024	United States	Cross-sectional	10,282	30	1.11	<0.001	2009-2014	5 years
8.	Zhengyun Ren et al	2024	United States	Cross-sectional	10,282	30	1.19	<0.001	2009-2014	5 years
9.	J. Li et al.	2022	China	Retrospective cohort study	808	>18	2.847	0.002	January 1, 2011 to December 31, 2019	19 years
10.	Tomasz Urbanowicz et al	2022	Poland	Cohort study (observational)	269	59-64	1.27	0.012	Jan and Dec 2014	8 years
11.	Jiang et al.	2023	China	Cross-sectional	474	>40	1.24	<0.001	March 2018-May 2023	6 years
12.	Cui et al.	2023	China	Retrospective cohort study	218	53.9 ± 8.5	>0.95	0.008	Jan 2010-June 2020	10 years
13.	M.O. Ozilhan et al.	2023	Turkey	Retrospective study	935	64.12	2.3	<0.001	Jan 2020 – Feb 2021	14 months
14.	Kong et al.	2023	United States	Observational study	13026	>18	1.16	<0.001	1999-2014 follow-up until Dec 2019	20 years
15.	Zhai et al.	2023	United States	Cross-sectional study	20,293	47.26±16.77	8.03	0.012	(NHANES) 2009-2012	4 years

(P<0.05 are statistically significant)

Figure 2. SIRI and Periodontitis

Evidence Synthesis

Literature Search and Study Characteristics

The flow chart of the literature search is presented in Figure 1. A total of 44 full text articles were retrieved from the PubMed, BMC Oral Health, Google Scholar, and ResearchGate databases. We excluded 28 articles that used the Systemic Inflammation Index (SII) and other inflammatory indices with systemic disease, and one article was excluded due to age factors. Ultimately, 15 studies were included in this systematic review. The study characteristics include author, year of publication, country, study design, sample size, mean age, SIRI (OR-Odds Ratio), significant P-value, duration and follow-up of the studies are mentioned in the table.

Yani Wang et al. 2024 Highlights the importance of monitoring SIRI as a potential indicator for CKD (Chronic Kidney Disease) risk in hypertensive patients, suggesting that early detection and intervention could help mitigate the prevalence of CKD in this population (Y. Wang et al. 2024).

Shengling hu et al. 2024 Emphasize the importance of monitoring systemic inflammation in tuberculosis patients. They advocate for paying closer attention to SIRI during examinations to identify high-risk patients with TOPD (Tuberculosis-Associated Obstructive Pulmonary Disease) early (S. Hu et al. 2024).

Shiyi Luo et al. 2024 Suggest that SIRI and other inflammatory markers could potentially serve as useful tools for clinicians in diagnosing and understanding the systemic inflammatory activity related to periodontitis (S. Luo et al. 2024).

Zhengyun ren et al. 2024 Suggest that there is a potential connection between systemic inflammation and periodontal disease, emphasizing the importance for periodontitis patients to be aware of their systemic health, especially concerning diseases that involve inflammatory processes (S. Luo et al. 2024).

The Use of SIRI in Both Systemic Inflammatory Diseases and Periodontitis

SIRI in Systemic Inflammatory Diseases

The Systemic Inflammatory Response Index (SIRI) serves as a marker of systemic inflammation by integrating the counts of neutrophils, monocytes, and lymphocytes—key components of the body's immune response. Elevated neutrophil and monocyte levels typically indicate heightened inflammatory activity, while reduced lymphocyte counts can signal a compromised immune system. By combining these parameters, SIRI offers a comprehensive reflection of the body's inflammatory status (Huang et al. 2023).

Monitoring systemic inflammatory responses is crucial in managing diseases like rheumatoid arthritis, sepsis, inflammatory bowel disease, and cardiovascular conditions. Therefore, elevated systemic inflammation can lead to organ dysfunction and worsen disease outcomes (Mangoni and Zinellu 2024).

In systemic inflammatory diseases, the NLR and other inflammation markers often fluctuate due to the dynamic nature of the immune response. Specifically, neutrophils typically increase during acute inflammation, while lymphocyte levels may decrease in response to stress or severe inflammation, leading to variations in the NLR. The SIRI was developed to integrate multiple inflammatory markers, specifically neutrophil, monocyte, and lymphocyte counts—into a single index, providing a more comprehensive assessment of the systemic inflammatory response (R.-H. Wang et al. 2023).

By evaluating SIRI, clinicians can assess the extent of inflammation, predict disease outcomes, and monitor responses to therapies such as immunosuppressant's or biologic drugs (Huang et al. 2023). Elevated SIRI has been linked with worse outcomes in several systemic inflammatory diseases, making it a valuable tool in clinical practice.

SIRI in Periodontitis

SIRI, can play an important role in understanding and managing periodontitis. It can reflect the overall inflammatory status of the body and correlate with the severity of periodontal disease (S. Luo et al. 2024). High SIRI values in patients with periodontitis have been associated with more severe periodontal damage, including greater attachment loss, bone loss, and increased clinical inflammation (e.g., gingival bleeding) (Y. Hu et al. 2024). By measuring SIRI, dental professionals can gain insight into the degree of systemic inflammation related to periodontal disease, potentially guiding treatment decisions. In periodontal therapy, especially in patients with more severe forms of periodontitis, systemic inflammation may persist even after localized interventions like scaling and root planning (Huang et al. 2023). SIRI can help monitor the effectiveness of periodontal treatment by tracking changes in the inflammatory response over time. A decrease in SIRI values post-treatment may indicate a successful reduction in systemic inflammation, which can be associated with better long-term outcomes. By identifying elevated SIRI levels in periodontitis patients, clinicians can potentially intervene not only in managing periodontal disease but also in reducing the risk of these comorbid conditions (the simultaneous presence of two or more medical conditions) (Y. Hu et al. 2024).

III. Result

This systematic review synthesized existing literature on the association between the Systemic Inflammatory Response Index (SIRI) and periodontitis, evaluating its potential as a biomarker for assessing the

severity of periodontal disease. A comprehensive search across multiple databases, including PubMed, ResearchGate, and Google Scholar, identified studies published from 2009 to 2024 that examined the relationship between SIRI, periodontal disease severity, and systemic inflammatory conditions.

The review identified a significant association between elevated SIRI levels and the presence and severity of periodontitis. Specifically, studies indicated that higher SIRI values correlated with more severe periodontal damage, including greater attachment loss, bone loss, and increased clinical inflammation, such as gingival bleeding. These findings suggest that SIRI can effectively reflect the overall inflammatory status of the body in patients with periodontitis.

Additionally, the review highlighted that SIRI not only serves as a marker for periodontal disease but also has implications for systemic health. Elevated SIRI levels in periodontitis patients were associated with an increased risk of comorbid conditions, such as cardiovascular disease, diabetes, and respiratory problems. This underscores the importance of monitoring systemic inflammation in patients with periodontitis to potentially mitigate the risk of these associated health issues.

Overall, the findings from this review support the use of SIRI as a non-invasive marker of systemic inflammation, with notable implications for both periodontal and systemic health. As research continues, the role of SIRI in periodontal disease management is likely to expand, offering additional insights into the complex interplay between oral health and overall systemic inflammation.

IV. Discussion

This systematic review set out to elucidate the relationship between the Systemic Inflammatory Response Index (SIRI) and periodontitis, focusing on its diagnostic and prognostic potential. Our findings indicate that elevated SIRI levels are consistently associated with greater periodontal destruction. By integrating neutrophil, monocyte, and lymphocyte counts into a single composite score, SIRI appears to capture the balance between pro-inflammatory and regulatory immune responses, a feature that may be especially useful given the multifactorial nature of periodontitis.

The reviewed studies demonstrated that higher SIRI values correlated with clinical indicators such as increased probing depth, clinical attachment loss, and radiographic bone loss. These associations support the idea that SIRI not only reflects local periodontal inflammation but also mirrors the systemic inflammatory status (Ren et al. 2024; Guo et al. 2024). This is in line with the growing body of evidence that links periodontitis with systemic conditions like cardiovascular disease, diabetes, and hypertension (Genco and Borgnakke 2013; Hajishengallis and Chavakis 2021). In several studies, subgroup analyses revealed that factors such as age, sex, and ethnicity may modify the strength of this association, suggesting that host factors and regional differences in immune responses could influence SIRI levels (H. Yang et al. 2025; Z. Luo et al. 2024; Yin et al. 2024).

Moreover, the composite nature of SIRI appears to offer advantages over traditional biomarkers like CRP or the NLR, which tend to provide a more generalized measure of inflammation. By capturing multiple dimensions of the immune response, SIRI has the potential to serve as an early-warning signal for patients at high risk of progressive periodontal destruction. However, it remains critical to note that most available data are derived from observational studies. Consequently, while the associations are compelling, they do not establish a clear causal pathway between elevated SIRI and periodontitis progression (Y. Hu et al. 2024).

Another noteworthy finding is the potential role of SIRI in monitoring the systemic inflammatory burden in patients with periodontitis who are at risk of or already suffering from systemic comorbidities. This dual relevance may pave the way for its use in multidisciplinary management, where dental and medical practitioners work together to reduce overall disease burden (Guo et al. 2024). Future interventional studies, including longitudinal and controlled trials, are necessary to determine whether reducing SIRI levels through periodontal therapy correlates with improved systemic health outcomes.

When combined with neutrophilia and relative lymphopenia, an increased SIRI may be an early sign of severe systemic inflammation. Some exploratory investigations have indicated increased SIRI values in patients with severe periodontitis compared to healthy controls, regardless of common confounding variables such as smoking and diabetes (Y. Hu et al. 2024; S. Luo et al. 2024; Ren et al. 2024; Escobar Arregocés et al. 2021) . Prospective, controlled studies are needed to elucidate this association and evaluate whether therapies aiming at lowering inflammation can result in equivalent decreases in SIRI levels.

V. Limitations

Although our findings show that elevated SIRI levels are linked with periodontal disease, there are several important limitations to consider.

First, the current body of research offers limited insight into how SIRI fits into the overall development of periodontitis. Many studies point out that higher SIRI levels go hand in hand with more severe periodontal damage, but we still don’t fully understand whether these elevated levels actually trigger the disease or if they

simply reflect its progression. More detailed, mechanism-focused studies are needed to clarify SIRI's exact role in the onset and advancement of periodontitis.

Second, most of the available research does not clearly separate gingivitis, a reversible, early stage of gum inflammation from periodontitis, which involves irreversible loss of supporting tissues. Without making this clear distinction, it's hard to tell how SIRI behaves in the early versus the later stages of periodontal disease. Future work should aim to differentiate between these two conditions so that we can better understand whether SIRI can help pinpoint the transition from gingivitis to periodontitis.

Third, there is considerable variation in how researchers define and measure the severity of periodontitis. Clinical measurements such as probing depth, attachment loss, and bone loss are not consistently used or reported, which makes it challenging to compare SIRI values across different studies. This lack of consistency means we are still far from establishing reliable SIRI thresholds that can effectively predict how severe a patient's disease is or how quickly it might progress.

Fourth, and importantly, there is no research on the use of SIRI in countries with large populations, such as India. In India, the implementation of SIRI-based techniques for periodontal screening remains limited due to resource constraints and the lack of standardized protocols. Given the high prevalence of periodontitis and the large population, integrating these advanced inflammatory biomarkers into routine screening could significantly enhance early diagnosis and treatment outcomes.

Another drawback of SIRI is its sensitivity to confounding variables. Several systemic disorders, including diabetes, obesity, and autoimmune diseases, might affect neutrophil, monocyte, and lymphocyte counts, resulting in SIRI values that are not necessarily related to periodontitis (Zhao et al. 2022; Chen et al. 2024; L. Wang et al. 2024; C.-H. Yang et al. 2025). In addition, lifestyle factors such as smoking, food, and stress might influence systemic immune responses, confounding the interpretation of SIRI in periodontal disease (Isola et al. 2023). Furthermore, acute infections and temporary inflammatory situations can produce immune cell count variations, making it difficult to identify periodontal inflammation from other inflammatory states (Hajishengallis and Chavakis 2021).

Finally, while SIRI captures the balance of key immune cells, it doesn't consider other important elements like specific cytokines or markers of oxidative stress. In real-life scenarios, many factors, ranging from individual immune responses to environmental exposures and lifestyle habits such as diet and smoking—can affect inflammation. Unfortunately, only a few studies have looked at how these variables interact with SIRI in the context of periodontal disease. Understanding these influences is crucial if we are to validate SIRI as a robust diagnostic and prognostic tool.

VI. Future Agenda

In the future, it is essential to conduct detailed mechanistic studies to clarify whether changes in SIRI are a cause or a consequence of periodontitis, while also clearly distinguishing between gingivitis and periodontitis to pinpoint when SIRI levels begin to shift; standardizing measurement protocols and establishing universal reference ranges will further enable reliable comparisons across studies and integration into routine clinical practice, and given the high prevalence of periodontitis in large-population countries like India, extensive multicenter research is urgently needed to account for genetic, environmental, and socioeconomic factors, ultimately paving the way for a more holistic and personalized approach to managing periodontal disease through precision medicine strategies.

VII. Conclusion

In summary, the evidence synthesized in this systematic review supports a significant association between elevated SIRI levels and the severity of periodontitis. The composite nature of SIRI reflecting the interplay among neutrophils, monocytes, and lymphocytes positions it as a promising biomarker for assessing both local periodontal inflammation and the broader systemic inflammatory status. Such a marker could enhance early detection, risk stratification, and personalized treatment strategies for patients with periodontitis, particularly those with associated systemic comorbidities.

However, before SIRI can be implemented in routine clinical practice, further research is warranted. Future studies should focus on standardizing laboratory methods, establishing reference ranges, and conducting well-designed prospective trials to better understand the temporal relationship between SIRI fluctuations and disease progression. Addressing these gaps will be essential for validating SIRI's clinical utility and integrating it into comprehensive periodontal and systemic disease management protocols.

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