Immunopathologia Persa
http immunopathol.com
DOI:10.34172/ipp.2026.44024

Systemic immune-inflammation index and breast neoplasm risk; a systematic review and meta-analysis

Zahed Karimi[1], Mahin Roozitalab[2], Faezeh Khajeh[3], Seyyed Amirkazem Vejdan[4], Zahra Amirian[4], Seyed Amir Banikarim[5], Sara Teihou Jorshari[5], Anna Ghorbani Doshantapeh[6], Sina Salem Ahim[7*]

[1]Department of Internal Medicine, School of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
[2]Cellular and Molecular Research Center, Yasuj University of Medical Sciences, Yasuj, Iran
[3]Department of Anesthesiology, School of Paramedical Sciences, Gonabad University of Medical Sciences, Gonabad, Iran
[4]Department of General Surgery, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
[5]Hematology-Oncology Department, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
[6]Department of Hematology-Medical Oncology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[7]Fasa University of Medical Sciences, Fasa, Iran

***Correspondence to**
Sina Salem Ahim,
Email:
sinasalemahim@gmail.com

Received 12 Dec. 2025
Revised: 6 Jan. 2026
Accepted 1 Feb. 2026
ePublished 15 Apr. 2026

Keywords: Breast neoplasms, Malignant tumor of breast, Breast tumor, Breast cancer, Systemic immune-inflammation

Abstract

Introduction: Breast carcinoma is the most common neoplasm among women. On the other hand, many inflammation markers are correlated with carcinoma prognosis. Our investigation sought to evaluate how the systemic immune-inflammation (SSI) index is associated with the likelihood of developing breast cancer.
Materials and Methods: Web of Science, Cochrane, Scopus, PubMed, Embase, and Google Scholar were searched for publications up to November 8, 2025, and the data were analyzed using STATA 14.
Results: In total, five observational studies with a sum of 520783 female participants were combined. Results of the studies demonstrated that high SII index levels strengthened the risk of breast neoplasm (OR: 1.09, 95% CI: 1.05, 1.13). The tertile 2 of the SII index was not associated with increased risk of breast neoplasm. However, the tertile 3 (9%), the quartile 2 (6%), the quartile 3 (6%), and the quartile 4 (32%) of the SII index increased the risk of breast neoplasm. Furthermore, high SII index levels among the women in the UK and the USA increased the probability of breast cancer by 7% and 18%, respectively, and in cohort and cross-sectional studies by 8% and 22%, respectively. Besides, female patients with diabetes mellitus who had high SII index levels faced a 3% higher risk of breast neoplasm than nondiabetic women.
Conclusion: A high SII index was a risk factor for the occurrence of breast neoplasm, and higher SII index levels in women were associated with higher risks of breast carcinoma. Additionally, women with high SII index levels who lived in the USA faced twice the risk of breast cancer compared with those who lived in the UK.
Registration: This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (ID: CRD420251237998) and Research Registry (UIN: reviewregistry2062) websites.

Citation: Karimi Z, Roozitalab M, Khajeh F, Vejdan SA, Amirian Z, Banikarim SA, Teihou Jorshari S, Ghorbani Doshantapeh A, Salem Ahim S. Systemic immune-inflammation index and breast neoplasm risk; a systematic review and meta-analysis. Immunopathol Persa. 2026;x(x):e44024. DOI:10.34172/ipp.2026.44024.

Introduction

Among women, breast cancer is the most common form of malignancy and the principal contributor to cancer-associated mortality (1). In 2022, approximately 2.3 million new cases and 670,000 deaths due to breast neoplasm were reported around the world, and according to estimates, by 2050, the new cases and deaths will reach 3.2 million and 1.1 million, respectively (2). Risk factors of breast carcinoma include age, obesity, use of oral contraceptive pills, family history, menopausal status, alcohol consumption, smoking, and dietary patterns (3).

The primary treatment methods for breast neoplasms include radiotherapy, surgery, and systemic treatments (4,5). Evidence in cancer research indicates that chronic inflammation may play a role in the onset of breast carcinoma (6). Furthermore, many inflammatory markers are related to cancer prognosis (7-9). The systemic immune-inflammation (SII) index, calculated by counting peripheral blood neutrophils, lymphocytes, and platelets, presents a comprehensive evaluation of the inflammatory and immune status (10). Accordingly, the purpose of the present study was to examine the association among the SII index and the risk of breast neoplasm. Studies on this subject published over the past few years have presented inconsistent results. Some studies (11,12) demonstrated that generally, high SII index levels increased the risk of breast carcinoma. Whereas, in another study (13) conducted on the second one-third, results indicated no statistically significant relationship between high SII index levels and the risk of breast neoplasm occurrence.

Key point

A high systemic immune-inflammation (SII) index is a risk factor for the occurrence of breast carcinoma, and higher SII index levels in women were associated with higher risks of breast cancer. Accordingly, investigating the SII index level in women can present an acceptable prognosis about the possibility of breast cancer occurrence in women.

Materials and Methods

The study was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (14), and the protocol was registered in both PROSPERO (International Prospective Register of Systematic Reviews) and the Research Registry.

Search strategy

A comprehensive literature search was carried out across multiple databases, including Embase, Web of Science, Scopus, PubMed, Cochrane, and the Google Scholar search engine, to identify all relevant studies available up to November 8, 2025. No restrictions were applied regarding language or publication date. The search strategy incorporated Medical Subject Headings (MeSH), including breast neoplasms, malignant tumor of breast, breast tumor, breast cancer, and systemic immune-inflammation along with corresponding free-text terms, and Boolean operators (AND, OR) were used to structure and refine the search combinations. In addition to the electronic search, an independent manual screening of reference lists and related sources was performed to ensure the inclusion of all pertinent studies.

PECO framework for study selection

- Population: Articles designed to investigate the effect of the SII index on the risk of breast neoplasm.
- Exposure: High SII index.
- Comparison: Women who did not have breast neoplasms.
- Outcomes: Risk of breast neoplasm.

Inclusion criteria

Articles designed to examine the role of the SII index on the risk of breast neoplasm.

Exclusion criteria

Studies with low qualitative score, posters, duplicate studies, abstracts, systematic reviews, studies on the association between the SII index and breast cancer metastasis, meta-analysis, studies on the association between the SII index and breast cancer recurrence, reviews, and those that did not provide our required data were excluded.

Quality assessment

The Newcastle–Ottawa Scale was used to evaluate methodological quality. Each item could receive a maximum of one star, except the comparability item. Overall scores varied from 0 to 10, where 0 represented poor quality and 10 indicated excellent quality. Studies with scores under 6 were deemed low quality (15).

Data extraction

Two authors were assigned to extract data. The extracted data included the following: sample size, country, SII index level, year, author's name, and type of study. Discrepancies were subsequently settled through evaluation by a third reviewer.

Statistical analysis

The natural logarithm of the odds ratio (OR) was applied for analysis, after which the results of all included studies were pooled. Heterogeneity was assessed using the statistic, and a random-effects model was employed to synthesize the findings. All analyses were performed in STATA version 14, with P values <0.05 regarded as statistically significant.

Results

The database search and Google Scholar screening initially identified 326 records, of which 192 duplicates were removed. After abstract screening, 14 studies without accessible full texts were excluded. An additional 59 articles were removed for lacking the necessary data. Of the 61 studies that proceeded to full-text assessment, 56 did not meet the inclusion criteria, leaving 5 studies for the final analysis (Figure 1).

The current study examined four cohort and one cross-sectional studies with a total of 520783 female participants with mean ages between 40 and 69 years. The following table presents additional required data (Table 1).

The five observational studies were combined and demonstrated that a high SII index level (OR: 1.09, 95% CI: 1.05, 1.13) increased the risk of breast neoplasm. Accordingly, a high SII index was a risk factor for the occurrence of breast carcinoma (Figure 2).

Subgroup analysis revealed that high SII index levels in women from the countries USA and the UK increased the risk of breast neoplasm by 7% and 18%, respectively. Additionally, in cohort and cross-sectional studies, the increase in the risk of breast neoplasm following high SII levels by 8% and 22%, respectively, was evident.

Furthermore, various levels of the SII index presented different results, as the T2 of the SII index did not increase the risk of breast tumors. Whereas, the T3 of the SII index strengthened the risk of breast carcinoma by 9%. While investigating different quartiles of the SII index, we concluded that the Q2 (6%), Q3 (6%), and Q4 (32%) quartiles increased the risk of breast neoplasm (Table 2).

Figure 3 demonstrates that women with diabetes mellitus with higher SII index levels had an increased risk of breast neoplasms (OR:1.03, 95% CI: 1.02, 1.05).

Discussion

Our findings demonstrated that elevated SII levels were

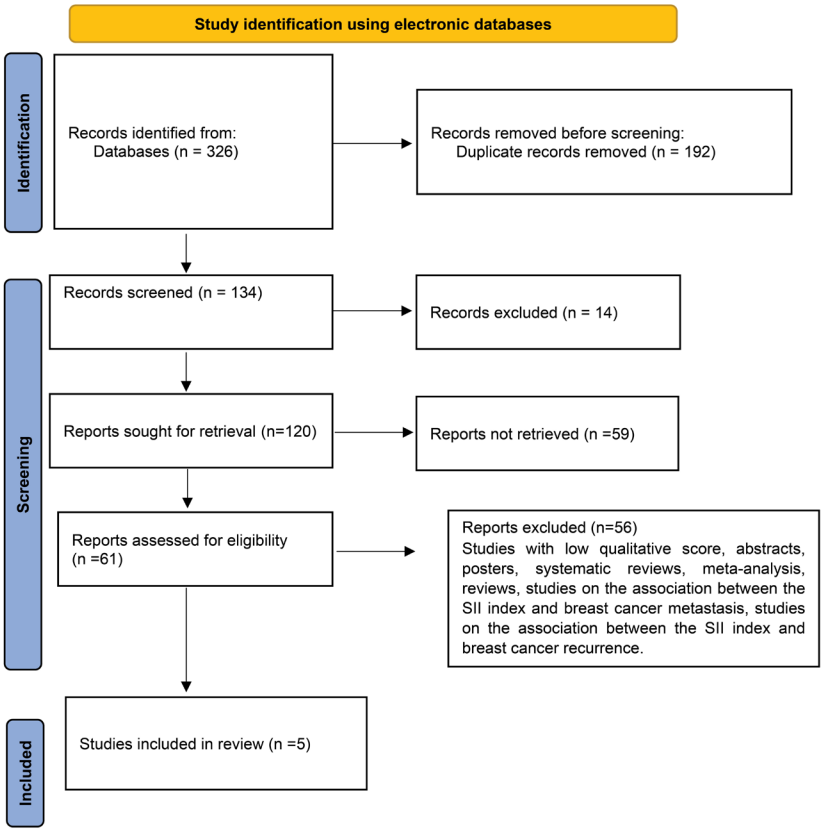

Figure 1. The PRISMA flow chart of study selection.

associated with an increased risk of breast carcinoma, indicating that women with higher SII values were more likely to develop the disease. In line with our findings, a cohort study by Li et al reported that elevated SII levels were linked to the occurrence of breast tumors, reinforcing the potential role of systemic inflammation in breast cancer development (16). Wen et al also found that women with elevated SII levels faced a greater risk of developing breast carcinoma, highlighting the potential role of systemic inflammation in tumor initiation (12). The cross-sectional study by Xiong et al further supports the role of systemic inflammation in breast cancer development, showing

Table 1. Summarized information of the articles

Author, year	Place	Type of study	Time of study	Sample size	Mean age (year)	Level of SII index	Odds ratio	95% CI	
								Lower	Upper
Xiong J, 2025(11)	USA	Cross-sectional	2001-2018	17044	48.73	Total	1.03	1.01	1.05
						Q2	1.14	0.87	1.49
						Q3	1.10	0.84	1.45
						Q4	1.44	1.11	1.88
Wen Y, 2025(12)	USA	Cohort	2001–2018	20843	48.72	Total	1.19	1.02	1.39
						Q2	1.05	0.76	1.43
						Q3	0.95	0.68	1.32
						Q4	1.48	1.05	2.08
Li Y, 2025(16)	USA	Cohort	1999-2018	21058	47.59	Total	1.02	1	1.04
						Q2	1.13	0.88	1.45
						Q3	1	0.78	1.30
						Q4	1.46	1.14	1.86
Zhang Y, 2024(6)	UK	Cohort	2006-2010	259435	57	Q2	1.05	0.99	1.12
						Q3	1.07	1.01	1.14
						Q4	1.11	1.04	1.18
Yang Z, 2023(13)	UK	Cohort	2006-2010	202403	40-69	T2	1.04	0.97	1.12
						T3	1.09	1.01	1.17

SII: Systemic immune-inflammation, Q: Quartile, T: Tertile.

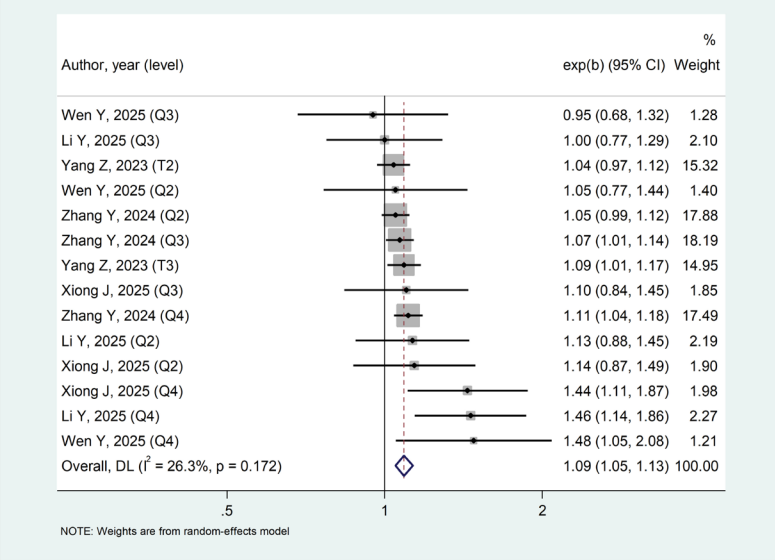

Figure 2. Forest plot showing the association between SII index and risk of breast neoplasm.

that increases in SII were accompanied by a higher risk, particularly among women with the greatest SII burden (11). According to the cohort findings of Yang et al, rising SII levels were associated with a higher probability of breast neoplasm, with the greatest risk observed among women in the highest tertile compared to the lowest (13). These studies have highlighted the potential role of systemic inflammation in breast carcinogenesis, with elevated SII levels repeatedly emerging as a relevant marker. Evidence from these cohort and cross-sectional investigations has consistently shown that women with higher SII values face a greater likelihood of developing breast tumors. These findings parallel the results of our meta-analysis, in which subgroup analyses demonstrated that elevated SII levels across both cohort and cross-sectional study designs were associated with increased breast carcinoma risk.

In comparison with previous meta-analysis studies, a study by Zhang et al reported that women with elevated SII levels experienced poorer outcomes, including reduced disease-free, overall, and metastasis-free survival, compared with those with lower SII values (17). Ciurescu et al reported in their meta-analysis that higher SII values were linked to reduced overall survival as well as shorter disease-free survival of individuals with breast malignancy (18). Recently, Ji and Wang, in their meta-analysis, found that women with breast cancer and elevated SII levels experienced poorer overall and disease-free survival compared with those with lower SII values (19). The mentioned meta-analyses indicated that women with breast carcinoma who had high SII index levels had lower survival rates than those with lower SII index levels. Accordingly, a high SII index level is a serious risk factor for breast carcinoma development as well as survival rate after the onset of the disease.

The cohort study by Fest et al further supports the role of systemic inflammation in breast cancer development, showing that women with higher SII levels were more susceptible to breast carcinoma (20). In another cohort study by Nost et al, evidence indicated a positive association amongst high SII index levels and the risk of esophageal, kidney, ovarian, and colon cancers (21). Regarding the other types of cancers, the cross-sectional study by Zhao et al further supports the role of systemic inflammation in carcinogenesis, demonstrating that individuals with higher SII levels were more susceptible to skin cancer (22). In a cross-sectional study by Tao et

Table 2. Subgroup analysis for the relationship between SII index and risk of breast neoplasm

Variables	Subgroups	Odds ratio (95% CI)	*P* value	I^2 (%)
Country	USA	1.18 (1.06, 1.32)	0.202	27.2
	UK	1.07 (1.04, 1.10)	0.647	0
Type of study	Cohort	1.08 (1.04, 1.12)	0.230	22.4
	Cross-sectional	1.22 (1.03, 1.44)	0.314	13.7
Level of SII index	Tertile 2	1.04 (0.97, 1.12)	-	0
	Tertile 3	1.09 (1.01, 1.17)	-	0
	Quartile 2	1.06 (1.00, 1.12)	0.891	0
	Quartile 3	1.06 (1.01, 1.13)	0.858	0
	Quartile 4	1.32 (1.09, 1.59)	0.021	69.2

SII: Systemic immune-inflammation.

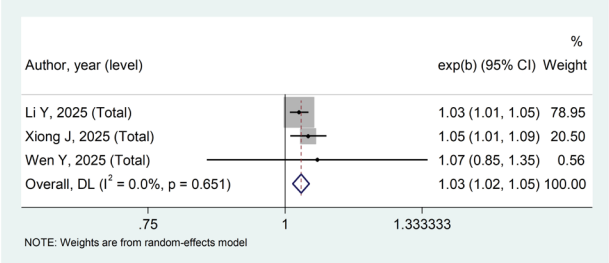

Figure 3. Forest plot showing the association between SII index and risk of breast neoplasm in diabetic patients.

al, individuals in the highest one-third of the SII index group faced a 48% higher risk of melanoma than those in the lowest one-third (23). The cross-sectional study by He et al further highlights the role of systemic inflammation in tumorigenesis, demonstrating that individuals with elevated SII levels were more susceptible to prostate neoplasms (24). Findings from Chen and Li also indicated that rising SII levels corresponded to a higher probability of prostate cancer occurrence (25). The abovementioned observational studies demonstrated that, in addition to the fact that a high SII index level is a risk factor for breast carcinoma, it can increase the risk of several other types of cancer, including prostate, esophageal, kidney, ovarian, and colon.

Conclusion

Elevated SII levels emerged as a meaningful risk factor for breast carcinoma, with higher SII values consistently associated with an increased likelihood of disease occurrence among women. These findings suggest that assessing the SII index may offer useful prognostic insight into the potential development of breast carcinoma, particularly in populations at elevated inflammatory risk. Notably, geographic variation appeared to influence this association, as women with high SII levels residing in the USA demonstrated a substantially greater risk of breast carcinoma compared with their counterparts in the UK. This pattern implies that factors related to nationality or race, such as genetic background, environmental exposures, lifestyle patterns, or healthcare access, may modify the relationship between systemic inflammation and breast cancer risk. Additionally, among women with elevated SII levels, those with diabetes exhibited a higher susceptibility to breast carcinoma than nondiabetic individuals, underscoring the potential interplay between chronic inflammation, metabolic dysregulation, and cancer development. Collectively, these observations highlight the importance of considering demographic and clinical characteristics when interpreting the prognostic value of the SII index in breast carcinoma.

Limitations of the study

A number of limitations should be acknowledged when interpreting the findings of this study. First, it was not feasible to stratify the results by age, which restricts our ability to determine whether the associations observed vary across different age groups or life stages. This is particularly relevant given the potential influence of age-related immunological and hormonal changes on inflammatory markers such as the SII index. Second, the evidence base was relatively limited, as only a small number of eligible studies met the inclusion criteria. This constraint may reduce the robustness of the pooled estimates and limit the capacity to conduct more detailed subgroup or sensitivity analyses. Finally, the available studies were conducted exclusively in the USA and the UK, which may limit the generalizability of the findings to populations in other geographic regions with different demographic, environmental, or healthcare characteristics. These factors should be considered when interpreting the results and highlight the need for more diverse, large-scale investigations in the future.

Acknowledgments

The authors would like to thank Diana Sarokhani and Hosein Mardanparvar (Guissu Research Corporation) for their guidance and editing of the manuscript registration on the PROSPERO website.

Authors' contribution

Conceptualization: Sina Salem Ahim and Zahed Karimi.
Data curation: Sina Salem Ahim and Sara Teihou Jorshari.
Formal analysis: Sina Salem Ahim and Zahra Amirian.
Funding acquisition: Sara Teihou Jorshari and Mahin Roozitalab.
Investigation: Zahed Karimi and Seyed Amir Banikarim.
Methodology: Mahin Roozitalab and Seyed Amiriazem Vejdan.
Project administration: Sina Salem Ahim and Anna Ghorbani Doshantapeh.
Supervision: All authors.
Validation: Faezeh Khajeh and Anna Ghorbani Doshantapeh.
Visualization: Zahra Amirian and Seyed Amiriazem Vejdan.
Writing–original draft: All authors.
Writing–review and editing: All authors.

Competing Interests

The authors declare that they have no competing interests.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors utilized Copilot and Grammarly to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

This study has been compiled based on the PRISMA checklist. Its protocol was registered on the PROSPERO website (ID: CRD420251237998) and the Research Registry website with (Unique Identifying Number (UIN) reviewregistry2062). Besides, ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

Funding/Support

None.

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