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The association between systemic immune-inflammation index and gestational diabetes mellitus; a systematic review and meta-analysis

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Abstract

Introduction: Gestational diabetes mellitus (GDM) is among the most common complications during pregnancy, and inflammatory indices, including systemic immune-inflammation (SII) index and systemic inflammation response index (SIRI), appear to be able to forecast GDM. Accordingly, in the present study, our goal was to examine the association between high levels of SII and SIRI indices and the risk of gestational diabetes.

Materials and Methods: Databases Web of Science, Cochrane, Scopus, PubMed, Embase, and Google Scholar Search Engine were used for articles published until August 7, 2025. Data was analyzed using STATA 14. Tests with p-values lower than 0.05 were considered statistically significant.

Results: High SII index levels increased the risk of GDM (OR=1.52, 95% CI: 1.25, 1.86), as the second (OR=1.11, 95% CI: 1.03, 1.19) and fourth (OR=1.31, 95% CI: 1.03, 1.66) quartiles increased the risk of GDM. Furthermore, high SII index levels in the USA and the cross-sectional study had no statistically significant association with GDM (OR=0.98, 95% CI: 0.59, 1.62). However, in China and cohort studies, high SII index levels increased the risk of GDM (OR=1.60, 95% CI: 1.30, 1.98). Additionally, high SIRI index levels increased the risk of GDM (OR=1.37, 95% CI: 1.17, 1.62), whereas high SIRI index levels in the USA and the cross-sectional study lowered the risk of GDM (OR=0.72, 95% CI: 0.53, 0.99). However, in China and cohort studies, high SIRI index levels increased the risk of GDM (OR=1.47, 95%CI: 1.24, 1.74).

Conclusion: High SII (52%) and SIRI (37%) indexes significantly increased the risk of GDM. Hence, individuals at risk of GDM can be identified and controlled through the evaluation and screening of the mentioned indices in pregnant women.

Registration: This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (ID: CRD420251128749) and Research Registry (UIN: reviewregistry2038) websites.

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Introduction

Gestational diabetes mellitus (GDM) is defined as abnormal glucose tolerance during pregnancy and is among the most frequent complications during pregnancy (1). In fact, GDM is the most common metabolic disorder worldwide, with a prevalence of approximately 14% (2-4). The incidence rate of GDM varies from 2.4% to 22.3% around the world, and China, with a 14.8% incidence rate, is among the highest global ranks (5-7). On the other hand, GDM increases the risk of adverse consequences during pregnancy, including hypertension, preeclampsia, premature rupture of membranes, stillbirth, cesarean section, neonatal respiratory distress, macrosomia, and metabolic and long-term effects on health, such as diabetes mellitus, obesity, and cardiovascular diseases (4,8-14). Accordingly, timely diagnosis of women at risk of GDM is critical, as interventions such as diets and exercise can be carried out at early stages to prevent GDM and its complications to a great extent (15).

Key point

High systemic immune-inflammation (SII) index (52%) and systemic inflammation response index (SIRI) (37%) levels increased the risk of gestational diabetes mellitus (GDM), as the second (11%) and fourth (31%) quartiles of SII increased the risk of GDM. Accordingly, those at risk of GDM can be identified and monitored through conducting evaluations and screening the mentioned indices among pregnant women.

Primary studies examined the role of inflammatory indicators, such as systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI), in predicting the incidence of GDM (16,17). SII and SIRI indices are newfound biological markers derived from the number of lymphocytes, platelets, neutrophils, and monocytes, and they provide us with a comprehensive assessment of the individual's immune and inflammatory condition (18,19). However, various studies reported different results regarding the relationship between SII and SIRI and the risk of GDM. For instance, one study (20) believed that there was no statistically significant association between SII index and the risk of GDM, whereas another (21) reported that high SII index levels increased the risk of GDM. Additionally, a study (22) demonstrated that the relationship between SIRI and GDM was statistically insignificant, while another study (23) indicated that high SIRI index levels increased the risk of GDM. Accordingly, the present study was conducted using systematic review and meta-analysis methods to examine the association between SII and SIRI indices and the risk of GDM by providing a general and up-to-date result.

Materials and Methods

Study design

Our article was designed based on Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (24). The protocol of this article was registered at the websites PROSPERO (International Prospective Register of Systematic Reviews) and Research Registry.

Search strategy

The search was conducted on the databases Web of Science, Cochrane, Scopus, PubMed, Embase, and Google Scholar Search Engine for articles published by August 7, 2025. The search included no limitations in the language and time of the studies. The Medical Subject Headings (MeSH) keywords and their equivalents were used in the search, and operators (AND, OR) were used to combine them. The search strategy in the database Web of Science was as follows: "Diabetes, Gestational" OR Gestational Diabetes Mellitus OR Pregnancy-Induced Diabetes (All Fields) AND Systemic immune-inflammation index (All Fields).

PECO

- Population: Articles that evaluated the association between the SII index and GDM.
- Exposure: High SII index.
- Comparison: Women who did not have GDM.
- Outcome: Estimating the association between high SII index and GDM.

Inclusion criteria

Articles that evaluated the association between the SII index and GDM.

Exclusion criteria

Articles without accessible full text, reviews, temporarily accepted articles, preprint studies, studies that lacked sufficient data, low-quality studies, duplicate studies, and posters.

Quality assessment

To assess the quality of studies, two authors independently used the Newcastle-Ottawa Scale. The scoring of the above tool is star-based, with 9 questions, 8 of which are rated with a maximum of one star, and the comparison question is rated with a maximum of two stars. Thus, the overall score is a number between 0 and 10, with zero indicating the lowest quality and ten indicating the highest quality. Studies with scores<5 were considered low-quality (25).

Data extraction

Two authors independently extracted data, including mean age, total number, country, type of study, year, SII index quartile, name of researcher, and the relationship between SII or SIRI indexes and risk of GDM. Then, using an agreement solution, the two authors addressed the discrepancies.

Statistical analysis

The odds ratio (OR) logarithm was used for data analysis, and the studies were combined. The I^2 index was used to assess heterogeneity among studies, and a random-effects model was employed to combine the results. Data analysis was conducted using STATA 14. Tests with $P<0.05$ were considered statistically significant.

Results

Overall, 85 articles were found in the search stage. Then, 34 duplicate studies were identified and removed. The abstracts were reviewed, and 6 studies without full text were excluded. Out of the remaining 45 studies, 21 articles that lacked the required data for analysis were removed. A total of 24 studies entered the next step and, 16 articles were excluded due to other exclusion criteria, and 8 studies remained (Figure 1).

At the end of the studies' screening, seven cohort studies and one cross-sectional study remained (Table 1).

Figure 2 demonstrated that high SII index levels increased the risk of GDM (OR=1.52, 95% CI: 1.25, 1.86). The second (OR=1.11, 95% CI: 1.03, 1.19) and fourth (OR=1.31, 95% CI: 1.03, 1.66) SII index quartiles increased the risk

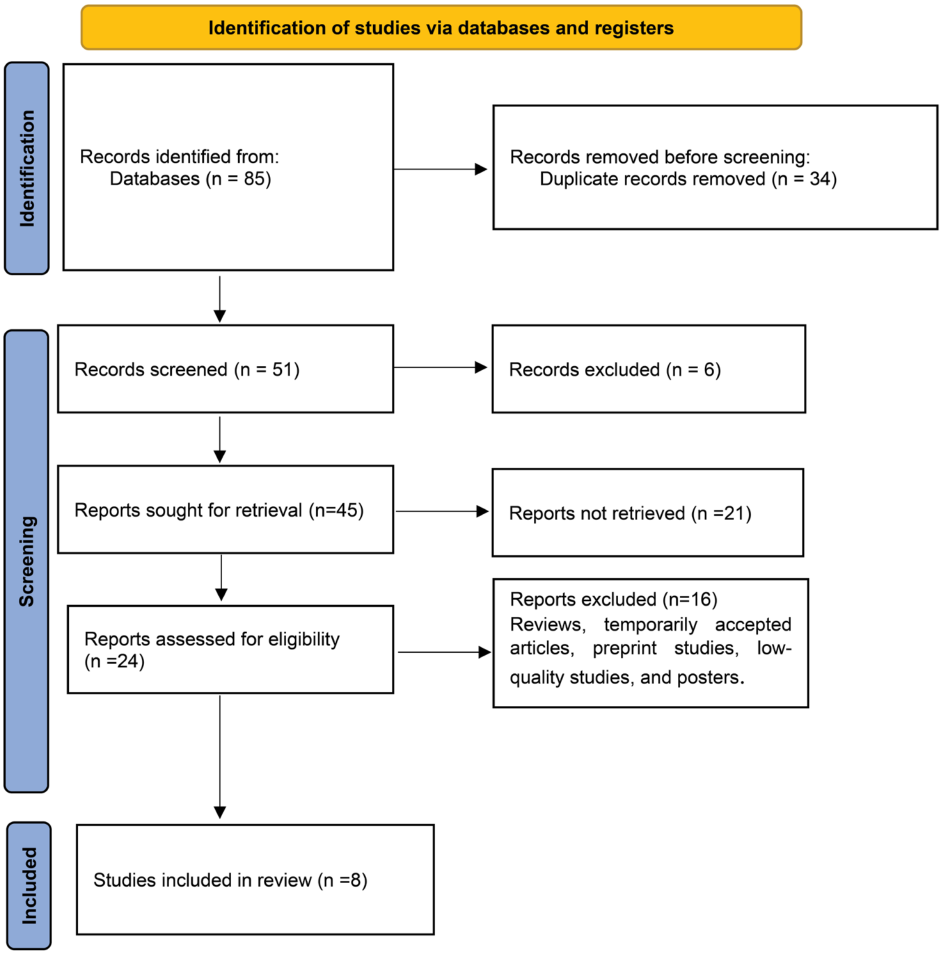

Figure 1. The PRISMA flow chart of study selection.

Table 1. Summarized information of the studies

Author, year	Country	Type of study	Duration of study	Total number	Mean age (total)	Number of women with GDM	Mean age of women with GDM	Number of women without GDM	Mean age of women without GDM	Stage of SII index
Qiu J, 2025 (20)	China	Cohort	2019	15807	31.26	2355	31.38	13452	31.23	Quartile 2 Quartile 3 Quartile 4
Sun Y, 2025 (21)	China	Cohort	between Aug 1, 2022, and Jun 30, 2024	777	29	476	29	301	29	Middle Highest
Li J, 2025 (22)	USA	Cross-sectional	2007–2018	2363	33.53	229	35.24	2134	33.35	Quartile 2 Quartile 3
Wang Y, 2025 (26)	China	Cohort	from 2019 to 2020	1505	≥ 18	337	35.56	1168	33.62	Quartile 2 Quartile 3 Quartile 4
Xie S, 2025 (27)	China	Cohort	from Feb 2018 to Dec 2020	28124	31.8	NR	NR	NR	NR	Quartile 2 Quartile 3 Quartile 4
Xiao Y, 2024 (28)	China	Cohort	from May 2020 to Apr 2022	536	NR	128	NR	408	NR	Total
Xiu X, 2024 (29)	China	Cohort	from Jan 2014 to Jan 2020	3229	31.75	NR	NR	NR	NR	Total
Zhang D, 2024 (23)	China	Cohort	between Mar 2019 and Dec 2022	17297	29.6	3673	30.5	13624	29.3	Quartile 2 Quartile 3 Quartile 4

NR: Not reported; SII: Systemic immune-inflammation index; GDM: Gestational diabetes mellitus.

of GDM. However, there was no statistically significant relationship between the third SII index quartile and the risk of GDM (OR=1.13, 95% CI: 0.98, 1.29).

Subgroup analysis revealed that the relationship between high SII index levels and the risk of GDM in the United States was not significant (OR=0.98, 95% CI: 0.59, 1.62). However, high SII index levels increased the risk of GDM in China (OR=1.60, 95% CI: 1.30, 1.98). Additionally, there was no statistically significant association between high SII index levels and the risk of GDM in the cross-sectional study (OR=0.98, 95% CI: 0.59, 1.62); whereas high SII index levels increased the risk of GDM (OR=1.60, 95% CI: 1.30, 1.98) in cohort studies (Figures 3 and 4).

Figure 5 demonstrated that high SIRI index levels increased the risk of GDM (OR=1.37, 95% CI: 1.17, 1.62). Furthermore, subgroup analysis showed that high SIRI index levels reduced the risk of GDM (OR=0.72, 95% CI: 0.53, 0.99) in the United States, while increasing the risk of GDM in China (OR=1.47, 95% CI: 1.24, 1.74). Additionally, high SII index levels reduced the risk of GDM in the cross-sectional study (OR=0.72, 95% CI: 0.53, 0.99), but increased the risk of GDM in cohort studies (OR=1.47, 95% CI: 1.24, 1.74) (Figures 6 and 7).

Figure 8 indicates that there was no publication bias in the present study ($P = 0.178$), and the resource search step was completed.

Discussion

Our study showed that high SII and SIRI index levels increased the risk of GDM. Furthermore, among Chinese women and in the highest SII quartile, high SII index levels significantly increased the risk of GDM.

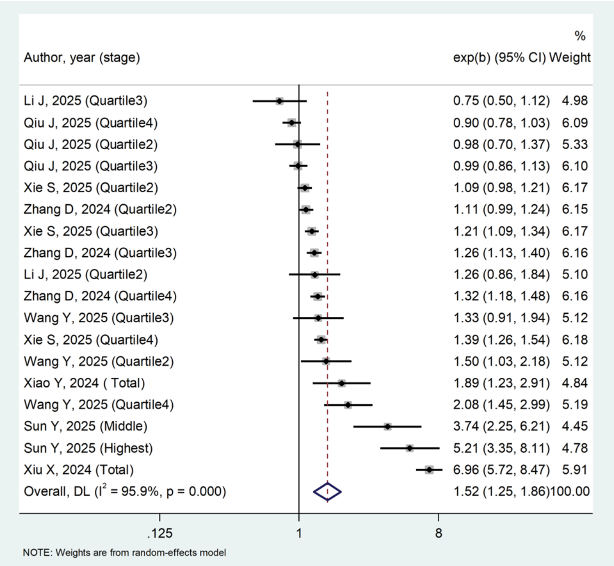

Figure 2. Forest plot showing the association between SII index and GDM.

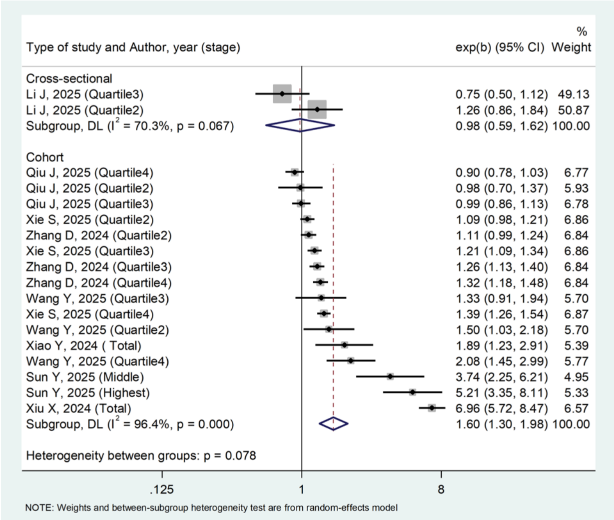

Figure 4. Forest plot showing the association between SII index and GDM by study design.

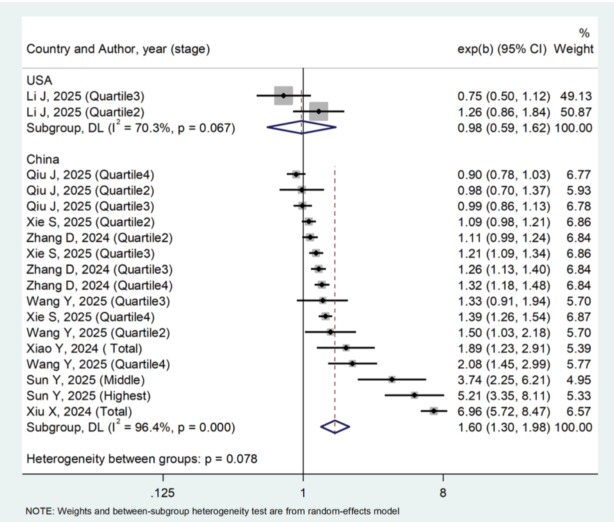

Figure 3. Forest plot showing the association between SII index and GDM by country

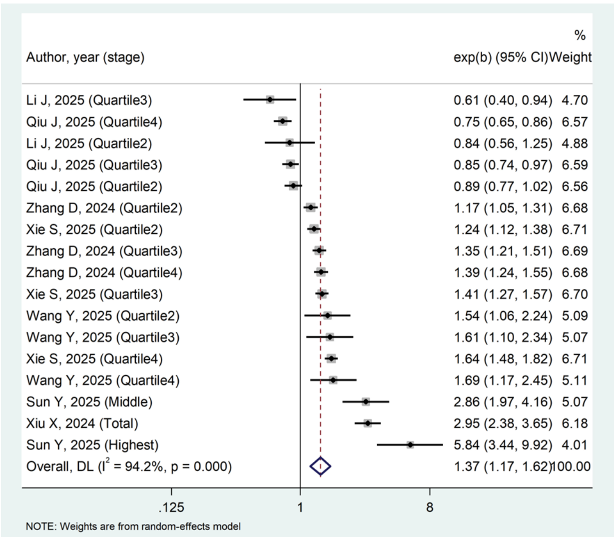

Figure 5. Forest plot showing the association between SIRI index and GDM.

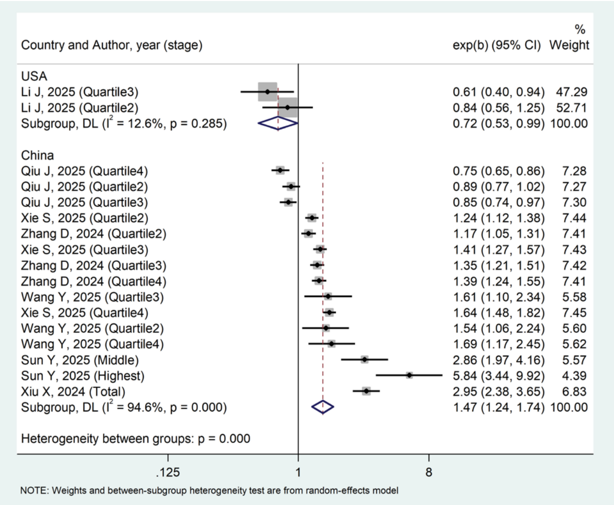

Figure 6. Forest plot showing the association between SIRI index and GDM by country.

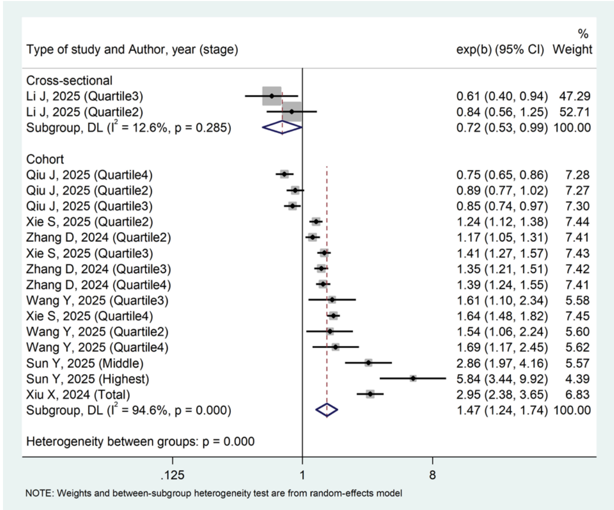

Figure 7. Forest plot showing the association between SIRI index and GDM by study design.

In a prospective cohort study on pregnant women by Wang et al, researchers reported that Ln (SII) (75%) and Ln (SIRI) (55%) increased the risk of GDM (26). Based on the results of a cohort study by Xie et al, higher quartiles of SII and SIRI were associated with increased risk of GDM. As odds ratios for the third and fourth quartiles of SI were 21% and 39%, respectively, while odds ratios of the second, third, and fourth quartiles of SIRI were 24%, 41%, and 64%, respectively (27). Another study by Zhang et al indicated that high levels of SII (2%) and SIRI (14%) were associated with higher GDM risks (23). The mentioned studies were consistent with the present research. These studies believed that high SII and SIRI index levels are suitable predictors for the incidence of gestational diabetes. Hence, pregnant women can be screened at the early stage of pregnancy using these indices.

According to the results of a cross-sectional study by Li et al on women aged between 20 and 44, there was no statistically significant relationship between log2-SII and log2-SIRI and the risk of GDM (22). The findings of these studies were inconsistent with the present study. However, the difference in parameters, including the age and race of the pregnant women, the number of samples, and the study type, may be the cause of the differences in outcomes, which requires additional examination.

In a cross-sectional study by Wang et al on 2566 diabetic patients, results revealed that high SII index levels increased the risk of diabetic depression (34%) (30). In a cohort study by Yan et al, researchers indicated that higher levels of SII increased the incidence risk of diabetes by 31% (31). In a study by Nie et al, findings demonstrated that high SII index levels were positively correlated with the incidence of diabetes (4%) (32). In a prospective study by Elbeyli et al, higher SII levels were a risk factor for the incidence of diabetic macular edema (OR: 1.14, 95% CI: 1.04, 1.25) (33). Findings of a cross-sectional study by Wang et al demonstrated that high SII and SIRI index levels

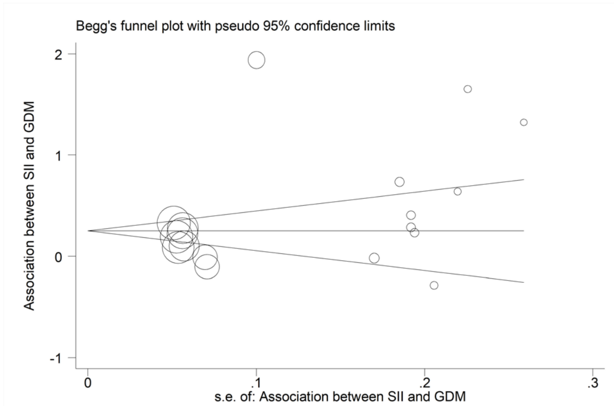

Figure 6. Publication bias plot.

increased the risk of diabetic retinopathy (34). Results of a cross-sectional study by Guo et al revealed that high SII index levels were associated with increased (42%) risk of diabetic kidney disease (35). Findings of a retrospective study by Liu et al on patients with diabetes mellitus type 2 indicated that high SIRI index levels increased the risk of diabetic kidney disease by about 100%, and high SII index levels were associated with increased risk of kidney disease progression in biopsy-confirmed diabetic kidney disease cases (36). These studies showed that high SII and SIRI index levels are risk factors for the occurrence of various diseases, including diabetes, diabetic depression, diabetic macular edema, diabetic retinopathy, and diabetic kidney disease; hence, obviously, they are associated with gestational diabetes, and in this regard, they were consistent with our study.

Conclusion

High SII index (52%) and SIRI index (37%) levels increased the risk of GDM, as the second (11%) and fourth (31%) quartiles of SII increased the risk of GDM. Accordingly, those at risk of GDM can be identified and monitored through conducting evaluations and screening the mentioned indices among pregnant women. Furthermore, high SII index levels in China and cohort studies increased the risk of GDM (60%), as high SIRI index levels in the USA and cross-sectional studies decreased the risk of GDM (28%), while in China and cohort studies, high SIRI index levels increased the risk of GDM (47%). It must be noted that the present study merely included one cross-sectional study, which was conducted in the United States; hence, the analysis results based on the country and study type are similar.

Limitations of the study

The age group of the pregnant women was within a range and could not be separated into several groups. Other than the one study conducted in the United States, others were conducted in China. Except for one cross-sectional study, other studies were cohort studies.

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Authors' contribution

Conceptualization: Sina Salem Ahim and Sadaf Rassouli.
Data curation: Mahsa Rezaee, Ahmadreza Siyasari, and Mahsa Hamidiadl.
Formal analysis: Sadaf Rassouli and Leylinaz Safaeihavadaragh.
Investigation: Zeinab Zamanpour and Moloud Alsadat Mousavi.
Methodology: Samaneh Saghafian Larijani and Leylinaz Safaeihavadaragh.
Project Management: Mahsa Rezaee.
Supervision: Sina Salem Ahim.
Validation: Moloud Alsadat Mousavi and Ahmadreza Siyasari.
Visualization: Samaneh Saghafian Larijani and Zeinab Zamanpour.
Writing–original draft: All authors.
Writing–reviewing and editing: All authors.

Conflicts of interest

There are no competing interests.

Ethical issues

This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO website (ID: CRD420251128749) and the Research Registry website with the (Unique Identifying Number [UIN] of reviewregistry2038). Besides, ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the author.

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