

The Effect of Vitamin D Levels on the Status of Bacterial Vaginosis in Non-Pregnant Women: A Systematic Review

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ABSTRACT

Background & Objective: Bacterial vaginosis (BV) is one of the most frequent vaginal infections and has been linked to unfavorable reproductive outcomes. Vitamin D is known to play a key role in regulating immune function, and its deficiency has been proposed as a potential factor that may increase vulnerability to BV. This systematic review aimed to evaluate the association between vitamin D status and bacterial vaginosis.

Materials & Methods: This systematic review analyzed studies published up to September 2023 using both national and international databases. Relevant keywords, including *bacterial vaginosis*, *vitamin D*, and *25-hydroxyvitamin D*, were used in English and Persian searches. The methodological quality of the included studies was evaluated using the Newcastle–Ottawa Scale and the Jadad checklist.

Results: A total of seven studies met the inclusion criteria. The overall methodological quality ranged from moderate to high. Approximately half of the studies reported a significant association between lower serum vitamin D levels and BV, while the remaining studies did not observe a statistically meaningful relationship.

Conclusion: Current evidence indicates a possible link between vitamin D status and bacterial vaginosis; however, the findings are not consistent across studies. Further well-designed prospective studies and randomized controlled trials are needed to clarify the role of vitamin D in the prevention and management of BV. Future research should also explore the effects of vitamin D on the vaginal microbiome, particularly in asymptomatic women.

Keywords: *Vitamin D; Bacterial Vaginosis; Serum 25-Hydroxyvitamin D; Systematic Review; Non-Pregnant Women; Vaginal Microbiome*



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1. Introduction

Bacterial vaginosis is a common form of vaginal microbial imbalance in reproductive-aged women, characterized by a shift from a *Lactobacillus*-dominant environment toward a diverse anaerobic bacterial community (1). BV accounts for approximately 30% of all causes of vaginal discharge in women of reproductive

age and has been associated with a range of adverse sexual and reproductive health outcomes, including increased susceptibility to sexually transmitted infections and reproductive tract complications (2-4). Beyond local symptoms, BV has been associated with multiple reproductive and obstetric complications, such as

pregnancy loss, adverse birth outcomes, infertility-related conditions, and inflammatory disorders affecting the female reproductive tract (5, 6). Given these potential complications, BV represents a significant public health concern worldwide. The global prevalence of BV varies widely across regions, highlighting the substantial burden of this condition among women of reproductive age (7). Although antimicrobial therapy is recommended for symptomatic BV, treatment outcomes remain suboptimal due to high recurrence rates (8, 9). Nearly half of treated women experience relapse within one year following standard antibiotic therapy, underscoring the persistent and recurrent nature of BV and the limitations of current treatment strategies (10, 11). Evidence suggests that BV does not arise from a single causative factor but rather from the interaction of multiple lifestyle, physiological, and social determinants. Among the factors most frequently implicated are tobacco use, intravaginal hygiene practices, reproductive hormonal changes, sexual exposure patterns, and socioeconomic circumstances. Despite the identification of numerous predisposing factors, the underlying mechanisms contributing to the development and recurrence of BV remain incompletely understood, suggesting that additional host-related factors may play an important role (12, 13). Given the limited effectiveness of current therapeutic approaches and the high recurrence rate of bacterial vaginosis, there is a clear need for the scientific community to explore alternative and adjunctive treatment strategies (9, 12, 14). In particular, micronutrients involved in immune regulation have emerged as potential modifiers of susceptibility to BV. In addition to its established functions in calcium homeostasis, vitamin D has been recognized as an important modulator of immune function. Experimental studies suggest that it may support mucosal defense mechanisms by influencing antimicrobial peptide production and maintaining immune balance through the regulation of inflammatory mediators such as IL-1 β (15). Because suboptimal vitamin D status is frequently observed among women in reproductive age groups, growing attention has been directed toward its possible role in vaginal health. The biological functions of vitamin D suggest that deficiency could affect host defense mechanisms and thereby influence the development of BV. However, the nature and magnitude of this association remain uncertain and require further clarification (16). Research exploring the potential association between vitamin D status and BV has generated inconsistent evidence across different populations and study settings. While some investigations have suggested that reduced circulating vitamin D concentrations may be linked to an increased risk of BV development or recurrence (17, 18), other studies have reported no statistically significant association between vitamin D levels and BV outcomes (19, 20). These discrepancies may be attributable to differences in study design, population characteristics, vitamin D assessment methods, and adjustment for confounding factors. These inconsistencies in findings may be attributed to differences in study design, population characteristics, methods used to assess vitamin D status, diagnostic

criteria for BV, and the extent to which confounding factors were controlled. In addition, stronger associations have been reported in certain populations, such as pregnant women and specific ethnic groups, warranting more comprehensive investigation (16). Given that vitamin D deficiency is a potentially modifiable and relatively low-cost factor, clarifying its role in preventing or reducing BV recurrence may have important clinical and public health implications. Accordingly, this systematic review aims to comprehensively evaluate and synthesize the existing evidence regarding the relationship between vitamin D status and both the occurrence and recurrence of BV in women.

2. Materials and Methods

2.1 Study Design and Registration

The present systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting standards (21). Nevertheless, the protocol was not prospectively recorded in the International Prospective Register of Systematic Reviews (PROSPERO), mainly due to administrative constraints and limited time at the beginning of the study. This lack of prior registration is considered a limitation of the current review.

2.2 Research Question and Eligibility Criteria (PICO Framework)

To guide the study, the Population, Intervention/Exposure, Comparison, and Outcome (PICO) framework was used to formulate the research question:

- Population (P): Non-pregnant women of reproductive age
- Intervention/Exposure (I): Serum vitamin D status or vitamin D supplementation
- Comparison (C): Normal vitamin D levels or placebo/no supplementation
- Outcome (O): Presence, recurrence, or improvement of bacterial vaginosis

Accordingly, this review aimed to investigate whether vitamin D status is associated with the occurrence or clinical outcomes of bacterial vaginosis in non-pregnant women.

2.3 Search Strategy

An extensive search strategy was implemented across multiple international databases, including PubMed, Scopus, Web of Science, Embase, and Google Scholar. Furthermore, supplementary searches were carried out in national information sources such as Magiran, the Scientific Information Database (SID), and IranDoc to ensure comprehensive coverage of relevant literature. All relevant studies published up to September 2023 were considered, with no restrictions on language, publication date, or geographical location. The search strategy incorporated both Medical Subject Headings (MeSH) terms and related keywords: (“Vitamin D” OR “25-hydroxyvitamin D” OR “Ergocalciferol” OR “Cholecalciferol”) AND (“Bacterial Vaginosis” OR “Vaginosis, Bacterial”) Equivalent Persian keywords

were searched using appropriate Boolean operators (AND/OR).

2.4 Identification of Studies

The initial literature search yielded 3,410 records from electronic and national databases, including PubMed (850 records), Scopus (740 records), Web of Science (620 records), Embase (520 records), Google Scholar (410 records), and the Iranian databases Magiran, SID, and IranDoc (270 records). In addition, 30 records were identified through manual screening of the reference lists of the included studies and searches of gray literature sources. All retrieved records were subsequently screened for eligibility according to the predefined inclusion and exclusion criteria.

2.5 Study Selection Process

The processes of screening, eligibility assessment, and study inclusion were performed following the PRISMA framework (21). All retrieved citations were managed using EndNote software, where duplicate entries were identified and eliminated. After removing duplicates, 1,980 unique records were retained for the initial screening of titles and abstracts. The screening process was performed independently by two reviewers. Following the initial evaluation of titles and abstracts, 1,830 records were excluded because they were not relevant to the review topic or did not satisfy the eligibility requirements. Consequently, 150 articles were considered potentially eligible and were retrieved for full-text review. A detailed assessment of the full texts resulted in the exclusion of 143 studies. The primary reasons for exclusion included inappropriate study populations, absence of outcomes relevant to the review question, inadequate methodological rigor, and insufficient reporting of data. Ultimately, seven studies fulfilled all predefined eligibility criteria and were included in the systematic review. Any discrepancies arising during the selection process were addressed through discussion between the reviewers until agreement was reached.

2.6 Inclusion and Exclusion Criteria

2.6.1 Inclusion Criteria

Studies were eligible for inclusion if they met the following criteria: 1. they were published in English or Persian; 2. they were conducted among non-pregnant women; 3. they employed observational or interventional study designs; 4. they assessed serum vitamin D levels or vitamin D supplementation; and 5. bacterial vaginosis was diagnosed using standard diagnostic criteria (8, 9).

2.6.2 Exclusion Criteria

Studies were excluded if they lacked accessible full-text versions, were review articles, editorials, or case reports, were considered to be of low methodological quality based on the predefined quality assessment tools, or were not directly relevant to the research question.

2.6.3 Data Extraction and Management

Data were extracted using a standardized data collection form by two reviewers independently. The extracted information included the first author and year of publication, country of origin, study design, sample size and participant characteristics, diagnostic criteria for bacterial vaginosis, methods used to assess vitamin D status, characteristics of the intervention (where applicable), statistical methods, and the main outcomes and conclusions. The extracted data were independently cross-checked by the reviewers, and any discrepancies were resolved through discussion and consensus.

2.6.3 Quality assessment of studies

The methodological rigor and potential risk of bias of the included studies were evaluated independently by two reviewers. The quality of observational studies was assessed using the Newcastle–Ottawa Scale (NOS) (22), while randomized controlled trials were assessed using the Jadad scale (23).

The Newcastle–Ottawa Scale (NOS) assigns a maximum of nine stars and is structured across three domains, including selection (maximum of four stars), comparability (maximum of two stars), and outcome assessment (maximum of three stars). Based on the total score, studies were categorized as high quality (8–9 stars), moderate quality (5–7 stars), or low quality (0–4 stars) (22).

The Jadad scale (also known as the Oxford Quality Scoring System), developed by Jadad *et al.* (1996), evaluates randomization, blinding, and withdrawals, with scores ranging from 0 to 5; studies scoring ≥ 3 were considered to have appropriate methodological quality and were included in the review (23).

2.7 Data Synthesis and Rationale for Not Performing Meta-analysis

Substantial variability was identified across the included studies with respect to study design, participant characteristics, approaches used to evaluate vitamin D status, intervention protocols, outcome measures, and diagnostic criteria.

Because of this heterogeneity, quantitative synthesis was not appropriate. Therefore, a meta-analysis was not conducted, and a narrative synthesis approach was adopted.

3. Result

3.1 Study Selection

A total of 3,410 records were retrieved from database searches.

After removing duplicates and screening titles, abstracts, and full texts, seven studies met the eligibility criteria and were included in the final analysis. The study selection procedure is illustrated in [Figure 1](#).

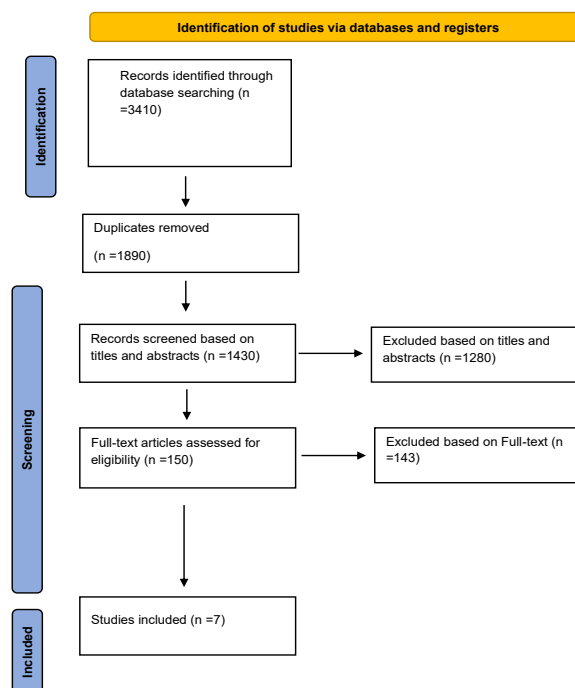


Figure 1. PRISMA 2020 Flow Diagram Illustrating Study Selection Process. (Prepared by Authors, 2026).

3.2 Study Characteristics

The studies included in this review were published between 2013 and 2023 and collectively enrolled 2,712 participants. Among them, three were randomized controlled trials (17, 18, 20), two were prospective cohort studies (19, 24), and two had a case-control design (25, 26).

Most studies were conducted among non-pregnant women of reproductive age. The methodological quality assessment showed that most studies were of high quality, with only one observational study rated as moderate quality and one randomized controlled trial classified as low quality. (Table 1 and Table 2).

Table 1. Methodological Quality Assessment of Observational Studies Using the Newcastle–Ottawa Scale (NOS).

Author (Year)	Selection (0–4)	Comparability (0–2)	Outcome/Exposure (0–3)	Total Score (0–9)	Quality Level
Moore et al. (2018) (19)	3	2	3	8	High
Turner et al. (2016) (24)	4	2	3	9	High
Rakhmatullaeva et al. (2022) (26)	3	2	2	7	Moderate
Mojtahedi et al. (2023) (25)	4	2	3	9	High

Note: Selection domain includes representativeness, selection of non-exposed cohort, ascertainment of exposure, and outcome absence at baseline. Comparability assesses control for confounders. Outcome/Exposure domain includes outcome assessment, follow-up adequacy, and follow-up duration.

Table 2. Quality Assessment of Randomized Controlled Trials Using the Jadad Scale.

Author (Year)	Randomization (0–2)	Blinding (0–2)	Withdrawals/Dropouts (0–1)	Total Score (0–5)	Quality Level
Turner et al. (2014) (20)	2	1	1	5	High
Taheri et al. (2015) (18)	1	2	1	4	High
Nikvarz et al. (2023) (17)	1	0	1	2	low

Note: Studies scoring ≥ 3 was considered to have acceptable methodological quality.

3.3 Findings from Randomized Controlled Trials

Three randomized controlled trials examined the impact of vitamin D supplementation on BV outcomes. In the study by Turner et al. (2014), a significant rise in serum

vitamin D levels was observed in the intervention group; however, no statistically significant reduction in BV recurrence was detected during the follow-up period (20). Taheri et al. (2015) found that daily supplementation with

2,000 IU vitamin D for 15 weeks significantly improved recovery rates in women with asymptomatic BV compared with placebo ($p<0.001$) (18).

Nikvarz *et al.* (2023) demonstrated that combined treatment with metronidazole and high-dose vitamin D resulted in significantly better clinical and laboratory outcomes than metronidazole alone (17). Overall, evidence from high-quality clinical trials was inconsistent, with two trials suggesting beneficial effects and one showing no significant benefit.

3.4 Findings from Cohort Studies

Two prospective cohort studies examined the relationship between serum vitamin D levels and the incidence of BV. Moore *et al.* (2018) observed a high rate of vitamin D deficiency among African American women; however, this deficiency was not linked to an increased risk of BV (19). Similarly, Turner *et al.* (2016) found no significant association between adequate vitamin D levels (>30 ng/mL) and BV prevalence among non-pregnant women (24), while a separate study reported associations in pregnant women at follow-up (27). These results indicate that vitamin D status may exert a limited effect on the occurrence of BV in non-pregnant populations.

3.5 Findings from Case-Control Studies

Two case-control studies compared vitamin D status between women diagnosed with BV and those without the condition. Rakhmatullaeva *et al.* (2022) found that women with moderate-to-severe BV had a higher prevalence of vitamin D deficiency compared with healthy controls (26). Mojtabehi *et al.* (2023) also found significantly lower serum 25-hydroxyvitamin D levels in women with BV and identified vitamin D deficiency as an

independent risk factor after adjustment for confounders (25).

These studies, both of moderate to high quality, consistently supported an association between low vitamin D levels and increased BV risk.

3.6 Heterogeneity of Included Studies

Considerable variability was identified across the included studies with respect to study design, participant characteristics, geographic setting, diagnostic criteria, vitamin D assessment methods, and intervention protocols. Differences were noted in BV diagnostic tools (Amsel criteria, Nugent scoring, self-report), vitamin D dosing regimens, follow-up duration, and baseline vitamin D status. These methodological variations limited direct comparability and precluded quantitative meta-analysis.

3.7 Overall Synthesis of Findings

A significant association between low serum vitamin D concentrations and BV was reported in four of the seven included studies (17, 18, 25, 26), whereas three found no significant relationship (19, 20, 24).

Positive associations were more consistently observed in case-control studies and some clinical trials, while cohort studies generally reported null findings. Taken together, evidence from higher-quality randomized and observational studies remains mixed. Most findings were derived from non-pregnant women, indicating that vitamin D may play a role in BV susceptibility in this population, although results are not uniform. Studies involving pregnant women were limited and mainly served as comparative evidence. Individual study outcomes are summarized in Table 3.

Table 3. Characteristics and Main Findings of the Included Studies.

Author (Year)	Study Design	Study Group (n)	Intervention / Exposure	Assessment Tool	Main Outcomes	p-value	Conclusion
Turner <i>et al.</i> , 2014 (20)	Randomized controlled trial	Women with symptomatic BV (n=118)	Intervention: Metronidazole + vitamin D (50,000 IU, 9 doses/24 weeks) Control: Metronidazole + placebo	Amsel criteria, Nugent score	No significant effect of vitamin D supplementation on BV recurrence (HR=1.11, 95% CI: 0.68–1.81); 24-week BV prevalence was 65% vs. 48% in the vitamin D and placebo groups.	>0.05	Vitamin D supplementation did not reduce BV recurrence
Taheri <i>et al.</i> , 2015 (18)	Randomized controlled trial	Women with asymptomatic BV (n=208)	Intervention: Vitamin D 2000 IU/day (15 weeks) Control: Placebo	Nugent score	Recovery rate: 63.5% vs 19.2%	<0.001	Vitamin D improved asymptomatic BV
Moore <i>et al.</i> , 2018 (19)	Prospective cohort	Non-pregnant African-American women (n=1459)	Serum vitamin D levels (observational)	Self-report questionnaire	75% vitamin D deficient; no association with BV incidence	>0.05	Vitamin D deficiency was not a risk factor
Turner <i>et al.</i> , 2016 (24)	Prospective cohort	Non-pregnant women (n=571)	Serum vitamin D levels	Amsel criteria, Nugent score	Mean vitamin D: BV group 29.7 vs control 20.9 ng/mL	>0.05	No association with BV prevalence
Rakhmatullaeva <i>et al.</i> , 2022 (26)	Case-control	BV group (n=36) Control (n=30)	Serum vitamin D levels	Microscopy, Femoflor-16	Vitamin D deficiency in 50% of moderate BV vs 20% controls	<0.05	Low vitamin D associated with dysbiosis
Mojtabehi <i>et al.</i> , 2023 (25)	Case-control	BV group (n=125) Control (n=125)	Serum 25(OH)D levels	Amsel criteria	Lower vitamin D in BV group	<0.001	Low vitamin D increased BV risk
Nikvarz <i>et al.</i> , 2023 (17)	Randomized controlled trial	Women with BV (n=40)	Intervention: Metronidazole + vitamin D 50,000 IU Control: Metronidazole	Amsel criteria	Significant improvement in intervention group	<0.05	Vitamin D improved treatment response

Note: BV: Bacterial vaginosis. Values are reported according to original studies. p-values indicate statistical significance of comparisons between study groups. When exact p-values were not reported, significance was extracted from authors' conclusions.

4. Discussion

Among women of reproductive age, BV represents one of the most prevalent vaginal infections (28, 29). Despite available antimicrobial therapies, recurrence rates remain high, and treatment outcomes are often suboptimal, partly due to microbial diversity and increasing antibiotic resistance (5).

The present systematic review investigated the relationship between serum vitamin D concentrations and BV in non-pregnant women. Of the seven included studies, four reported a significant association, whereas three did not, indicating inconsistent evidence.

4.1 Evidence from Clinical Trials

Among the randomized controlled trials, findings were mixed. Turner et al. (2014) reported no significant reduction in BV recurrence following high-dose vitamin D supplementation combined with metronidazole therapy (20). Despite the observed increase in serum vitamin D concentrations among participants receiving the intervention, many participants remained below optimal thresholds, and potential confounding factors, such as differences in sexual behavior, may have influenced outcomes. In addition, partial application of the Amsel criteria may have limited diagnostic accuracy. These methodological limitations reduce confidence in the null findings.

In contrast, Taheri et al. (2015) demonstrated that moderate-dose vitamin D supplementation significantly improved recovery in women with asymptomatic BV (18). Similarly, Nikvarz et al. (2023) reported improved clinical and laboratory outcomes following combined antibiotic and vitamin D therapy (17). These trials suggest a potential therapeutic role for vitamin D; however, differences in dosage, duration, baseline vitamin D status, and outcome assessment limit direct comparability. Overall, although two high-quality trials showed beneficial effects, the evidence remains insufficient to draw firm conclusions.

4.2 Evidence from Observational Studies in Non-Pregnant Women

Results from the cohort studies consistently indicated the absence of a clear relationship between vitamin D status and BV. Moore et al. (2018) found no increased risk of BV among vitamin D-deficient women, despite a high prevalence of deficiency (19). Similarly, Turner et al. (2016) reported no association between adequate vitamin D levels and BV prevalence in non-pregnant women (24). Both studies were of high methodological quality but relied partly on self-reported data or included populations with limited variation in severe deficiency, which may have reduced their ability to detect associations.

In contrast, case-control studies by Mojtahedi et al. and (2023) Rakhmatullaeva et al. (2022) consistently showed lower serum vitamin D levels among women with BV (25, 26). These studies benefited from objective diagnostic methods and laboratory measurements; however, their observational nature restricts the ability to establish causality and leaves the findings vulnerable to residual confounding.

4.3 Biological Plausibility

Vitamin D receptors are expressed in reproductive tissues and regulate immune responses and antimicrobial peptide production. Vitamin D may influence oxidative stress and inflammatory pathways associated with BV (30, 31). These mechanisms provide biological plausibility for a protective role of vitamin D. Nevertheless, clinical evidence remains inconsistent, suggesting that vitamin D may act as a modifying factor rather than a primary determinant of BV.

4.4 Influence of Behavioral and Lifestyle Factors

Mojtahedi et al. (2023) identified smoking, hookah use, and early sexual debut as significant risk factors for BV (25).

These findings are consistent with previous research and highlight the importance of behavioral determinants. Semen exposure, contraceptive practices, and hygiene behaviors may also affect vaginal microbiota composition. These factors may influence the observed relationship between vitamin D status and BV and should therefore be adequately accounted for in future research.

4.5 Heterogeneity and Limitations

Considerable heterogeneity was observed across studies regarding design, population characteristics, diagnostic criteria, vitamin D assessment methods, supplementation protocols, and follow-up duration. These variations limited comparability and precluded meta-analysis. Additional limitations include small sample sizes in some trials, reliance on self-reported outcomes, incomplete adjustment for confounders, and geographic and socioeconomic differences among populations.

Furthermore, most studies assessed short-term outcomes, and long-term effects of vitamin D supplementation on BV recurrence remain unclear. Selection bias may also have influenced findings, as several studies recruited participants from healthcare facilities. Additionally, publication venue quality and indexing status varied across the included studies, which should be considered when interpreting the findings.

4.6 Implications and Future Research Directions

Given the inconsistent findings and methodological limitations, a definitive conclusion regarding the role of vitamin D in BV prevention and treatment cannot currently be made. Evidence from randomized trials suggests possible benefits in selected populations, whereas cohort studies largely report null associations. Overall, the strength of evidence remains moderate to low.

Further research should emphasize rigorously designed, large-scale randomized trials incorporating standardized diagnostic approaches, adequate follow-up periods, and careful control of behavioral and environmental confounders. Studies should also investigate dose-response relationships, optimal supplementation regimens, and interactions between vitamin D status and vaginal microbiome composition. Special attention should be given to asymptomatic BV and longitudinal changes in microbiota.

5. Conclusion

The findings of this systematic review suggest a possible relationship between vitamin D status and bacterial vaginosis; however, the available evidence remains limited and inconsistent. While some studies indicate a potential protective role of adequate vitamin D levels, others report no significant relationship. Differences in study design, population characteristics, and diagnostic methods may partly explain these inconsistencies. The role of vitamin D in both the prevention and management of bacterial vaginosis remains unclear, highlighting the need for further rigorous prospective studies and randomized controlled trials.

6. Declarations

6.1 Acknowledgments

Not applicable

6.2 Conflict of Interest

The authors declare that they have no conflict of interest.

6.3 Financial Support

This study received no specific financial support or funding.

6.4 Ethical Considerations

As this study is a systematic review of previously published studies and does not involve the collection of new data from human participants, ethical approval was not required.

6.5 Author Contributions

Conceptualization: AT, AS; Investigation: AT, SY, MA, TJ, AS; Writing-original draft: AT, SY, MA; Writing-review and editing: TJ, AS

6.6 Using Artificial Intelligence Tools (AI Tools)

The authors declare the use of artificial intelligence-assisted technologies for text editing during the preparation of this manuscript. The authors take full responsibility as to the accuracy of the content.

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