REVIEW ARTICLE

Evaluation of the effects of probiotic supplementation on the ecology and inflammatory factors of female vaginal flora: a systematic review and meta-analysis

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Abstract

This meta-analysis systematically evaluated the effects of probiotic supplementation on vaginal microbiota and inflammatory factors in women. PubMed, Embase, Web of Science, CNKI, and Wanfang were searched from inception to January 2026 for randomized and controlled studies. Outcomes included vaginal pH, Nugent score, and inflammatory cytokines (IL-4, IL-6, IL-10, TNF-α). Fifteen studies were included. Compared with controls, probiotics did not significantly reduce IL-4, IL-6, IL-10, or TNF-α levels, nor did they significantly improve Nugent score. However, probiotic supplementation significantly reduced vaginal pH (OR = 0.36, 95% CI: 0.15–0.89; P = 0.03), indicating improved maintenance of a weakly acidic vaginal environment. Sensitivity analyses showed generally stable results, although heterogeneity remained substantial for several outcomes. Overall, probiotics appear effective in modulating vaginal acid–base balance but show limited evidence for improving inflammatory cytokine profiles or restoring vaginal microbiota structure. Current data are insufficient to support routine probiotic use for optimizing vaginal microbiota and inflammatory status. Further high-quality, well-designed randomized controlled trials are required to clarify their clinical benefits. *(Afr J Reprod Health 2026; 30 [9]: 124-136).*

Keywords: Probiotics; Vaginal microbiota; Inflammatory factors; Meta-analysis

Résumé

Cette méta-analyse a évalué de manière systématique les effets de la supplémentation en probiotiques sur le microbiote vaginal et les facteurs inflammatoires chez les femmes. Les bases de données PubMed, Embase, Web of Science, CNKI et Wanfang ont été consultées depuis leur création jusqu'en janvier 2026 afin d'identifier des études randomisées et contrôlées. Les critères de jugement comprenaient le pH vaginal, le score de Nugent et les cytokines inflammatoires (IL-4, IL-6, IL-10, TNF-α). Quinze études ont été incluses. Comparativement aux groupes témoins, les probiotiques n'ont pas réduit significativement les concentrations d'IL-4, IL-6, IL-10 ou TNF-α, ni amélioré significativement le score de Nugent. En revanche, la supplémentation en probiotiques a significativement réduit le pH vaginal (OR = 0,36 ; IC à 95 % : 0,15–0,89 ; P = 0,03), indiquant un meilleur maintien d'un environnement vaginal faiblement acide. Les analyses de sensibilité ont montré des résultats globalement stables, bien qu'une hétérogénéité substantielle persiste pour plusieurs critères. Dans l'ensemble, les probiotiques semblent efficaces pour moduler l'équilibre acido-basique vaginal, mais les preuves restent limitées quant à leur capacité à améliorer les profils cytokiniques inflammatoires ou à restaurer la structure du microbiote vaginal. Les données actuelles sont insuffisantes pour recommander l'utilisation systématique des probiotiques dans l'optimisation du microbiote vaginal et du statut inflammatoire. Des essais contrôlés randomisés de haute qualité sont nécessaires pour confirmer leurs bénéfices cliniques.. *(Afr J Reprod Health 2026; 30 [9]: 124-136).*

Mots-clés: Probiotiques; Microbiote vaginal; Facteurs inflammatoires; Méta-analyse

Introduction

The vaginal microecosystem is maintained through interactions among the vaginal microbiota, local immunity, endocrine activity, and vaginal anatomical structure. In healthy women, this system is generally dominated by protective lactobacilli, which helps resist pathogenic invasion and restrain excessive inflammatory activation. Disruption of this balance has been associated with conditions such as bacterial vaginosis, increased susceptibility to human immunodeficiency virus infection, and pelvic inflammatory disease.[1] Although antibiotics are effective against pathogenic microorganisms, they may also disrupt beneficial vaginal flora and thereby increase the risk of recurrent dysbiosis.[2] By contrast, probiotics may help restore vaginal homeostasis by competing with pathogens for ecological niches, modulating local immune responses, and supporting mucosal barrier function.[3] Accordingly, probiotic supplementation has gradually been explored as an alternative or adjunctive strategy for preserving vaginal health. However, clinical studies have reported inconsistent findings: some have shown beneficial effects on the vaginal microenvironment,[4] whereas others have found no meaningful improvement in women with abnormal vaginal flora.[5] In addition, few evidence syntheses have simultaneously evaluated vaginal microecological outcomes and inflammatory markers. Therefore, the present meta-analysis systematically assessed the effects of probiotic supplementation on vaginal pH, Nugent score, and inflammatory factors (IL-4, IL-6, IL-10, and TNF-α) in women, with the aim of providing evidence for the rational clinical use of probiotics in vaginal health management.

Methods

Literature retrieval strategy

Databases including China National Knowledge Infrastructure (CNKI), Chinese Biology Medicine (CBM), Wanfang, PubMed, Embase, The Cochrane Library, and Web of Science were searched from database inception to January 2026. A combination of subject headings and free-text terms was used for literature retrieval .Search terms in English and Chinese included probiotic, vaginal microbiota, vaginal pH, Nugent, IL-4, IL-6, IL-10, TNF-α, and inflammation. The PubMed search strategy was constructed using combinations of these terms as follows: (vaginal microbiota[Title/Abstract]) AND (probiotic[Title/Abstract])AND(IL6[Title/Abstract] OR TNF-α[Title/Abstract] OR IL-10[Title/Abstract]OR inflammation[Title/Abstract] ORIL4[Title/Abstract])AND(Nugent[Title/Abstract] OR vaginal pH[Title/Abstract]).

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) female participants; (2) published randomized controlled trials (RCTs), retrospective controlled studies, or prospective controlled studies; (3) the experimental group received probiotic treatment, while the control group received placebo, no probiotic treatment, or standard care without probiotics; (4) at least one of the following outcomes was reported: vaginal pH, Nugent score, IL-4, IL-6, IL-10, or TNF-α; and (5) full-text articles published in Chinese or English peer-reviewed journals.

Exclusion criteria were as follows: (1) duplicate publications; (2) conference abstracts, reviews, systematic analyses, animal experiments, case reports, and master's theses; (3) studies involving male participants or children; (4) studies from which valid data could not be extracted; (5) studies with poor methodological quality or incomplete data; (6) non-Chinese and non-English literature; and (7) studies with an unclear treatment course.

Literature screening and data extraction

Two reviewers independently screened the literature and extracted data, with cross-checking performed afterwards. Any disagreements were resolved by consulting a third reviewer. Every effort was made to contact the original authors for clarification or supplementation of missing data. The following data were extracted: first author name, year of publication, sample size, age, patient type, intervention method, intervention duration, study design, and outcome measures.

Quality assessment

Two reviewers independently assessed the risk of bias of the included controlled studies using the risk of bias tool recommended by the Cochrane Handbook for Systematic Reviews of Interventions. Additionally, the methodological quality of prospective or retrospective controlled studies was evaluated with the Newcastle-Ottawa Scale (NOS), which encompasses three dimensions: patient selection, comparability of study groups, and outcome assessment. Each study was scored on a scale of 0 to 9, with a score of ≥7 indicating high quality, 5–6 indicating moderate quality, and ≤4 indicating low quality.

Statistical methods

Meta-analysis was performed using RevMan 5.3 and Stata MP software. For continuous data, the mean difference (MD) or standardized mean difference (SMD) with corresponding 95% confidence intervals (CI) was used. Heterogeneity was evaluated using the χ^2 test combined with the I^2 statistic. If $I^2 \leq 50\%$ and $P \geq 0.10$, no significant statistical heterogeneity was observed among studies, and a fixed-effect model was applied. Otherwise, a random-effect model was adopted, and sensitivity analysis was performed using the stepwise elimination method to assess the influence of individual studies on the overall results and verify the robustness of the meta-analysis. The test level was set at $\alpha = 0.05$.
Note: For studies without numerical data but with available figures, data were extracted using WebPlotDigitizer. SMD was used for continuous data with inconsistent units

Results

Literature search and screening

A total of 1238 articles were initially retrieved. After screening according to the predefined inclusion and exclusion criteria, 15 studies were finally included in this meta-analysis. The flow chart of study selection is presented in Figure 1.

Basic characteristics of included studies

A total of 15 studies were finally included in this meta-analysis. The basic characteristics of the included studies are summarized in Table 1.

Quality assessment

A total of 13 randomized controlled trials (RCTs) were included in this study. The risk-of-bias assessment based on the Cochrane Risk of Bias tool is presented in Figures 2 and 3. In addition, 1 prospective controlled study and 1 retrospective controlled study were included. Methodological quality evaluation using the Newcastle-Ottawa Scale (NOS) indicated that both non-randomized studies were of high quality (score = 7).

Meta-analysis

IL-4

IL-4 was reported in 3 studies, with a total of 206 patients (105 in the probiotic group and 101 in the non-probiotic group). Significant heterogeneity was detected across studies ($I^2 = 83\%$, $P = 0.002$); thus, a random-effects model was adopted for meta-analysis. The results showed that, compared with the non-probiotic group, probiotic administration did not significantly reduce IL-4 levels (SMD = -0.04, 95% CI: -0.73 to 0.65; P = 0.91; Figure 4).

Sensitivity analysis revealed that, after exclusion of the study by Zhao and Bai (2025)[19], the pooled effect size of the remaining 2 studies changed from negative to positive but remained statistically non-significant (P = 0.34; Figure 5). This reversal suggests that study-level clinical heterogeneity may be an important source of inconsistency. Specifically, Zhao and Bai enrolled postpartum women with mycotic vaginitis,[19] whereas Ang et al. studied pregnant women with vaginal candidiasis[6] and Yang et al. included low-risk pregnant women with abnormal Nugent scores.[7] Moreover, the Zhao study used clotrimazole vaginal expansion suppositories combined with live lactobacillus capsules,[19] which differs mechanistically from the mainly oral probiotic regimens used in the other studies. These differences in patient population and co-intervention may explain the discordant direction of effect.

IL-6

IL-6 was reported in 3 studies, enrolling a total of 253 patients (126 in the probiotic group and 127 in the non-probiotic group). Significant heterogeneity was observed across studies ($I^2 = 95\%$, $P < 0.001$); therefore, a random-effects model was used for meta-analysis. The results demonstrated that probiotic treatment did not significantly reduce IL-6 levels compared with no probiotic treatment (SMD = -1.00, 95% CI: -2.30 to 0.29; P = 0.13; Figure 6). Sensitivity analysis indicated that the overall result was robust (Figure 7).

Table 1: Characteristics of patients included in the study

Reference	Study design	therapeutic time	patient types	non-Probiotic group			Probiotic group			Indicator
				n	age	Intervention	n	ane	Intervention	
ANG X Y 2022[6]	RCT	8 weeks	vaginal candidiasis	25	28.20±1.04	indistinguishable placebo tablet (containing maltodextrin carrier only)	31	29.16±0.74	probiotic tablets (9.5 log CFU/capsule of total lactobacilli)	IL-4, IL-10, TNF-α
YANG S 2020[7]	RCT	12weeks	asymptomatic pregnant women who had an Intermediate or Bacterial Vaginosis Nugent score at 13 weeks	34	34.4±3.3	Placebo	32	33.8±4.2	GR-1 and RC-14	IL-4, IL-6 IL-10, TNF-α
VACCALLUZZO A2024[8]	RCT	10 days	signs and symptoms of vaginal dysbiosis	20	33.2±7.02	did not receive any treatment	60	34.7±6.96	1 capsule of the probiotic strain	Nugent score , pH
SGIBNEV A2020[9]	RCT	14 days	Trichomonas vaginalis (TV) in the presence BV	42	23.6±2.1	in addition to metronidazole received a placebo instead of a probiotic.	44	25.3±2.4	gimens for therapy combination with metronidazole and vaginal probiotics. For 7 days, the probiotics group patients received metronidazole at 500 mg twice a day and 1 capsule of probiotic GynopHilus® vaginally twice a day	Nugent score , pH
VITALI B2012[10]	Prospective controlled design	4weeks	healthy women during late pregnancy	12	21-42	Probiotics free	15	21-42	the oral intake of the probiotic VSL#3	IL-10
GILLE C 2016[11]	RCT	8weeks	women with <12 completed weeks of pregnancy	160	33（24-44）	Placebo	160	33（21-45）	Oral Lactobacillus rhamnosus GR-1and L reuteri RC-14 (109 colony-forming units)	Nugent score
BUI H T2025[12]	RCT	7 days	Bacterial vaginosis	48	36.98±10.23	NaCl 0.9% + standard care treatment	48	37.67±9.72	LiveSpo X-SECRET + standard care treatment	pH
VAN DE WIJGERT J2020[13]	RCT	2 months	HIV-negative, non-pregnant Rwandan BV patients	17	29(24-36)	behavioral counseling only	17	30(27-35)	GynopHilus LP vaginal tablet	Nugent score

HEMALATHA R2012[14]	RCT	8 days	Non-HIV, non-pregnant, sexually active women, living with husband, aged 20–40 years	73	20-40	pH lowering vaginal tablet	75	20-40	probiotic vaginal tablet "Florisia™" (lactobacilli tablet)	Nugent score , pH
PARK S H2023[15]	RCT	12weeks	women with a Nugent score of 4–6	37	37.03±7.15	Placebo	39	39.56±6.58	MED-01 (5.0 × 109 CFU)	Nugent score
YA W 2010[16]	RCT	7 days on, 7 days off, and 7 days on	healthy Chinese women with a history of recurrent BV	62	37.2±10.9	1 placebo capsule	58	37.4±10.6	vaginal propHy-laxis with 1 capsule	pH
ZHANG Y2021[17]	RCT	30 days	with abnormal vaginal discharge symptoms and Nugent point≥7	56	33.3±7.5	metronidazole vaginal suppositories	52	34.2±7.0	orally administered probiotic drinks containing L. rhamnosus GR-1 and L. reuteri RC-14 (≥1 × 109 CFU per day, for 30 days) and vaginally administered metronidazole suppositories (0.2 g per day, for 7 days)	Nugent score , pH
DE SETA F 2014[18]	Retrospective Comparative Study	4weeks	vulvovaginal candidiasis	40	18-45	2% clotrimazole vaginal cream+vaginal application of a capsule containing lubricant	40	18-45	2% clotrimazole vaginal cream+vaginal application of a capsule containing Lactobacillus plantarum P17630	pH
ZHAO J Y2025[19]	RCT	7 days	Postpartum mycotic vaginitis	43	30.25±3.41	clotrizole vaginal expansion suppository	43	29.84±3.16	clotrizole vaginal expansion suppository+live lactobacillus capsule for vaginal use	pH, IL-4, IL-6, TNF-α
WANG J 2022[20]	RCT	-	Pregnant women with vaginal group B streptococcus (GBS) infection in late pregnancy.	51	32.02±6.23	Intravenous infusion of antibiotics 4 hours before delivery	52	31.98±6.09	Oral probiotics until delivery+Intravenous infusion of antibiotics 4 hours before delivery	IL-6, TNF-α

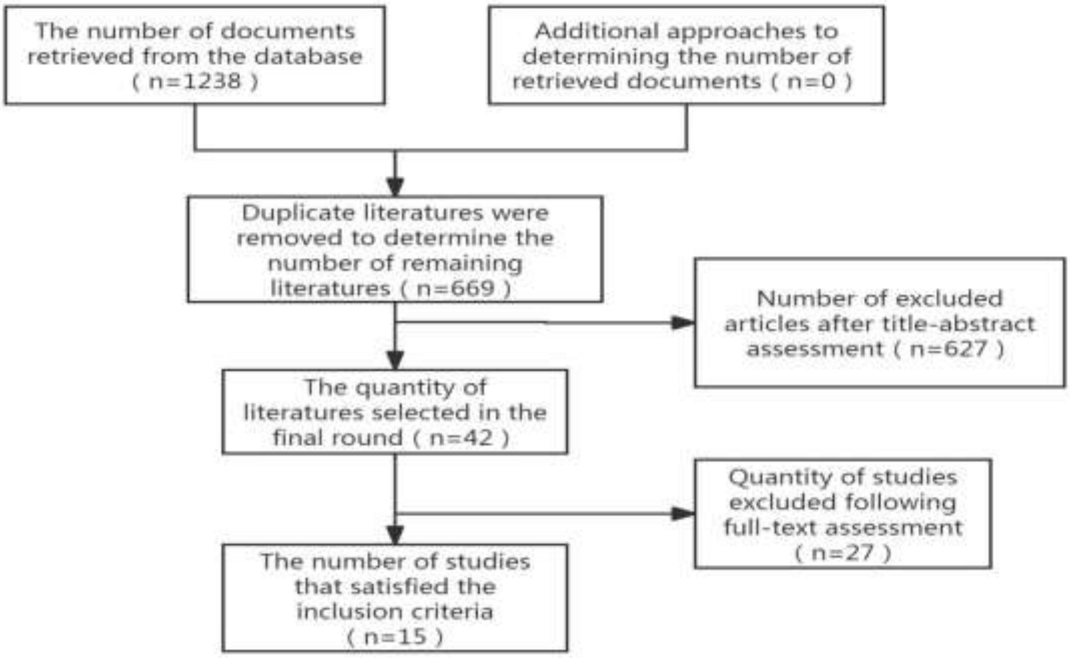

Figure 1: Literature retrieval flow chart

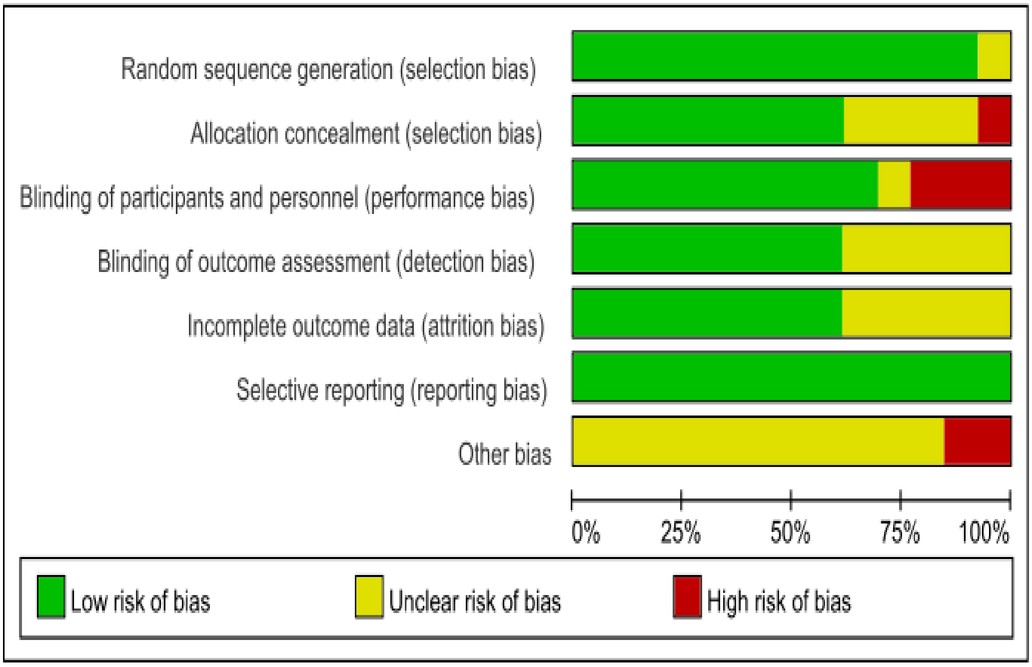

Figure 2: Proportion of projects with risk of bias in the included studies

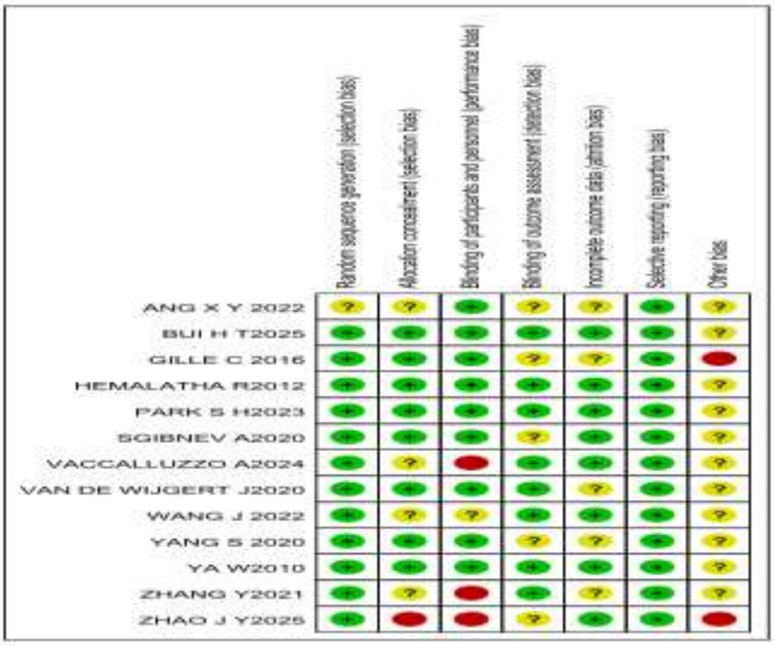

Figure 3: Risk of bias of included studies

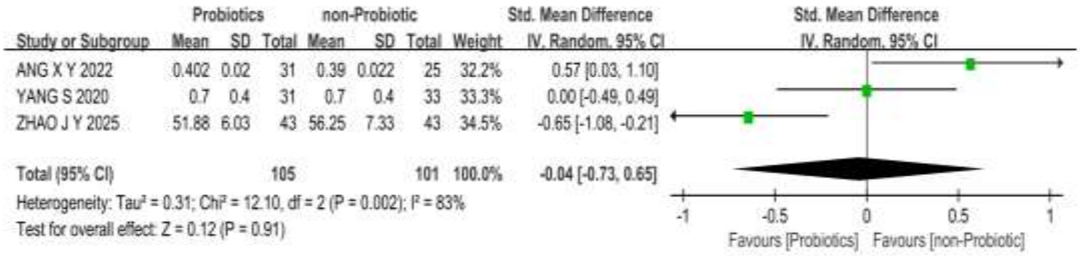

Figure 4: Forest plots of the IL-4

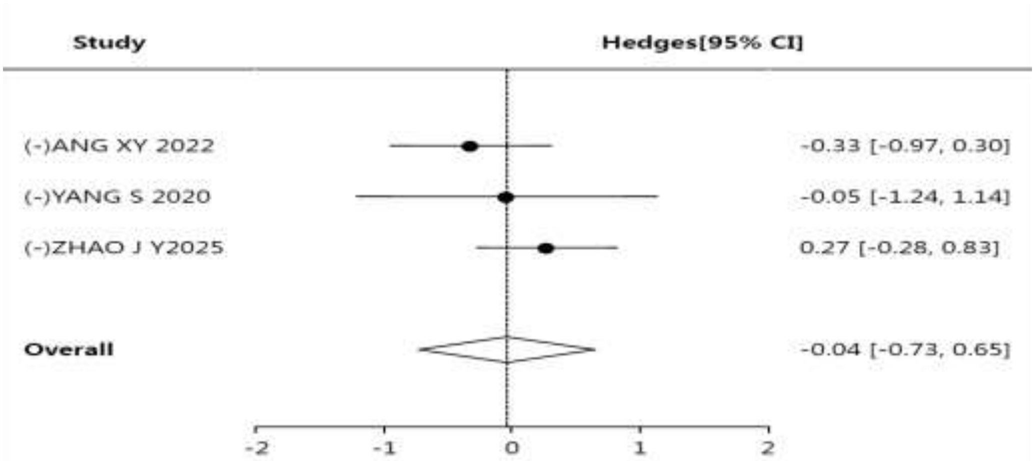

Figure 5: Sensitivity analysis of the IL-4

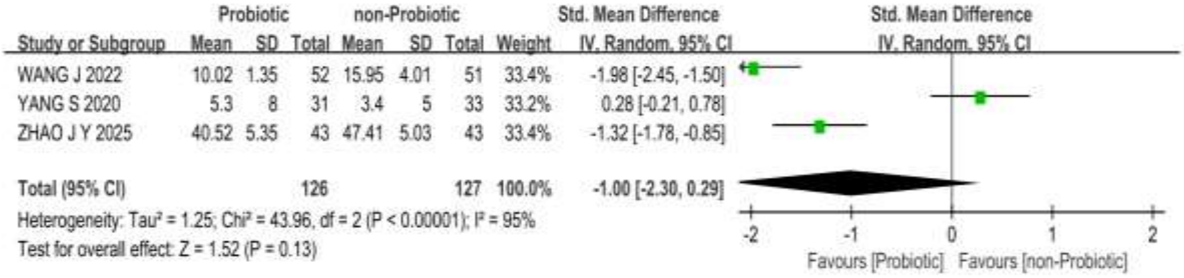

Figure 6: Forest plots of the IL-6

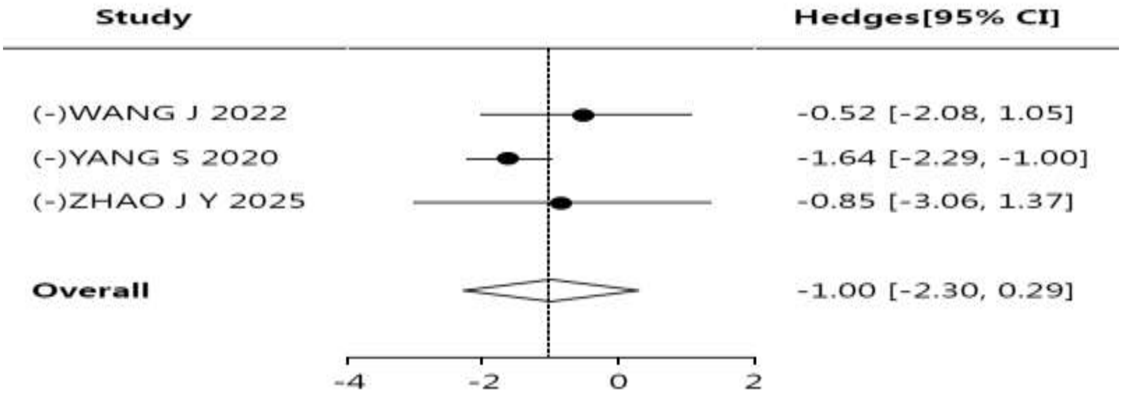

Figure 7: Sensitivity analysis of the IL-6

IL-10

IL-10 was reported in 3 studies, with a total of 147 patients (70 in the probiotic group and 77 in the non-probiotic group). Significant heterogeneity was detected across studies ($I^2 = 88\%$, $P < 0.001$). Therefore, a random-effects model was applied for meta-analysis. The results showed that probiotic intervention did not significantly reduce IL-10 levels compared with the non-probiotic group (SMD = -0.13, 95% CI: -1.12 to 0.86; P = 0.80; Figure 8).

Sensitivity analysis showed that, after exclusion of Ang et al. (2022)[6], the pooled effect size of the remaining 2 studies changed from negative to positive and heterogeneity decreased to 0%, indicating that this study was a major source of between-study heterogeneity (Figure 9). A plausible explanation is that Ang *et al.* enrolled pregnant women with vaginal candidiasis,[6] whereas the other two studies involved asymptomatic pregnant women.[7,10] In addition, Ang et al. combined probiotic treatment with clotrimazole suppositories,[6] while no comparable background antifungal therapy was used in the other studies. These differences may have altered the inflammatory response profile and contributed to the observed heterogeneity.

TNF-α

TNF-α was reported in 4 studies, enrolling a total of 310 patients (157 in the probiotic group and 153 in the non-probiotic group). Significant heterogeneity was observed across studies ($I^2 = 87\%$, $P < 0.001$). Therefore, a random-effects model was used for meta-analysis. The results demonstrated that probiotic treatment did not significantly reduce TNF-α levels compared with the non-probiotic group (SMD = -1.28, 95% CI: -2.74 to 0.18; P = 0.08; Figure 10). Sensitivity analysis indicated that the overall result was robust (Figure 11).

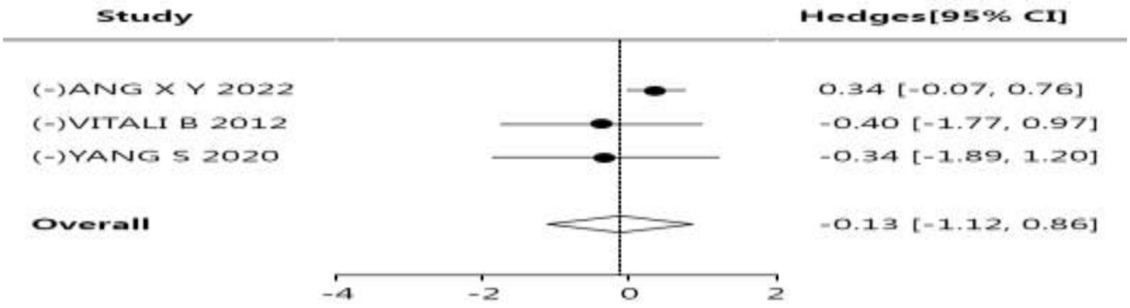

Figure 9: Sensitivity analysis of the IL-10

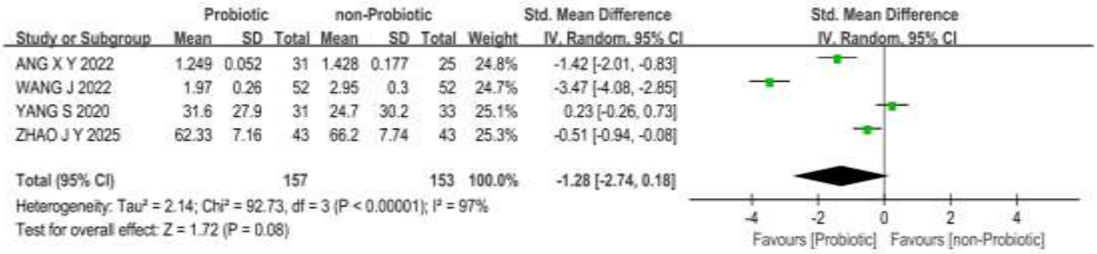

Figure 10: Forest plots of the TNF-α

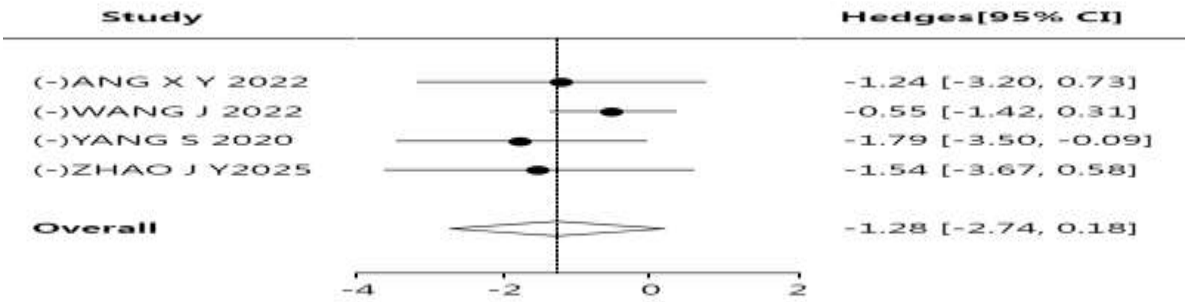

Figure 11: Sensitivity analysis of the TNF-α

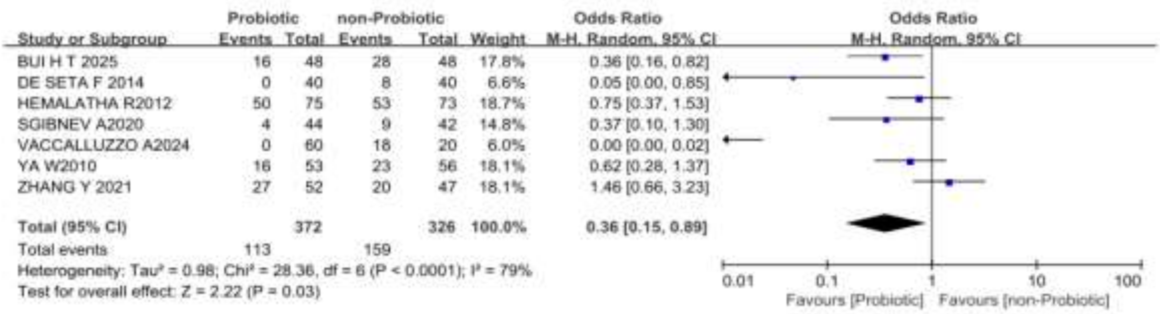

Figure 12: Forest plots of the vaginal pH

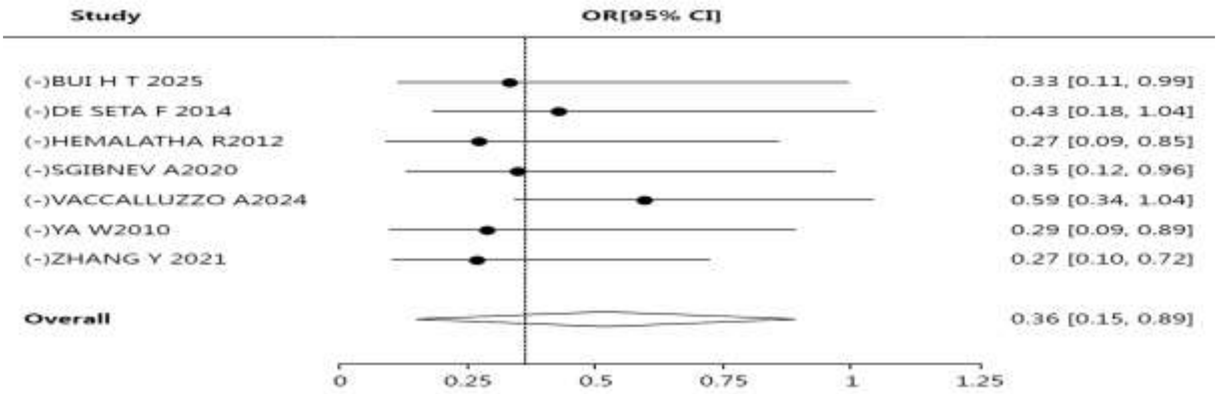

Figure 13: Sensitivity analysis of the Vaginal pH

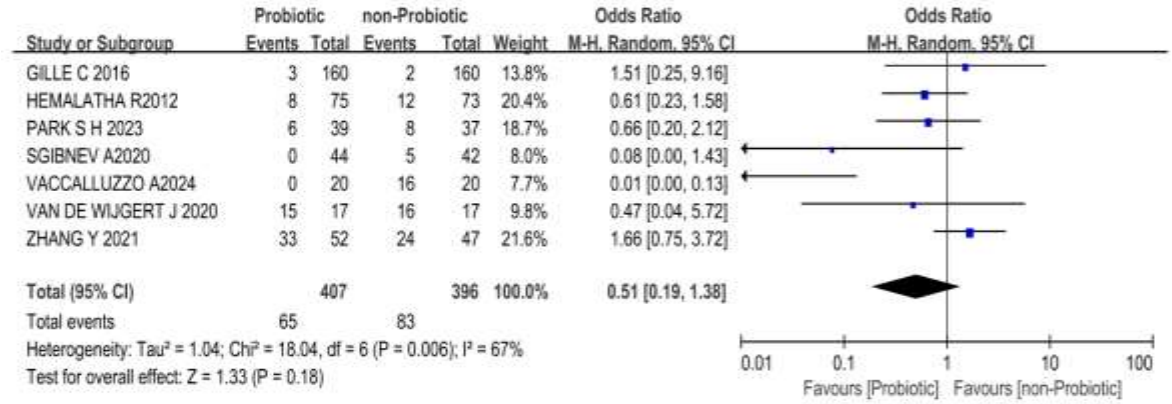

Figure 14: Forest plots of the Nugent point

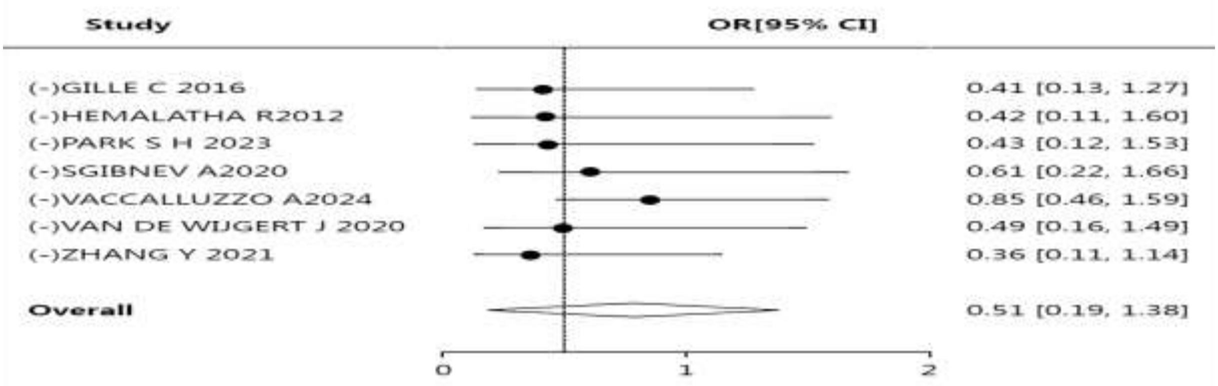

Figure 15: Sensitivity analysis of the Nugent point

Vaginal pH

Vaginal pH was reported in 7 studies, with a total of 698 patients (372 in the probiotic group and 326 in the non-probiotic group). Significant heterogeneity was detected across studies (I^2 = 79%, P < 0.001); thus, a random-effects model was used for meta-analysis. The results showed that probiotic intervention significantly reduced vaginal pH compared with the non-probiotic group (OR = 0.36, 95% CI = 0.15 to 0.89; P = 0.03; Figure 12). Sensitivity analysis indicated that the result was robust (Figure 13).

Nugent Score

Nugent score was reported in 7 studies, with a total of 803 patients (407 in the probiotic group and 396 in the non-probiotic group). Significant heterogeneity was observed across studies (I^2 = 67%, P = 0.006). Therefore, a random-effects model was used for meta-analysis. The results demonstrated that probiotic treatment did not significantly reduce Nugent score compared with the non-probiotic group (OR = 0.51, 95% CI = 0.19 to 1.38; P = 0.18; Figure 14). Sensitivity analysis indicated that the overall result was robust (Figure 15).

Discussion

In women of reproductive age, the vaginal ecosystem is commonly dominated by Lactobacillus species, whose production of lactic acid, bacteriocins, and hydrogen peroxide helps maintain a low vaginal pH and suppress colonization by opportunistic pathogens.[1,2] When this balance is disrupted, vaginal pH increases, protective metabolites decline, and dysbiosis may progress to symptomatic infection, including bacterial vaginosis and other lower genital tract disorders.[22] Restoration of a lactobacillus-dominant state is therefore a biologically plausible therapeutic target in vaginal health management.

Our pooled analysis suggests that probiotics are more likely to influence the physicochemical vaginal environment than inflammatory cytokine profiles or the overall Nugent-defined microbiota pattern. The significant reduction in vaginal pH supports the concept that probiotic supplementation may reinforce acidification of the vaginal milieu, which is an important component of colonization resistance. However, the absence of significant effects on IL-4, IL-6, IL-10, TNF-α, and Nugent score indicates that acidification alone may be insufficient to produce consistent restructuring of the vaginal microbiota or measurable anti-inflammatory effects within the treatment windows evaluated. A prior meta-analysis by López-Moreno and Aguilera[23] reported similarly limited evidence for durable correction of dysbiosis, which is broadly consistent with our findings.

Strengths, implications for policy and practice, and limitations

This study has several strengths. It synthesized evidence from both international and Chinese databases, evaluated microecological and inflammatory outcomes together, and incorporated sensitivity analyses to examine the stability of the pooled estimates. By assessing vaginal pH, Nugent score, and cytokine markers within the same review, this study provides a more integrated appraisal of whether probiotics influence both the ecological and inflammatory dimensions of vaginal health.For clinical practice and policy, the present findings support a cautious and targeted rather than routine use of probiotics. The available evidence suggests that probiotics may help maintain a weakly acidic vaginal environment, but current data do not justify recommending universal probiotic supplementation as a standard strategy to normalize inflammatory markers or fully restore vaginal flora.[24] In practice, clinicians should consider patient subgroup, probiotic strain, route of administration, and co-therapy before recommending these products. At the policy level, future guideline development should emphasize product standardization, transparent strain reporting, and high-quality randomized trials before broad recommendations are made.

Several limitations should also be acknowledged. First, there was substantial heterogeneity in baseline characteristics and intervention regimens across the included studies. Marked differences existed in probiotic strains, dosage, route of administration, treatment duration, and background therapy. Moreover, the study populations included healthy pregnant women, postpartum patients with mycotic vaginitis, and women with bacterial vaginosis or other forms of dysbiosis, whose underlying vaginal microecological status differed considerably. Second, the number of included studies was relatively small, which limited further exploration of heterogeneity through meta-regression or subgroup analyses for several outcomes. Third, most outcome measures showed considerable heterogeneity that could not be fully resolved by sensitivity analysis, which may affect the precision and generalizability of the pooled estimates. Fourth, the indicators used to evaluate vaginal microbiota ecology were limited by the reporting of the original studies. Vaginal pH and Nugent score are useful screening indicators, but they cannot precisely characterize microbial diversity, strain-level composition, or interactions among microbial taxa.

Conclusion

Probiotic supplementation can significantly improve vaginal pH in women by helping maintain a weakly acidic vaginal microenvironment. However, its effects on inflammatory factors, including IL-4, IL-6, IL-10, and TNF-α, remain uncertain, and it does not significantly improve the vaginal microbiota pattern reflected by Nugent score. Current evidence therefore does not support routine probiotic use for all women with the goal of improving both vaginal ecology and inflammatory status. Further well-designed randomized controlled trials with standardized strains, doses, and outcome reporting are warranted.

Funding

Not applicable.

Conflict of interests

The authors declared no conflict of interest.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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