Urologia Colombiana

Permanyer

Check for updates

REVIEW ARTICLE

Probiotic supplementation improved sperm parameters in idiopathic infertility male: a systematic review and meta-analysis

La suplementación con probióticos mejoró los parámetros espermáticos en hombres con infertilidad idiopática: una revisión sistemática y metaanálisis

Johannes C. Prihadi[1-3], Antoninus Hengky[4], Steven Alvianto[5], Hans Putranata[5], Pradipta A. Putra[1], and Havian D. Telium[1]*

[1]Division of Urology, Department of Surgery, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta; [2]Division of Urology, Department of Surgery, Atma Jaya Hospital, Jakarta; [3]Faculty of Medicine, IPB University, Bogor; [4]Division of Urology, Department of Surgery, Universitas Padjadjaran, Bandung, West Java; [5]Fatima General Hospital, Ketapang Regency, West Kalimantan. Indonesia

How to cite this article: Prihadi J.C. et al. Probiotic supplementation improved sperm parameters in idiopathic infertility male: a systematic review and meta-analysis. Urol. Colomb. 2026;35(1):39-48. doi: 10.24875/RUC.25000029

Abstract

Several reproductive disorders and infertility issues have been associated with dysbiosis in the reproductive tract. Recent research indicates that addressing this imbalance can lead to improvements in spermatogenesis and sperm quality. A comprehensive search was conducted using databases such as PubMed, EBSCO, ProQuest, and Google Scholar to identify studies relevant to probiotic utilization on sperm quality in idiopathic infertile males. The search strategies included specific medical subject headings and keywords related to "sperm quality," "male infertility," and "probiotics." Random-effect meta-analyses were performed to estimate the effect size. All studies showed significant improvement in = sperm qualities. A total of four studies were included for both qualitative and quantitative synthesis. The data showed significant improvements in sperm concentration, volume, and motility, with standardized mean differences of 1.96 (95% CI: 0.08-3.84, p = 0.04), 1.28 (95% CI: 0.28-2.28, p = 0.01), and 0.89 (95% CI: 0.10-1.67, p = 0.03), respectively. Probiotic supplementation showed promising results in improving sperm quality in males with idiopathic infertility. However, larger-scale studies are needed to confirm these findings, and the mechanisms behind these effects should be further explored.

Keywords: *Probiotics. Sperm quality. Sperm parameter. Male infertility.*

Resumen

Diversos trastornos reproductivos y problemas de infertilidad se han asociado con la disbiosis en el tracto reproductivo. Investigaciones recientes indican que abordar este desequilibrio puede conducir a mejoras en la espermatogénesis y la calidad del esperma. Se realizó una búsqueda exhaustiva en bases de datos como PubMed, EBSCO, ProQuest y Google Scholar para identificar estudios relevantes sobre el uso de probióticos en la calidad espermática en hombres con infertilidad idiopática. Las estrategias de búsqueda incluyeron encabezados de temas médicos específicos y palabras clave

***Correspondence:**
Johannes C. Prihadi
E-mail: johannes.cansius@atmajaya.ac.id

Date of reception: 03-06-2025
Date of acceptance: 01-12-2025
DOI: 10.24875/RUC.25000029

Available online: 11-03-2026
Urol. Colomb. 2026;35(1):39-48
www.urologiacolombiana.com

relacionadas con "calidad espermática", "infertilidad masculina" y "probióticos". Se llevaron a cabo metaanálisis de efectos aleatorios para estimar el tamaño del efecto. Todos los estudios mostraron una mejora significativa en las cualidades del esperma. Se incluyeron un total de cuatro estudios tanto para la síntesis cualitativa como cuantitativa. Los datos mostraron mejoras significativas en la concentración, el volumen y la motilidad del esperma, con diferencias medias estandarizadas (DME) de 1.96 (IC del 95%: 0.08 a 3.84, p = 0.04), 1.28 (IC del 95%: 0.28 a 2.28, p = 0.01) y 0.89 (IC del 95%: 0.10 a 1.67, p = 0.03), respectivamente. La suplementación con probióticos mostró resultados prometedores en la mejora de la calidad espermática en hombres con infertilidad idiopática. Sin embargo, se necesitan estudios a mayor escala para confirmar estos hallazgos, y los mecanismos detrás de estos efectos deben explorarse más a fondo.

Palabras clave: *Probióticos. Calidad espermática. Parámetro espermático. Infertilidad masculine.*

Introduction

As a major health concern worldwide, infertility is estimated to affect 8-12% of reproductive-age couples. Besides being solely responsible for 20-30% of infertility cases, males also contribute to 50% of overall infertility cases[1]. The World Health Organization (WHO) has defined male infertility as the inability of a male to make a fertile female pregnant for a minimum of at least 1 year of regular unprotected intercourse[2,3]. WHO defined different subtypes of sperm abnormalities: asthenozoospermia, oligozoospermia, teratozoospermia, or their combination[4]. Genetic mutations, congenital reproductive abnormalities, endocrine/metabolic dysfunction, environmental toxicant exposure, and lifestyle factors have been associated with male infertility or subfertility[5].

A significant proportion of male infertility is idiopathic in nature, without known causes, called idiopathic male infertility (IMI). IMI is a multifactorial heterogeneous disease where the infertile male has normal sperm and semen parameters[2,6]. IMI is a widely debated term, as various degrees of infertility are prevalent in the general population, with the most severe forms being azoospermia and asthenozoospermia[6]. IMI is often treated empirically, utilizing either hormonal or non-hormonal remedies[2].

Numerous reproductive disorders and infertility have been linked to reproductive tract dysbiosis, or the predominance of pathogen-driven microorganisms in the reproductive system[7]. To date, more attention has focused on the potential roles of probiotics in restoring reproductive tract eubiosis while minimizing the use of antibiotics[8]. Probiotics are defined by the Food and Agriculture Organization of the United Nations and the WHO (FAO/WHO) in 2002 as "live microorganisms that, when administered in adequate amounts, confer a beneficial health effect on the host"[9]. In humans, probiotics have been shown to enhance spermatogenesis, increase epididymal sperm count, and improve the normal sperm percentage to reduce sperm morphological abnormalities and DNA damage[7].

Therefore, due to increasing interest in utilizing probiotics as an adjunctive therapy to improve sperm parameters, the obvious research gap in advanced clinical trials on probiotics, and the lack of a comprehensive meta-analysis, this study was designed to evaluate the beneficial effects of probiotics on sperm parameters among adult men diagnosed with idiopathic infertility.

Materials and methods

This systematic review was performed based on Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines and registered on PROSPERO.

Eligibility criteria

The studies will be chosen according to the PICO framework, which is explained below.

- Study Designs: randomized controlled trials (RCTs) or non-randomized trials.
- Population (P): adult man diagnosed with idiopathic infertility.
- Intervention (I): probiotics supplementation.
- Comparator (C): placebo, standard treatment, or no treatment.
- Outcome (O): primary outcomes, including sperm quality in concentration, volume, and motility, while secondary outcomes include any other sperm quality outcome and adverse events.

There was no restriction on language or year of publication.

Search strategy

Our search methods were created with a combination of medical subject headings and free text terms linked to sperm quality in IMI and probiotics. Our primary sources of information were Google Scholar, EBSCO, ProQuest, and PubMed. To find any possibly missing papers, we manually searched the reference lists of the included research and pertinent reviews. To guarantee a thorough search, we used synonyms and versions of the terms "sperm quality," "idiopathic male infertility," and "probiotics" (Supplementary data).

Data management, selection, collection, and extraction

Mendeley™ was used to manage the studies that were identified throughout our search. Two co-authors (AH and SA) separately gathered the identified papers, eliminated the duplicates, and assessed them for eligibility based on titles and abstracts. After the first screening, full-text evaluations of potentially pertinent research were carried out. Any disagreements that arose throughout the selection process and quality evaluation will be discussed and addressed.

Data collection entailed a thorough extraction of information from the selected studies. The following data were methodically extracted: author, publication year, study nation, study design, length of study, number of participants and allocation, inclusion and exclusion criteria, and intervention. Sperm quality, including concentration, volume, and motility, was the main objective; adverse effect was the secondary endpoint. Two reviewers independently extracted the data, assuring both reliability and accuracy. After that, a cross-check was performed on the extracted data to guarantee accuracy and consistency. When there were gaps in the data, we tried to get in touch with the relevant study authors to get the missing details.

Quality assessment

The quality of the included studies was assessed using established criteria to ensure the validity and reliability of the findings. We employed standardized tools appropriate for the study designs included in our review. The Cochrane Rob 2 tool was used to assess RCT studies, whereas ROBINS-I was used to assess non-randomized studies.

Data analysis and synthesis

The data were synthesized using both qualitative and quantitative methodologies to provide a comprehensive picture of the research findings. This study provided a narrative summary of the included studies in qualitative synthesis, detailing study characteristics, interventions, and outcomes. In a quantitative study, statistical software (Review Manager 5.4) was used to examine the included studies and conduct meta-analyses. Each outcome was entered in continuous forms, and 95% confidence intervals (CIs) were used to determine the standardized mean difference (SMD). The I^2 statistic and Chi-square test were used to assess the heterogeneity among the studies. Random-effects models were employed when I^2 values were above 50%, while fixed-effects models were used otherwise. We used Egger's test and funnel plots to evaluate publication bias.

Results

Study characteristics

A total of four studies were found through database searches and manual investigation (Fig. 1). The initial screening of 450 studies was done using their titles and abstracts, and 21 duplicates were removed. From these, 11 studies were thoroughly assessed to determine their eligibility, all in English. Four studies were included in the final review as a result of this method (Table 1)[10-13]. The risk of bias was assessed and presented in table 2.

Three of the four studies were RCTs, and one was a single-arm trial involving 156 middle-aged participants. All studies included patients with IMI and utilized specific probiotics, most commonly from the *Lactobacillus* and *Bifidobacterium genera*, with concentrations ranging from 10^9 to 10^{11} CFU. The duration of the studies varied between 10 weeks and 6 months.

Sperm quality change

A meta-analysis using a random-effects model revealed significant improvements in several sperm parameters (Fig. 2). Sperm concentration increased with an SMD of 1.96 (95% CI: 0.08-3.84, p = 0.04) and an I^2 of 95%. The percentage of sperm motility also showed significant improvement, with an SMD of 1.28 (95% CI: 0.28-2.28, p = 0.01) and an I^2 of 86%. In addition, ejaculate volume increased significantly, with an SMD of 0.89 (95% CI: 0.10-1.67, p = 0.03) and an I^2 of 79%. Two studies investigating the impact of probiotic supplementation on DNA fragmentation reported significant improvements, along with reductions in inflammatory and oxidative markers.

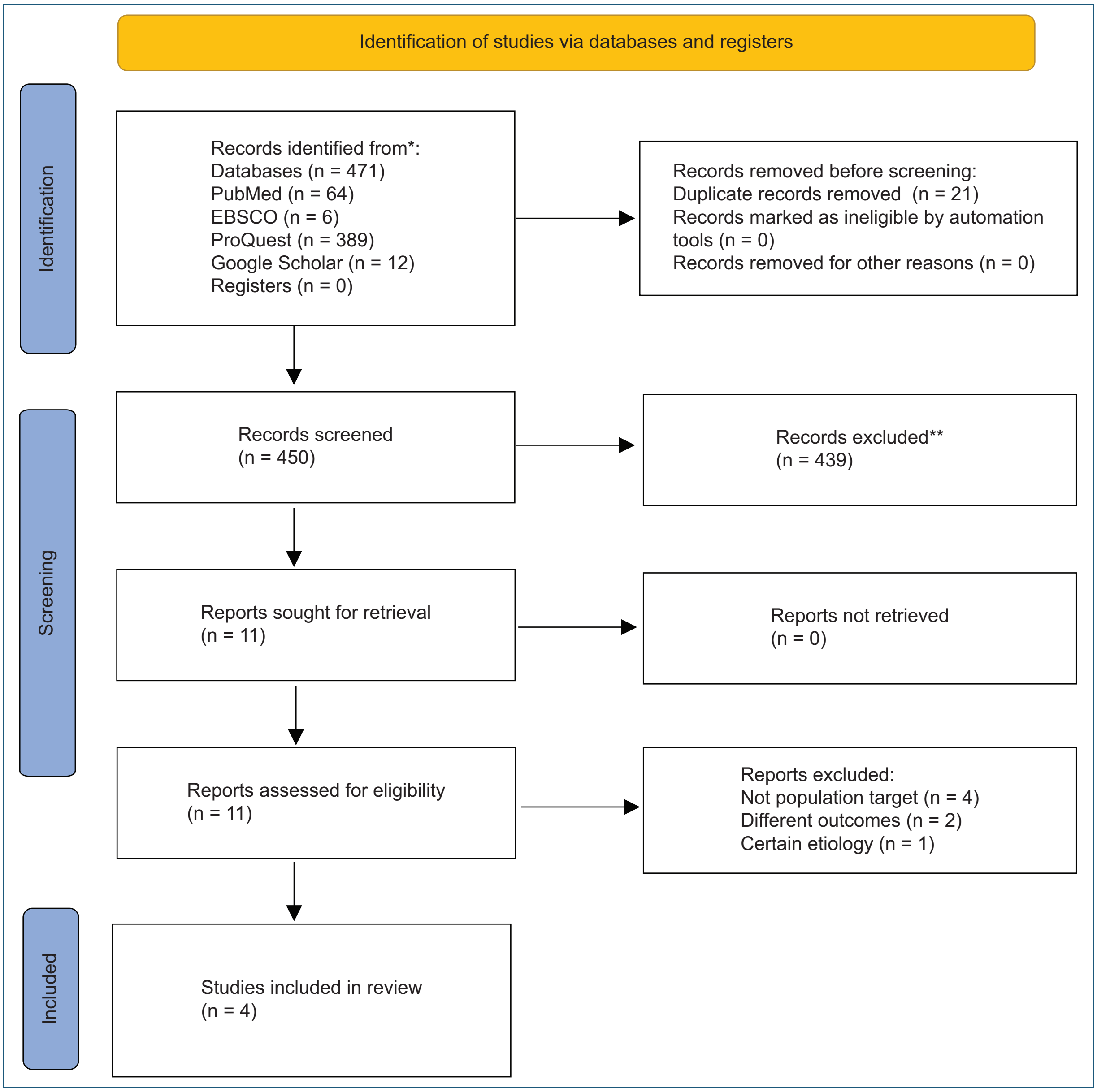

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 flow diagram.

Discussion

All selected studies had shown that probiotics with or without prebiotics, administered over different durations, short-term (3 weeks) or long-term (up to 6 months), successfully showed constant results of improved infertility. Probiotics with/without prebiotics improved male infertility significantly through various mechanisms: increased sperm motility, increased sperm concentration, increased viable sperm, increased ejaculate volume, and reduction in oxidative and inflammatory markers.

Male infertility was responsible for almost 50% of overall infertility, with 30% of these cases being idiopathic in nature[14]. IMI was postulated to be linked with elevated reactive oxygen species (ROS) and decreased antioxidant capacity due to environmental and/or genetic factors. These pathological conditions disturb the testicular microenvironment and disrupt normal spermatogenesis[6]. However, low ROS levels were required for normal sperm physiologic function: capacitation, hyperactivation, and acrosomal reaction[15]. High levels of ROS caused lipid peroxidation, DNA damage,

Table 1. Characteristics of included studies

No.	Author, Year	Design	Inclusion criteria	Exclusion criteria	Participants				Intervention	Control	Study duration	Outcome
					N		Age (years)					
					Case	Control	Case	Control				
1	Valcarce et al., 2017[10]	Single arm trial	Asthenozoospermic patients	Not specified	9	N/A	N/A	N/A	*L. rhamnosus* CECT8361 and *B. longum* CECT7347 at 50% each, containing 10^9 CFU/capsule, once daily	N/A	12 weeks (+ 4 pre-intervention sampling	Sperm motility was improved significantly, but concentration and volume were not. DNA fragmentation was drastically reduced. Intracellular H_2O_2 was decreased.
2	Maretti et al., 2017[11]	RCT Pilot	Patient with idiopathic oligo-astheno-terato-zoospermia (according to WHO)	Refusal, leukocytosis, signs of infection, drug, tobacco, alcohol abuse, ongoing medical treatment (gonadotropins, anabolic steroids, cancer chemotherapy, NSAIDs), previous cancer radiotherapy/chemotherapy, X-ray exposure in the previous 8 months, and genetic abnormalities	20	21	37 (32-42	36 (30-43)	Probiotic-containing supplement with *L. paracasei* 86 B21060 5×10^9 CFUs	Alimentary starch	6 months	There was significant improvement in sperm count, volume, concentration, motility, morphology, FSH, LH, and testosterone levels in the prebiotic group. E2 and PRL were not improved.
3	Helli et al., 2020[12]	RCTs	Age 20-45, idiopathic oligo-astheno-terato-zoospermia, and normal levels of genodatropin, testosterone, and prolactin	Known causes of infertility include drug/ alcohol, diabetes, kidney disease, chronic liver disease, varicocele, infection, drugs that interfere with sex hormones, contact with pesticides, heavy metals, taking antioxidants, and a BMI ≥ 30	25	25	32.23 ± 4.11	33.01 ± 3.91	Probiotic capsule containing *L. casei*, *L. rhamnosus*, *L. bulgaricus*, *L. acidophilus*, *B. breve*, *B. longum*, *S. thermophiles* with a total of 2×10^{11} CFU	Maltodextrin	10 weeks	There was a significant improvement in volume, concentration, motility, and antioxidant capacity in the intervention group compared to the placebo. Concentration of malondialdehyde and inflammatory markers was significantly reduced.

(Continued)

Table 1. Characteristics of included studies *(continuation)*

No.	Author, Year	Design	Inclusion criteria	Exclusion criteria	Participants				Intervention	Control	Study duration	Outcome
					N		Age (years)					
					Case	Control	Case	Control				
4	Abbasi et al., 2021[13]	RCTs	Male with idiopathic male infertility (according to WHO)	Known causes (cryptorchidism; varicocele, chromosome abnormalities, leukocytospermia, epididymal-orchitis, genito-urinary traumas, prostatitis, testicular torsion, history of inguinal/genital surgery, history of hormone therapy, endocrinopathies, history or ongoing use of cytotoxic drugs and immunosuppressants, anticonvulsants, androgens, and recent history of sexually transmitted infections	28	28	34.5	33.8	Probiotics containing *L. rhamnosus*, *L. casei*, *L. bulgaricus*, *L. acidophilus*, *B. breve*, *B. longum*, and *S. thermophilus* with a total of 10^9 CFU	Placebo with an identical capsule	80 days	There was significant improvement in concentration, motility, abnormal morphology, sperm lipid peroxidation, and DNA fragmentation.

L. casei: Lacticaseibacillus casei; L. rhamnosus: Lacticaseibacillus rhamnosus; L. bulgaricus: Lacticaseibacillus bulgaricus; L. acidophilus: Lacticaseibacillus acidophilus; B. breve: Bifidobacterium breve; B. longum: Bifidobacterium longum; S. thermophiles: Streptococcus thermophiles; RCT: randomized controlled trials.

Table 2. Risk of bias assessment

RoB 2								
No.	**Author, Year**	**Random sequence generation (selection bias)**	**Allocation concealment (selection bias)**	**Blinding of participants and personnel (performance bias)**	**Blinding of outcome assessment (detection bias)**	**Incomplete outcome data (attrition bias)**	**Selective reporting (reporting bias)**	**Overall**
1	Maretti et al., 2017	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Unclear
2	Helli et al., 2020	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
3	Abbasi et al., 2021	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
ROBINS-I								
No.	**Author, Year**	**Bias due to confounding**	**Bias in selection of participants into the study**	**Bias in classification of interventions**	**Bias due to deviations from intended interventions**	**Bias due to missing data**	**Bias in measurement of outcomes**	**Bias in selection of the reported result**
1	Valcarce et al., 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

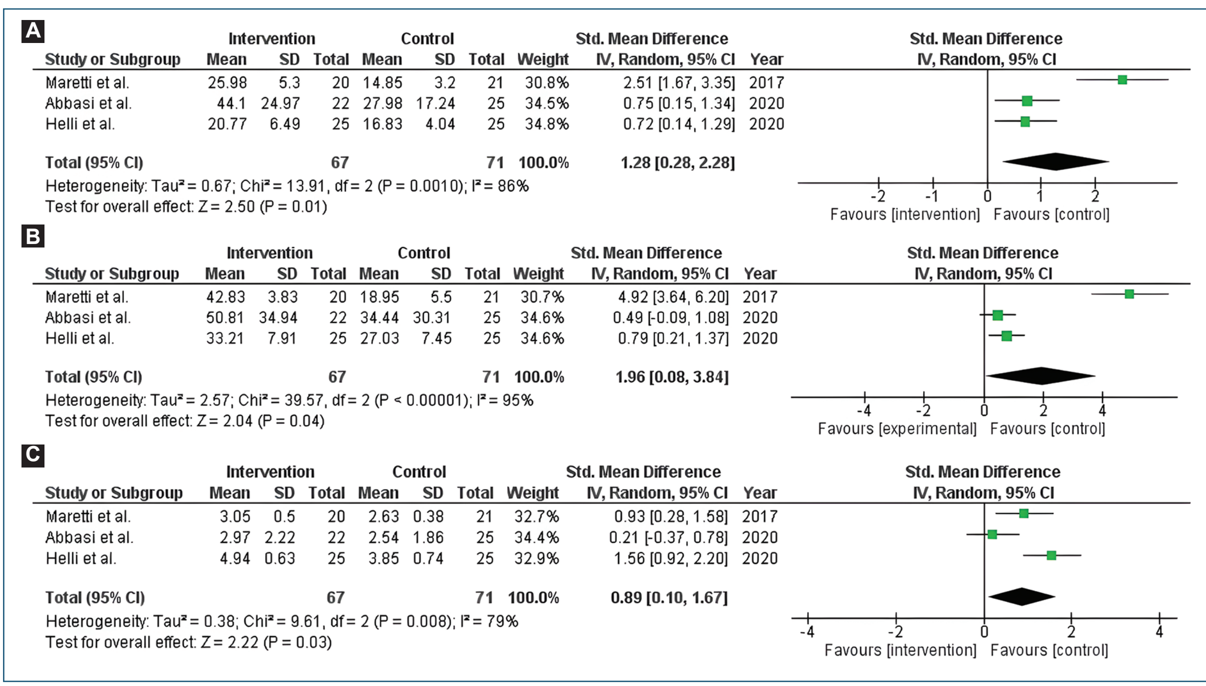

Figure 2. Forest plot of probiotic effects on sperm parameters. **A:** forest plot of probiotic effects on sperm concentration (per mL × 10^6). **B:** forest plot of probiotic effects on sperm motility (%); **C:** forest plot of probiotic effects on ejaculate volume (mL).

enzyme inactivation, and spermatozoa protein oxidation[15]. Current management for IMI is composed of hormonal therapies and non-hormonal therapies. Hormonal therapies have long been studied and were regarded as a safe and effective treatment for male infertility, especially follicle-stimulating hormone (FSH) and selective estrogen receptor modulators (SERMs). FSH directly increases spermatogenesis and spermiogenesis. SERMs block negative feedback in the hypothalamic-pituitary-gonadal axis, which increases GnRH and gonadotropins (FSH and LH)[16]. Non-hormonal therapies focused on reducing ROS that disturb the spermatogenetic process. Spermatozoa were especially susceptible to ROS due to their plasma membrane structure containing high polyunsaturated fatty acids content[16]. Antioxidant supplementation acts to counterbalance elevated ROS. Supplementation such as carnitines, coenzyme Q10, vitamins (Vit C, Vit D, and Vit E), and trace elements (zinc and selenium) demonstrated high antioxidant capacity that was effective for IMI[15,17].

Lactobacillus and *Bifidobacterium strains* were some of the most common lactic acid bacteria marketed as probiotics that had been studied to own antioxidant properties. Oral probiotics exert their immune regulatory property by producing various cytokines and chemokines responsible for increased mucus immunoglobulin A (IgA), activation of regulatory T cells, increased mucin production and tight junction protein, and preventing dysbiosis by suppressing potential pathogenic overgrowth[18]. *In vivo* study in mice models by Qiao et al. demonstrated that increased total antioxidant capacity was positively associated with higher *Lactobacilli* growth in gut microbiome[19].

Furthermore, this immune regulatory property was not limited to the gastrointestinal tract. A RCT study by Jing et al. found that *Bifidobacterium* probiotic supplementation for 6 months in cow's milk allergy infants successfully reduced allergic scores, improved anti-inflammatory responses, significantly reduced pro-inflammatory cytokines (tumor necrosis factor-alpha, interleukin [IL]-6, and IL-1β), and significantly increased anti-inflammatory cytokine (IL-10)[20]. Another study by Zeng et al. demonstrated that gut microbiota-based therapies for autoimmune diseases (such as celiac sprue, systemic lupus erythematosus and lupus nephritis, juvenile idiopathic arthritis, psoriasis, fibromyalgia syndrome, progressive systemic sclerosis, multiple sclerosis, type 1 diabetes mellitus, Crohn's disease, and ulcerative colitis) showed improved symptoms, reduced inflammatory factors, and were not associated with significant adverse events[21]. Similar to the gastrointestinal tract, the male reproductive system is also home to complex microbial communities that aid in normal physiologic processes. Disruption in maintaining a balanced and healthy microbiome could lead to elevated oxidative stress, imbalance in the redox state, and an increase in susceptibility to infection and thus, infertility[22].

An *in vitro* study by Barbonetti et al. demonstrated that a combination of three selected *Lactobacilli* strains (*Lactobacillus Brevis* [CD2], *Lactobacillus Salivarius* [F2], and *Lactobacillus plantarum* [FV9]) has a protective effect on sperm lipid peroxidation level, thus preserving sperm viability and motility[23]. *In vivo* studies in rat models by Chen et al. also found significantly reversed alterations due to a high-fat diet in the probiotic-supplemented group, resulting in an increase in all semen parameters and a lower percentage of sperm with DNA damage[24]. Dardmeh et al. have also suggested that *Lactobacillus rhamnosus*, as a potential agent, positively impacts weight loss and reproductive hormones, significantly improving sperm motility and kinetic parameters in diet-induced obese male mice[25]. While in human studies, Valcarce et al. studied the effect of a probiotic containing *L. rhamnosus CECT8361* and *Bifidobacterium longum CECT7347* in nine asthenozoospermic men for 12 weeks, and found a significant improvement in sperm motility and a decrease in DNA fragmentation. Helli et al. also found a significant increase in sperm mean count, concentration, and motility compared to the placebo group in 25 men with oligoasthenoteratozoospermia supplemented with a probiotic containing *Lacticaseibacillus casei, L. rhamnosus, Lacticaseibacillus bulgaricus, Lacticaseibacillus acidophilus, Bifidobacterium breve, B. longum, Streptococcus thermophiles* for 10 weeks.

Studies have shown that the prebiotic content of synbiotics, intended to promote the survival of probiotic strains in the gastrointestinal tract, synergistically offers superior functionality compared to probiotic or prebiotic solutions alone[26]. Abbasi et al. studied the effect of FamiLact, containing a broad spectrum of beneficial *Lactobacillus, B. breve/longum,* and *S. thermophiles*, along with prebiotics (fructooligosaccharides) administration in 22 males with IMI for 80 days were found to improve the semen parameters significantly[13]. Maretti et al. also studied another synbiotic named Flortec, a synbiotic containing *L. paracasei* B21060 (5×10^9 cells), arabinogalactan, oligo-fructosaccharides, and L-glutamine, on 20 males with idiopathic oligoasthenoteratospermia over a 6-month therapy period, demonstrating significant improvements in sperm parameters by optimizing free radical concentration in seminal fluid, enhancing the prostatic microenvironment, and ameliorating intestinal flora[11]. In addition, elevated blood levels of FSH, luteinizing hormone (LH), and testosterone (T) were also observed, which are believed to be a consequence of interaction with kisspeptin hypothalamic pulsatile secretion, a key signaling in human fertility.

Emerging evidence has revealed that microorganisms inhabit numerous human body sites, including the urinary tract, which has long been assumed sterile[27]. Variations in each microbiota composition may not impact the overall function of the microbiome, as it produces the same metabolites and induces similar changes in human cells. The correlation between dysbiosis and increased oxidative stress was established. Specific bacterial species may produce ROS via bacteriospermia, adhesion and agglutination events, bacterial toxins, and the inflammatory process[28].

Oral probiotics have demonstrated effectiveness in addressing female reproductive issues and may similarly hold potential in optimizing the male microbiome[29]. The production of antioxidants and gamma-amino butyric acid by the probiotics is thought to be the primary mechanism to improve sperm quality, particularly regarding sperm concentration, motility, and decrease of DNA fragmentation[30]. In addition, the male urogenital tract and the gut microbiota interact to control testicular function (gut-testes axis). Dysbiosis of the gut microbiome alters the structure and function of the intestinal barrier, leading to inflammation, endocrine disruption, insulin resistance, and metabolic diseases, all of which affect spermatogenesis pathways[31].

Our study had some limitations. The number of studies able to be included in the quantitative synthesis was relatively small. Although this systematic review and meta-analysis had different intervention durations that represent varying therapeutic onset and duration of probiotics in IMI, further high-quality studies are needed to strengthen our findings.

Conclusion

Probiotic supplementation has shown promising results in improving sperm quality, including significantly elevated SMD of sperm concentration, percentage of sperm motility, and ejaculate volume in IMI. Nevertheless, large-scale studies are needed to validate these findings, and the underlying mechanisms of these effects should be further explored.

Funding

The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence (AI). The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

Supplementary data

Supplementary data are available at DOI: 10.24875/RUC.25000029. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

References

1. Borght MV, Wyns C. Fertility and infertility: definition and epidemiology. Clin Biochem. 2018;62:2-10.
2. Leslie SW, Soon-Sutton TL, Khan MA. Male infertility. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2024.
3. World Health Organization. Infertility. Fact Sheets. Switzerland: World Health Organization; 2024.
4. World Health Organization. WHO Laboratory Manual for the Examination and Processing of Human Semen. 6th ed. Geneva: WHO; 2021.
5. Bhattacharya I, Sharma SS, Majumdar SS. Etiology of male infertility: an update. Reprod Sci. 2024;31:942-65.
6. Kothandaraman N, Agarwal A, Abu-Elmagd M, Al-Qahtani MH. Pathogenic landscape of idiopathic male infertility: new insight towards its regulatory networks. NPJ Genom Med. 2016;1:16023.
7. Hashem NM, Gonzalez-Bulnes A. The use of probiotics for management and improvement of reproductive eubiosis and function. Nutrients. 2022;14:902.
8. Khalesi S, Bellissimo N, Vandelanotte C, Williams S, Stanley D, Irwin C. A review of probiotic supplementation in healthy adults: helpful or hype? Eur J Clin Nutr. 2019;73:24-37.
9. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. Expert consensus document. The international scientific association for probiotics and prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastroenterol Hepatol. 2014;11:506-14.
10. Valcarce DG, Genovés S, Riesco MF, Martorell P, Herráez MP, Ramón D, et al. Probiotic administration improves sperm quality in asthenozoospermic human donors. Benef Microbes. 2017;8:193-206.
11. Maretti C, Cavallini G. The association of a probiotic with a prebiotic (flortec, bracco) to improve the quality/quantity of spermatozoa in infertile patients with idiopathic oligoasthenoteratospermia: a pilot study. Andrology. 2017;5:439-44.
12. Helli B, Kavianpour M, Ghaedi E, Dadfar M, Haghighian HK. Probiotic effects on sperm parameters, oxidative stress index, inflammatory factors and sex hormones in infertile men. Hum Fertil (Camb). 2022;25:499-507.
13. Abbasi B, Abbasi H, Niroumand H. Synbiotic (FamiLact) administration in idiopathic male infertility enhances sperm quality, DNA integrity, and chromatin status: a triple-blinded randomized clinical trial. Int J Reprod Biomed. 2021;19:235-44.
14. Corsini C, Boeri L, Candela L, Pozzi E, Belladelli F, Capogrosso P, et al. Is there a relevant clinical impact in differentiating idiopathic versus unexplained male infertility? World J Mens Health. 2023;41:354-62.

15. Barati E, Nikzad H, Karimian M. Oxidative stress and male infertility: current knowledge of pathophysiology and role of antioxidant therapy in disease management. Cell Mol Life Sci. 2020;77:93-113.
16. Duca Y, Calogero AE, Cannarella R, Condorelli RA, La Vignera S. Current and emerging medical therapeutic agents for idiopathic male infertility. Expert Opin Pharmacother. 2019;20:55-67.
17. Jung JH, Seo JT. Empirical medical therapy in idiopathic male infertility: promise or panacea? Clin Exp Reprod Med. 2014;41:108-14.
18. Maldonado Galdeano C, Cazorla SI, Lemme Dumit JM, Vélez E, Perdigón G. Beneficial effects of probiotic consumption on the immune system. Ann Nutr Metab. 2019;74:115–24.
19. Qiao Y, Sun J, Ding Y, Le G, Shi Y. Alterations of the gut microbiota in high-fat diet mice is strongly linked to oxidative stress. Appl Microbiol Biotechnol. 2013;97:1689-97.
20. Jing W, Liu Q, Wang W. *Bifidobacterium bifidum* TMC3115 ameliorates milk protein allergy by affecting gut microbiota: a randomized double-blind controlled trial. J Food Biochem. 2020;44:e13489.
21. Zeng L, Yang K, He Q, Zhu X, Long Z, Wu Y, *et al*. Efficacy and safety of gut microbiota-based therapies in autoimmune and rheumatic diseases: a systematic review and meta-analysis of 80 randomized controlled trials. BMC Med. 2024;22:110.
22. Kaltsas A, Zachariou A, Markou E, Dimitriadis F, Sofikitis N, Pournaras S. Microbial dysbiosis and male infertility: understanding the impact and exploring therapeutic interventions. J Pers Med. 2023;13:1491.
23. Barbonetti A, Cinque B, Vassallo MR, Mineo S, Francavilla S, Cifone MG, *et al*. Effect of vaginal probiotic lactobacilli on *in vitro*-induced sperm lipid peroxidation and its impact on sperm motility and viability. Fertil Steril. 2011;95:2485-8.
24. Chen XL, Gong LZ, Xu JX. Antioxidative activity and protective effect of probiotics against high-fat diet-induced sperm damage in rats. Animals (Basel). 2013;7:287-92.
25. Dardmeh F, Alipour H, Gazerani P, Van Der Horst G, Brandsborg E, Nielsen HI. *Lactobacillus rhamnosus* PB01 (DSM 14870) supplementation affects markers of sperm kinematic parameters in a diet-induced obesity mouse model. PLoS One. 2017;12:e0185964.
26. Quigley EM. Prebiotics and probiotics in digestive health. Clin Gastroenterol Hepatol. 2019;17:333-44.
27. Whiteside SA, Razvi H, Dave S, Reid G, Burton JP. The microbiome of the urinary tract--a role beyond infection. Nat Rev Urol. 2015;12:81-90.
28. Tvrdá E, Benko F, Ďuračka M. Oxidative stress as an underlying mechanism of bacteria-inflicted damage to male gametes. Oxygen. 2022;2:547-69.
29. Magill RG, MacDonald SM. Male infertility and the human microbiome. Front Reprod Health. 2023;5:1166201.
30. Bahar AF, Lestari SW, Abutari CA, Pramesti MP, Narulita P. A review of probiotics role in enhancing sperm quality. J Glob Pharma Technol. 2019;11:230-5.
31. Wang Y, Xie Z. Exploring the role of gut microbiome in male reproduction. Andrology. 2022;10:441-50.