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Effects of Probiotic Supplementation on PCOS Outcomes

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Abstract

Polycystic ovarian syndrome (PCOS) is a multifactorial metabolic, endocrinologic, and gynecologic condition affecting up to 5 million women in the United States. It is a disease characterized by oligo- or anovulation, hyperandrogenism, and/or polycystic ovaries. Phenotypic presentation can include irregular menstrual cycles, obesity, hirsutism, insulin resistance, or difficulty conceiving. If untreated, PCOS can result in a sequelae of chronic disease burden. Current standard of care consists of metformin for blood sugar control, oral contraceptives for menstrual regularity, and spironolactone for androgen imbalance, but newer research is identifying gut dysbiosis as a possible contributing etiology to disease development and symptomology. This literature review aims to investigate the effectiveness of probiotic supplement regimens in improving the gut microbiome and subsequent outcomes for patients with PCOS, specifically inflammatory, anthropometric, androgen, and blood sugar markers. A comprehensive literature review was performed using PubMed and Clinical Key databases. A variety of keywords and similar articles were used to identify studies that were further screened for inclusion and exclusion criteria. Studies were excluded if they were systematic reviews, published over 10 years ago, utilized non-human subjects, had poor study design, or looked at conditions outside of PCOS. There were 16 articles that met final criteria and were included in this review. Results showed significant improvement in androgen and inflammatory markers but were inconsistent in anthropometric and blood sugar findings. Further studies with longer duration and increased generalizability are needed to more adequately compare probiotics to standard of care in the treatment of PCOS.

Keywords: PCOS, probiotics, synbiotics, microbiome, testosterone, androgens, anthropometrics, glycemic control

Introduction

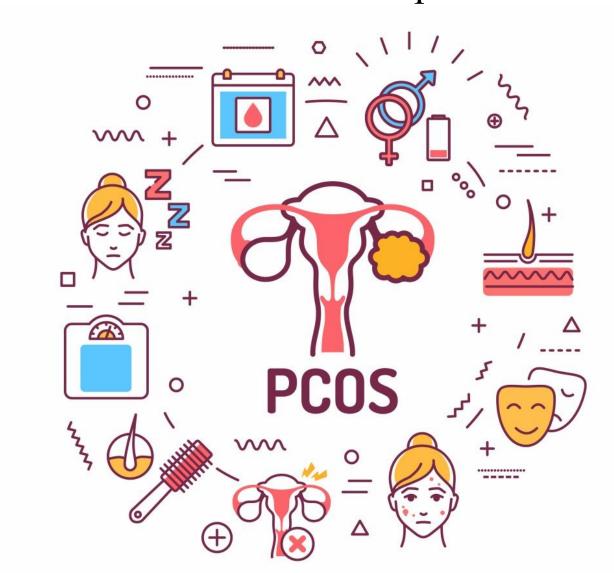
- PCOS affects 6-12% of reproductive age women in the United States (CDC, 2023)
- Phenotypic presentation can include obesity, hirsutism, irregular periods, and insulin resistance.
- Etiology is thought to be a combination of genetic and environmental factors, but further research has been done on the connection between the gut microbiome and PCOS.
- Studies have identified decreased fecal bacterial diversity and richness in PCOS patients which is negatively correlated with ghrelin and positively correlated with testosterone, luteinizing hormone (LH), anti-Mullerian hormone, and body mass index (BMI).

Statement of the Problem

PCOS is an increasingly common and underdiagnosed condition that, if unrecognized or undertreated, can increase risk for diabetes, metabolic syndrome, infertility, cardiovascular disease, and endometrial cancer. Standard of care currently focuses on treating insulin resistance (metformin), androgen imbalance (spironolactone), and anovulation (oral contraceptives) but does not address gut dysbiosis as a potential root cause of PCOS and its associated symptoms. A 2021 mixed-method study by Kaur et al. identified that PCOS patients were dissatisfied with the extended time to an official diagnosis, adequacy of information shared with them, and treatment options available. Patients included in this study cited that the internet, rather than their provider, was the primary source of information on their condition, resulting in conflicting and confusing recommendations for symptom management. This literature review aims to study the effectiveness of pre- and probiotic supplementation on PCOS outcomes. Supplementation and nutrition practices aimed at correcting imbalances in the gut microbiome could be a low-cost alternative or conjunctive therapy to standard of care in improving PCOS outcomes and satisfaction.

Research Question

What is the effect of probiotic regimens on metabolic and endocrinologic parameters in women with PCOS compared to standard of care?



https://www.kmobgyn.com/understanding-polycystic-ovarian-syndrome/

Literature Review

Probiotic Effect on Inflammatory Markers

- Daily probiotic supplementation for 12 weeks resulted in a significant decrease in high-sensitivity C-reactive protein (hs-CRP) and increase in nitric oxide (NO) (Nasri et al., 2018).
- Supplementation with prebiotic inulin-type fructans for 12 weeks led to decreased hs-CRP but did not have an impact on NO or blood pressure (Ziaei et al., 2022).

Probiotic Effect on Anthropometrics

- Synbiotic supplementation, in combination with lifestyle modifications, resulted in a significant decrease in BMI for women with PCOS (Chudzicka-Strugata et al., 2021).
- Twelve weeks of probiotic supplementation resulted in a small but statistically significant decrease in weight and BMI when compared to control group (Ahmandi et al., 2017).
- A different 12-week study did not find statistically significant improvements in BMI, waist circumference (WC), hip circumference (HC), or waist to hip ratio (WHR) after supplementation with synbiotic (Karimi et al., 2020).
- An eight-week study showed that synbiotic supplementation significantly improved WC and WHR did not have significant effects on weight or BMI when compared to baseline (Darvishi et al., 2021).

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				Bifidobacterium breve	
Streptococcus				Streptococcus	
thermophilus				thermophilus	

Figure 2: Probiotic Effect on Anthropometrics

Literature Review

Probiotic Effect on Androgen Levels

- Selenium and probiotic co-supplementation for 12 weeks significantly decreased total testosterone and hirsutism but not sex hormone binding globulin (SHBG) (Jamilian et al., 2018).
- Co-supplementation of vitamin D and probiotic for 12 weeks also showed improvement in total testosterone and hirsutism (Ostamohammadi et al., 2019).
- Pairing probiotic with diet and lifestyle changes for six months resulted in significant decrease in testosterone and LH/FSH ratio when compared to lifestyle changes alone with placebo (Kaur et al., 2022).

Probiotic Effect on Insulin and Blood Sugar Levels

- Synbiotic supplementation for 12 weeks resulted in a significant decrease in serum insulin, decrease in homeostatic model of assessment for insulin resistance (HOMA-IR), decrease in fasting plasma glucose (FPG), and increase in quantitative insulin sensitivity check index (QUICKI) when compared to placebo (Samimi et al., 2018).
- Comparatively, Karimi et al. (2018) found that there were no significant differences in FPG, two-hour post-prandial blood sugar, hemoglobin A1c (HbA1c), HOMA-IR, or QUICKI after 12 weeks of probiotic supplementation.

Study	Final Subject Number	Duration of Intervention	Probiotic Composition	Relevant Outcome Measures
Samimi et al. (2018)	n = 56	12 weeks	8 x 10 ⁹ CFU/day each Lactobacillus acidophilus Lactobacillus casei Bifidobacterium bifidum + 800 mg inulin	FPG: -4.1 mg/dL ($p = 0.04$) Serum Insulin: -2.8 μ IU/mL ($p = 0.002$) HOMA-IR: -0.7 ($p = 0.002$) QUICKI: +0.01 ($p < 0.001$)
Karimi et al. (2018)	n = 88	12 weeks	500 mg/day Lactobacillus acidophilus Lactobacillus casei Lactobacillus bulgaricus Lactobacillus rhamnosus Bifidobacterium longum Bifidobacterium breve Streptococcus thermophilus + inulin	FPG: insignificant PGF-2hr: insignificant HbA1c: insignificant HOMA-IR: insignificant QUICKI: insignificant

Figure 3: Probiotic Effect on Blood Sugar Control

Discussion

- A total of 16 studies were analyzed to assess probiotic effects on inflammatory, metabolic, anthropologic, and endocrinologic factors in PCOS. Cumulative results showed significant improvement in hs-CRP, total testosterone, hirsutism, LH/FSH ratios, and waist circumference. Impacts on other inflammatory markers, weight, BMI, insulin, and blood sugar levels continue to be inconsistent in research.
- The literature lacks generalizability as most studies were conducted in Iran. Because of this, participants may have a different baseline microbiome from cultural and geographic diet differences, as well as genetic differences, that may decrease applicability to other populations and regions.
- Future studies should continue to include randomized control trials but with larger and more diverse populations. Studies should have a longer intervention timeframe to assess efficacy more adequately. Additionally, fecal analyses should be included at baseline and at the end of intervention to examine alterations in the gut microbiome. Lastly, studies should be conducted that analyze the effect of probiotics compared to and in conjunction with standard of care, such as metformin, spironolactone, and contraceptive management.

Applicability to Clinical Practice

This research is relevant to clinical practice as probiotic supplementation is a low-risk therapeutic measure that may play a larger role with consistency over time in PCOS outcomes. The gut-brain axis and dysbiosis have been studied more heavily in the past several years and are being linked to negative health outcomes. A probiotic supplement, in addition to diet and lifestyle interventions, to improve patients' microbiome may be a helpful step in alleviating the polypharmacy and disease burden of conditions such as PCOS.

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