ORIGINAL ARTICLE

The role of probiotic in preventing recurrent urinary tract infections in pregnant women

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ABSTRACT

Background and Objective: Urinary tract infections (UTIs) are a major public health disease after upper respiratory tract infections, affecting more than 150 million people worldwide The study was aimed to identify the effects of probiotics in preventing recurrent UTIs in pregnant women.

Methods: This randomized controlled trial was conducted on pregnant females (1st and 2nd trimester), aged between 18 and 40 years presenting with UTIs. A total of 60 participants were equally and randomly allocated into two groups, i.e., Group A, who received probiotics along with conventional treatment, and Group B which acted as a control and received the placebo along with the conventional treatment. Urine D-R evaluations were performed pre and post intervention. The pre-post analysis was performed using a paired *t*-test as the data were normally distributed. To compare analysis among groups, an independent sample *t* test was applied. *p* (<0.05) was considered as statistically significant.

Results: Group-A (Probiotic) showed greater improvement among variables where the Leukocyte count improved from 15.2 ± 4.3 (cells/HPF) to 10.5 ± 3.1 (cells/HPF) (*p* = 0.001), and the level of nitrites improved from 0.8 ± 0.2 to 0.5 ± 0.1µmol/ml (*p* = 0.02) as compared to Group-B (*p* = 0.05).

Conclusion: The addition of probiotics in the conventional treatment regimen in pregnant females with recurrent UTIs leads to earlier recovery as depicted by the clinico-pathological assessment.

Keywords: Probiotics, urinary tract infection, pregnant females, prevention, treatment.

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Introduction

Urinary tract infections (UTIs) are a significant public health challenge, affecting more than 150 million people worldwide annually [1] and causing an economic burden of approximately US$ 6 billion each year.[2] As the second most common infectious disease after upper respiratory tract infections, UTIs are particularly prevalent among pregnant women, with a reported global prevalence of 23.9% in this population.[3] The recurrent nature of UTIs underscores the critical need for effective prevention and treatment strategies.[4–5] In the United States, UTIs are among the most common external infections, with incidence increasing markedly in young women aged 14-24 years.[6] Approximately 20% of women over the age of 65 and 11% of the general population are affected, with nearly 50% to 60% of older women experiencing at least one UTI during their lifetime.[7] Postmenopausal women, in particular, have a 10% annual prevalence of UTIs.[8] Most UTIs are caused by bacteria from the Enterobacteriaceae family, with uropathogenic *Escherichia coli* responsible for nearly 80% of cases, including 95% of the community- and hospital-acquired infections.[1] These bacteria can colonize the urinary tract either through adhesion to epithelial surfaces or biofilm formation.[9] The increased risk of UTIs during pregnancy is linked to physiological and hormonal changes, as well as other factors such as advanced maternal age, urinary incontinence, diabetes, and poor hygiene practices.[10,11]

Antibiotic therapy remains the standard treatment for UTIs but is increasingly challenged by the global rise in

antibiotic resistance, resulting in recurrent infections and escalating healthcare costs. Consequently, there is growing interest in alternative preventive strategies, including the use of probiotics.[12] Probiotics, defined as live microorganisms that confer health benefits when administered in adequate amounts, offer a promising intervention for recurrent UTIs. These beneficial bacteria, particularly strains of *Lactobacillus*, can inhibit uropathogenic microorganisms through various mechanisms. These include competing for adhesion sites on the urothelium, producing antimicrobial compounds such as bacteriocins and hydrogen peroxide, and modulating the host immune response.[13] Clinical studies have shown that probiotics can restore the vaginal and urinary microbiota, thereby reducing the recurrence of UTIs, especially in women prone to such infections.[14] Despite the growing body of evidence supporting probiotics, their role in preventing recurrent UTIs during pregnancy has been less extensively explored. Given the unique physiological changes in pregnancy, understanding the potential of probiotics as a non-invasive and safe alternative to antibiotics is crucial.

This study aims to investigate the effects of probiotics in preventing recurrent UTIs among pregnant women. By addressing this gap in the literature, the study seeks to provide valuable insights into the efficacy of probiotics as a preventive measure, ultimately contributing to improved maternal health outcomes.

Methods

The study was a randomized controlled trial conducted at a tertiary care hospital in King Abdullah Hospital Mansehra and Shaheena Jamil Teaching Hospital affiliated with Frontier Medical and Dental College, Abbottabad, Pakistan. The trial was registered with the clinical trials repository (TRN: NCT06429358) on 28-05-24. A total of 60 pregnant women with a history of recurrent UTIs were recruited, with 30 participants in each group. The selection criteria involved pregnant women (1st and 2nd trimester) aged 18-40 years, a history of recurrent UTIs (defined as two or more episodes in the past year), and singleton pregnancy. The exclusion criteria involved multiple gestations, history of preterm labor, chronic medical conditions (e.g., diabetes mellitus, immunodeficiency disorders), and use of antibiotics or probiotics within the past month. The study was approved by the Research Committee of Frontier Medical and Dental College Abbottabad following the guidelines as provided by the Belmont report for human subjects. All participants were given complete autonomy to exit from the research without assigning any reason. Moreover, all the information taken from the participants during the research was kept confidential, and the complete purpose of the research was informed to the participants prior to taking consent to participate in the research.

Participants were randomly allocated into two groups, i.e., Group A, who received probiotics, and Group B, control received the placebo treatment. The probiotic group received a daily oral supplement with *Lactobacillus rhamnosus* GG (10^9 colony-forming units per day).[13] The probiotic supplement was delivered in the form of easy-to-swallow capsules that were specifically prepared to maintain the viability and stability of the *L. rhamnosus* GG strain throughout the research period. Participants were told to take the probiotic supplement with water, ideally after meals, to maximize absorption and efficiency. Participants in the control group were given a placebo that looked and felt just like the probiotic pill. The placebo pills contained components that lacked any active probiotic strains or therapeutic benefits. This ensured that both participants and researchers were blinded, thereby minimizing potential biases in the evaluation of outcomes. Conventional treatment for UTI was administered to both groups. The procedure was tracked via regular follow-up after every 4 weeks visits and participant self-reporting. Participants in both groups were instructed to continue with the intervention until delivery to determine the long-term benefits of probiotic supplements on urinary tract health during pregnancy.

Urinary D-R evaluations were performed at two important times: pre-intervention and post-intervention. These evaluations sought to measure changes in urine parameters that were suggestive of urinary tract health. Parameters included: *Leukocyte count*: Leukocyte count (cells/HPF) in urine was evaluated before and after intervention to determine inflammation and probable UTIs. *Nitrites:* The presence of nitrites in urine (µmol/ml) before and after intervention was investigated as a marker of bacterial activity, particularly in UTIs caused by nitrate-reducing bacteria. *pH:* Urinary pH values were measured to assess changes in urine acidity, which can affect bacterial growth and UTI susceptibility.

Urine samples were collected aseptically before and after intervention and cultured to detect bacterial pathogens linked with UTIs.

Statistical analysis

Data were analyzed using Statistical Package for Social Science version 23. The pre and post test analysis was performed using paired *t*-test as the data were normally distributed. To compare analysis among group, independent sample *t* test was applied. p (<0.05) was considered as statistically significant.

Results

The demographic description of the participants as shown in Table 1 revealed that the mean age of the participants in group A was 25.63 ± 3.26 years whereas in group B the age was 26.23 ± 2.65 years.

Within the group, analyses were performed to compare pre-post differences in the outcome measures of the given intervention where the values of leukocytes, nitrites, pH, and urine culture were found to be significantly improved $p<0.05$ in both the groups that were group A and group B (Table 2).

Moreover, between groups comparison was performed using an independent *t*-test and the findings revealed that Group-A (probiotic)showed a significant reduction in the levels of inflammatory markers ($p < 0.05$) in comparison to Group-B (placebo) (Table 3) with a positive trend in culture sensitivity testing also.

Discussion

The findings of our study showed improvement in biochemical variables associated with UTI among both groups receiving probiotics and placebo along with the standard care. However, the results were more significant in the group that received probiotics along with the standard care ($p < 0.05$). However, the question of whether probiotics help prevent UTIs is difficult to answer yet. Studies using different populations, delivery systems, or probiotics have shown inconsistent results, and data may be available to support arguments for and against the benefits of probiotics. Currently, most of the literature claims antibiotics as a significant contributor to managing UTI. When it comes to growing the immune system, good probiotics can be very beneficial.[14]

In a review published in 2023, on the impact of probiotics on clinical and public health, the findings showed that the use of probiotics to prevent and treat UTIs will reduce the overuse of antibiotics, which is important for preventing

Table 1. *Showing clinico-demographic details of participants.*

Variables		Group A (*n* = 15)	Group B (*n* = 15)
Age (Mean ± SD)		25.63 ± 3.26	26.23 ± 2.65
Gestational age (Mean ± SD)		17.86 ± 5.35	18.66 ± 5.44
History of UTIs	3 months	4 (26.7%)	3 (20%)
	6 months	5 (33.3%)	5 (33.3%)
	9 months	-	3 (20%)
	1 year	6 (40%)	4 (26.7%)

Table 2. *Within the group analyses of variables for UTI assessment.*

Variables	Mean ± SD Pre	Mean ± SD Post	*p*-value
Group A (Probiotic group)			
Leukocyte (cells/HPF)	15.2 ± 4.3	10.5 ± 3.1	0.001
Nitratis µmol/ml	0.8 ± 0.2	0.5 ± 0.1	0.02
pH	6.2 ± 3.2	6.4 ± 1.5	0.04
Group B (Control group)			
Leukocyte (cells/HPF)	16.5 ± 2.3	14.25 ± 2.1	0.04
Nitrites µmol/ml	0.9 ± 0.3	0.8 ± 0.2	0.05
pH	6.49 ± 1.5	6.6 ± 0.9	0.04

SD; Standard Deviation.

Table 3. *Comparison of variables between groups.*

Variables	Group A	Group B	*p*-value
Leukocytes (cells/HPF)	14.25 ± 2.1	10.5 ± 3.1	<0.001
Nitratis (µmol/ml)	0.8 ± 0.2	0.5 ± 0.1	0.03
pH	6.6 ± 0.9	6.4 ± 1.5	0.04

infections.[15] Additionally, probiotics can prevent UTIs in vulnerable populations such as pregnant women and the elderly. Probiotic use may also improve the quality of life in patients with recurrent UTIs.[16] Sadeghi-Bojd et al.[17] in 2020 conducted a randomized controlled trial on 181 children who were equally divided into two of the treatment groups namely: probiotics and placebo. The findings showed that in children with normal urine output, probiotics were more effective than placebo in reducing the risk of recurrent UTIs after an initial febrile UTI.[17] In another study, conducted on 174 postmenopausal women that suffered from recurrent UTIs were given oral probiotics, vaginal probiotics, and a combination of both. The findings showed that prophylactic vaginal probiotic supplementation or combined with oral probiotics was effective in preventing symptoms of UTIs.[18]

In a recent systematic review and meta-analysis published in 2024, the effects of probiotics on UTI were analyzed. The findings showed that the odds ratio of having recurrent UTI was 0.94 (95% CI; 0.88-0.999; *p*-value = 0.046) among patients who were in placebo treatment as compared to those children who were on probiotics.[19] Contrary to these findings, a systematic review published in 2021 on the efficacy of probiotics in managing UTI among postmenopausal women revealed that probiotics showed no significant benefit compared to placebo in reducing UTI recurrence. Studies showing significant benefits may be biased by the presence of cranberry extract in probiotic supplements.[12] Likewise, in another systematic review published in 2022, a total of 9 articles with a total sample of 772 with a mean age of 34.2 participants were taken in which the effects of probiotics were determined in the prevention of recurrent UTI. The findings showed that two studies favored probiotic effects and the rest showed inconclusive results.[20] Using probiotics to treat cystitis and UTIs is promising, but not all studies show positive results; some have shown side effects.[21] These findings suggest that more research on a large scale with different target populations needs to be done to identify the conclusive effects of probiotics in preventing recurrent UTI, particularly among pregnant females.

Limitations of the study

Despite being a prevalent condition, the sample size used in the study was small owing to the vulnerability of the selected patient population, i.e., pregnant females. This may impact the generalizability of the results. Furthermore, the precise results of culture sensitivity testing are not made part of this study as a variable.

Conclusion

Supporting the conventional treatment regimen with probiotics in pregnant females having recurrent UTIs leads to a significant reduction in urinary inflammatory biomarkers thus resultantly an earlier recovery is seen.

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List of Abbreviations

UTIs	Urinary tract infections
SD	Standard deviation

Conflict of interest

None to declare.

Grant support and financial disclosure

None to disclose.

Ethics approval

The study was approved by the Ethics Committee of Frontier Medical and Dental College Abbottabad vide Letter No. 3388 dated 15-5-2024 through Clinical Trials Repository (TRN: NCT06429358) dated 28-05-24.

Author's contributions

SK, SUR, SB: Main concept and design of the study, acquisition and analysis of data, drafting of manuscript, critical intellectual input.

SJK, SAK, SZ: Drafting of manuscript and data acquisition and analysis, critical scientific and technical input.

ALL AUTHORS: Approval and responsibility for the final version of the manuscript to be published.

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