Patient Preference and Adherence

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Exploring Factors Affecting Acceptance of Fecal Microbiota Transplantation for Patients with Recurrent Urinary Tract Infections: a Descriptive Qualitative Study

Hongyuan Liu[1,*], Yaodi Wei[1,*], Zhenyi Xu[2,*], Hao Lin[2,*], Yu Zhao[1], Shiyu Wang[1], Fengbao Gao[1], Ninghan Feng[2], Alan J Wolfe[3], Fengping Liu[1]

[1]Wuxi School of Medicine, Jiangnan University, Wuxi, People's Republic of China; [2]Department of Urology, Affiliated Wuxi No. 2 Hospital, Nanjing Medical University, Wuxi, People's Republic of China; [3]Department of Microbiology and Immunology, Stritch School of Medicine, Loyola University Chicago, Maywood, IL, USA

*These authors contributed equally to this work

Correspondence: Alan J Wolfe, Department of Microbiology and Immunology, Stritch School of Medicine, Loyola University Chicago, Maywood, IL, USA, Email awolfe@luc.edu; Fengping Liu, Wuxi School of Medicine, Jiangnan University, Wuxi, People's Republic of China, Email liulaoshiyc@jiangnan.edu.cn

Purpose: Patients with recurrent urinary tract infections face complex management challenges. Fecal microbiota transplantation is a superior treatment for chronic infectious diseases, but limited patient knowledge affects treatment decisions. This study aims to identify factors associated with hesitancy towards fecal microbiota transplantation among patients with recurrent urinary tract infections, to help physicians and nurses in providing accurate and useful information to patients.

Patients and Methods: A descriptive qualitative approach was employed, utilizing semi-structured interviews conducted with patients experiencing recurrent urinary tract infections who expressed hesitancy towards fecal microbiota transplantation. The interviews took place between September 2021 and December 2022. Thematic analysis was conducted on the semi-structured interviews to identify perceived facilitators and barriers associated with fecal microbiota transplantation.

Results: The analysis included interviews with thirty adult female patients with recurrent urinary tract infections. Four facilitators influencing patients' decision-making regarding fecal microbiota transplantation were identified: (1) the motivating role of hope and expectations for active patient participation; (2) the influence of healthcare providers, as well as family members and friends on patients' decisions to pursue fecal microbiota transplantation; (3) the patients' perception of fecal microbiota transplantation as a low-risk treatment option; and (4) the dedication to the advancement of medical treatments. In contrast, two primary barriers to accepting fecal microbiota transplantation were identified: (1) that conventional treatment controls disease activity, while fecal microbiota transplantation effects remain uncertain; and (2) that safety concerns surrounding fecal microbiota transplantation.

Conclusion: Comprehensive information about fecal microbiota transplantation, including donor selection, sample processing, the procedure, and potential discomfort, is essential for patients and families to make informed treatment decisions.

Registration: CHiCTR2100048970.

Keywords: barriers, decision making, facilitators, fecal microbiota transplantation, qualitative study, recurrent urinary tract infections

Introduction

Urinary tract infection (UTI) is a prevalent bacterial infection, particularly among women.[1] It is estimated that over 50% of women experience a UTI in their lifetime, with 30%-40% of cases progressing to recurrent urinary tract infections (rUTIs).[2] The high prevalence and recurrence rates of rUTIs impose significant economic burdens on healthcare systems and individuals.[3] Globally, UTIs account for approximately 150 million cases annually, resulting in healthcare expenditures exceeding 6 billion dollars.[4] Aside from the financial costs and physical pain, rUTIs often are accompanied by

Received: 29 November 2023
Accepted: 23 March 2024
Published: 17 June 2024

symptoms of anxiety, depression, and even suicidal ideations, further impacting patients' well-being.[5,6] If left untreated, rUTIs can worsen and lead to complications such as bacteremia and septic shock.[7] Additionally, patients with UTIs face an increased risk of urinary incontinence, renal scarring, and renal injury.[8–10]

Traditional treatment approaches for rUTIs rely heavily on antibiotics. However, the escalating rates of antibiotic resistance have rendered these treatments increasingly ineffective.[11] Moreover, antibiotic resistance in UTIs has been associated with higher mortality and disability rates.[12] Therefore, there is an urgent need to explore non-antibiotic alternatives for the management of rUTIs.

Fecal microbiota transplantation (FMT), the transfer of stool from healthy individuals to patient with disease, has been proved its efficacy in treating of various diseases. And it is generally considered to be tolerable and safe, with a variety of delivery options available, such as oral cryocapsule ingestion, enema administration, introduction via nasojejunal tube, and direct delivery through colonoscopy.[13] Recent years, emerging research has highlighted the significance of the "gut microbiota-UTI axis" and its impact on rUTIs.[14,15] For example, Magruder et al noticed that the composition of gut microbes played a role in rUTIs.[16] As fecal microbiota transplantation (FMT) has been demonstrated to have a substantial effect for Crohn's disease,[17] and UTI is the most common genitourinary complication in Crohn's disease,[18] attempts have been made to apply FMT to the treatment of rUTIs. Tariq et al observed a decrease from 4 to 1 rUTI episode per year post-FMT.[19] Similarly, Biehl et al documented that a case of a 50-year-old kidney transplant patient with 8 UTI episodes in 2 years, who remained free of infection for 9 months after receiving frozen capsulized microbiota.[20] Jeney et al conducted a study in which they recruited 10 patients with rUTIs who received FMT. The results showed that the median number of episodes in rUTIs patients generally decreased after FMT compared to the pre-FMT period.[21] Finally, Aira et al reported on a 93-year-old woman with rUTIs who experienced 3 episodes a year, showing that she achieved a complete remission after undergoing FMT.[22]

The promising results of recent studies indicate that FMT is a potential strategy for the treatment of rUTIs. However, it is important to note that a significant proportion of the general population lacks knowledge and awareness about FMT.[23] This lack of understanding may influence patients' decisions when considering FMT as a treatment option for rUTIs. While limited research attribute to identify the factors associated with FMT for rUTI patients. Therefore, it is essential for us to identify the factors associated with FMT for rUTI patients, which can aid physicians and nurses in providing accurate and useful information to their patients, enabling them to make informed decisions about whether FMT is a suitable option for their rUTI treatment.

Methods

Study Design

A qualitative study reported in compliance with the Consolidated Criteria for Reporting Qualitative Research (COREQ).[24]

Participants

This study was conducted in the urology outpatient departments of the Second People's Hospital of Wuxi, China. Semi-structure interviews took place between September 2021 and December 2022 with patients diagnosed with rUTIs. Eligibility for participation in our study was extended to patients who were approached to participate in a clinical trial (CHiCTR2100048970) evaluating the efficacy of FMT for rUTIs, irrespective of their acceptance or refusal to participate in the trial.

In total, 30 patients were interviewed, 22 had opted for fecal microbiota transplantation (FMT) as a treatment method, while the remaining 8 individuals declined FMT. Inclusion criteria for interviewers were as follows: ① age 18 years or older; ② female patients with rUTIs: rUTIs were defined as experiencing ≥3 UTIs within a 12-month period or ≥2 UTIs within 6 months. UTI consisted of a clean-catch midstream urine quantitative culture with a bacterial colony count $\geq 10^3$/mL and the presence of urinary tract symptoms.[25] ③ Good communication and understanding skills. Exclusion criteria encompassed the following: organic secondary causes for recurrent UTI such as vesicoureteral reflux, cystocele, neurogenic bladder, etc.

Data Collection

Patients were informed about the clinical trial by professional teams (FPL, HYL, YDW, YZ, and SYW). We extended an invitation to all patients visiting our urology outpatient department who expressed their willingness to participate in interviews, regardless of whether they underwent FMT. However, We employed purposive sampling combined with maximum differentiation sampling to choose participants. We aimed to include participants with diversity in age, educational background, disease duration, and disease severity to encompass a wide range of perspectives. In total, all the interviews began after they made a decision about fecal microbiota transplantation. The purpose of the study was thoroughly explained to the patients before the interview, and they were informed that the interview would be recorded, and that the data would be used for research purposes. Patients were assured that they could withdraw from the interview at any time without any repercussions. The present study received ethical approval from the Ethical Review Board of Wuxi No.2 People's Hospital (ref: 2021Y-8).

To ensure the quality of the interviews, the interviewer underwent advanced training in qualitative research methods. In addition, we incorporated the decision-aids theory into the interview process, utilizing questions such as "Have you ever heard of FMT?" and "What factors influenced your decision regarding FMT for rUTIs?" The interviewers skillfully employed techniques like restatement or clarification when necessary to ensure comprehensive and authentic data collection.[26] Non-verbal cues, including the patients' emotional body language and facial expressions, were also recorded. On average, each interview lasted approximately 60 minutes. We conducted interviews until three consecutive subjects did not provide any new analytical information, indicating that saturation of codes had been reached.

Data Analysis

Data analysis was conducted by researchers HYL, YDW, YZ and FPL using a thematic analysis.[27] We independently reviewed the initial transcripts for overall comprehension and identified preliminary coding categories. Subsequently, we held meetings to discuss the transcripts line by line and assigned initial codes to relevant categories. Any disagreements were resolved through team consensus on the meaning of quotations. One investigator (FPL) then used the codes to review the remaining transcripts, determining that saturation had been reached after 30 interviews. In our final meetings, we developed broader categories and identified overarching themes by comparing the data across transcripts. This iterative process continued until all investigators agreed upon the final themes and quotations within each theme.

Rigour

Interviewers had no pre-existing relationships with participants, and pre-interviews with interviewers were conducted to clarify their assumptions regarding the research questions before the interviews. Researchers reflected on each step of data analysis, and the team analysis and theme development method helped reduce bias.[28]

Results

Demographic Characteristics

An in-depth qualitative study was undertaken to explore the experiences of 30 patients who had recurrent urinary tract infections (rUTIs) during the period between September 2021 and December 2022. The study participants consisted of individuals aged between 26 and 79 years. Among the participants, 22 had opted for fecal microbiota transplantation (FMT) as a treatment method, while the remaining 8 individuals declined FMT. For a more comprehensive overview of the participants' characteristics please refer to Table 1. To assess the severity of UTI symptoms, the participants maintained symptom diaries, and the collected data were used to assign symptom scores.[29] The primary objective of the interviews was to gain insights into the factors that either facilitated or hindered the adoption of FMT, as recounted by the participants.

Drivers of FMT Participation

The Motivating Role of Hope and Expectations for Active Patient Participation

Current Available Therapies are Ineffective and Associated with Significant Adverse Effects

Most participants expressed their dissatisfaction with the existing therapies for rUTIs, reporting antibiotic insensitivity.

Table 1 Patient Characteristics

Characteristics	Number	Percentage (%)
Age		
18–29	1	3
30–39	5	17
40–49	6	20
50–59	6	20
60–69	7	23
70+	5	17
Educational level		
Elementary School and below	9	30
Junior Middle School	9	30
Senior middle school or secondary	6	20
College graduate or above	6	20
Personal monthly income		
≤3000	16	53
3001–6999	8	27
≥7000	6	20
rUTI Duration (yrs)		
≤5	15	50
5–10	8	27
10–15	2	6
15–20	3	10
≥20	2	6
Symptoms at inclusion		
Mild	5	17
Moderate	7	23
Severe	18	60
Knowledge of FMT since…		
First visit	8	27
Had never visit	22	73
Effect of Traditional Treatments		
Ineffective	17	57
Poor efficacy	4	13
Very effective	9	30

Notes: *P6/P7/P13/P24/D1/D4: The interviewees were patients and their family members who lived with the patients.
Abbreviations: FMT, Fecal Microbiota Transplantation; rUTI, recurrent Urinary Tract Infection.

They had tried various treatments such as Chinese herbal medicine, acupuncture, probiotic preparations, and unconventional methods like blood-letting therapy, but none of these showed significant efficacy. This led to frustration and a feeling of having exhausted all other options. FMT emerged as a last resort for these patients, representing their only hope for a potential cure or symptom relief.

I have tried a variety of treatments for rUTIs but have not experienced any improvement. I have undergone multiple courses of antibiotics such as Cephalosporin and Nitrofurantoin, which were previously effective but no longer work for me. In searching for alternative options, I have visited Traditional Chinese Medicine hospitals and received various Chinese herbs and therapies, but these treatments also failed to provide any relief. I have further explored online probiotic supplements, hoping for a solution without adverse effects, but those did not improve my condition either… Feeling frustrated and with limited choices remaining, I made the decision to participate in a clinical trial involving FMT without hesitation. FMT represents my last chance for a potential cure or symptom relief. [Participant 1]

Many participants expressed concerns about the adverse effects of long-term antibiotic use and the potential disruption of immunity and the gut microbiome. The concerns about the side effects and experiences of serious reactions to antibiotics further motivated patients to explore alternative therapies like FMT.

I have been diagnosed with rUTIs for more than 20 years, and I was used to taking antibiotics when it comes back after treatment. Now, unfortunately, the antibiotics have become ineffective, resulting in pulmonary fibrosis. I deeply regret not having explored alternative therapies sooner. [Participant 18]

I wholeheartedly support my mother's decision to undergo FMT. I firmly believe that the prolonged use of antibiotics for managing infections can have a detrimental effect on the delicate balance of the gut microbiome. This disruption can subsequently lead to various problems, including intestinal infections, which based on the information I have received, may be linked to UTIs. [Participant 7]

Perceived Disease Severity

Patient-perceived severity of recurrent urinary tract infections (rUTIs) was identified as a crucial motivator for the participants' positive response to FMT. While most UTIs are not considered serious or life-threatening, the experience of individuals with rUTIs can vary significantly. Some individuals may have more severe symptoms, frequent recurrences, or complications that greatly impact their daily lives. The participants in this study represent a subgroup of patients who have been significantly affected by their rUTIs and are actively seeking a more effective solution to alleviate their symptoms and improve their quality of life.

I was diagnosed with my first UTI 8 years ago. At the beginning, the urinary symptoms were mild, so it did not immediately prompt me to visit the hospital or seek further examination. I questioned why it recurred. Usually, the frequency of urination was every ten minutes, accompanied by pain during peeing and afterward. Sometimes, I cry because of the unbearable pain. I decided to participate in this trial because of my serious symptoms of frequent urination and pain. I have been suffering from this condition, and I had excruciating pain. [Participant 1]

Certain participants became aware of the incurable nature of rUTIs, which heightened their feelings of hopelessness. The terms "incurable" and "refractory" were spontaneously mentioned by respondents when discussing FMT, reflecting their perception of the characteristics of rUTIs from frequently searching for specific information online. Due to their apprehension regarding UTI recurrence, these individuals are highly motivated to explore FMT or other emerging therapies.

I am excessively worried that my condition may worsen over time, leading to other health problems such as various types of damage to my bladder. I become agitated and aggressive knowing that the disease is incurable. I constantly worry about what my future will look like if there is no way for me to recover. I am not sure about the severity of rUTIs. Therefore, I have diligently pursued alternative remedies in my quest for a solution. Unfortunately, despite my efforts, it is disheartening to acknowledge that no other viable options are currently accessible to me. [Participant 2]

These statements highlight the profound impact of rUTIs on the participants' lives and their urgent desire to find a more effective treatment option, such as FMT, to address the severity of their symptoms and the limitations of current therapies.

Low Quality of Life

rUTIs have a significant impact on patients' daily lives, affecting various aspects such as work, sleep, sexual relationships, and social activities. Most participants expressed dissatisfaction with their restricted mobility due to frequent urination, leading to a lack of social connections.

My rUTIs have affected every part of my life. I avoid using public transit and prefer driving my car because I need to pee three or four times even for short distances of 15 minutes. I have a urinal bottle toilet in my car. At work, I often drink less water to reduce bathroom trips. The urgent need to use the bathroom frequently interferes with important moments such as conversations with important people and decision-making. Nowadays, I have withdrawn from social life except for work. Life feels meaningless as I get stuck dealing with these rUTIs. I have to suppress the urgency to use the bathroom whenever I go out. [Participant 10]

More than half of the participants reported experiencing serious sleep disorders. Three individuals resorted to taking hypnotics due to frequent urination, anxiety, and depression.

I cannot sleep well at night because I am constantly waking up to pee. If the frequency of nighttime urination reduced, I am sure I would be able to sleep better. However, I struggle with falling asleep, and sometimes I have to take sleeping pills. [Participant 14]

Many participants affected by rUTIs highlighted the impact on intimacy and sexuality. Younger participants expressed a sense of dissatisfaction as they believed there were bacteria residing in their bladder. Additionally, frequent urination decreased their sexual desire both in terms of frequency and intensity. Five young individuals reported a loss of sex drive.

In addition to this, I have noticed a puzzling pattern: every time I engage in sexual activity with my husband. I experience a urinary tract infection within the following day or two. This recurring phenomenon has raised concerns for both of us. My husband has undergone medical examinations, and no issues were detected. Furthermore, this situation has led to anxiety regarding sexual activity due to the accompanying frequency of urination. [Participant 5]

Patients' uncomfortable feelings such as anxiety, depression, and fear heightened their expectations of FMT. For example, some participants developed a fear of drinking water due to the associated frequent urination and pain. Driven by desperation, the participants expressed a strong interest in FMT.

Sometimes I just feel like I am a walking corpse, and my body parts are dead. FMT is my last hope. [Participant 1]

I feel anxious. In fact, I have contemplated suicide. My entire daily routine revolves around urination. I have sought various therapies without success. Thus, I want to try FMT. [Participant 8]

These statements underline the profound negative impact of rUTIs on patients' quality of life, including physical discomfort, emotional distress, and social isolation. The participants' experiences further emphasize the urgent need for effective treatments, such as FMT, to alleviate their symptoms and improve their overall well-being.

The Influence of Healthcare Providers, as Well as Family Members and Friends on Patients' Decisions to Pursue FMT

The participants in the study actively sought advice from various sources, and their decision-making process was significantly influenced by healthcare professionals, family members, friends, and other trial participants. The support and affirmation received from these individuals played a crucial role in shaping the participants' confidence and ultimately their decision to participate in FMT.

Confidence Placed on Physicians

The level of trust placed in healthcare professionals emerged as a key factor motivating patients' decisions. More than half of the patients expressed a strong willingness to engage in FMT, primarily driven by their trust in healthcare professionals. As physicians often serve as the initial point of contact for rUTI patients within the healthcare system, participants readily accepted the option of FMT when it was presented to them. They believed that physicians had the responsibility to make treatment decisions on their behalf, which overshadowed concerns about potential adverse effects.

I believe that you would not treat us as guinea pigs, right? I trust that you are responsible for my well-being. I have to believe in it and give it a shot; otherwise, I cannot find a cure. It's my last chance. I am sure you would not carry out a trial without any scientific theories, right? Even though my education level is low, I have a high level of acceptance for FMT. One of my friends recommended a private hospital, but I have not visited because I do not trust them. [Participant 16]

In addition to consulting with physicians within the research group, participants sought recommendations from other healthcare providers, particularly those with extensive experience in urology. Positive attitudes toward FMT expressed by these experienced physicians further strengthened patients' confidence and engagement.

Before experiencing this latest attack, I visited a hospital where I consulted with a highly experienced doctor who has been practicing for over 30 years. During my visit, I took the opportunity to discuss FMT with the doctor and asked if she was familiar with this procedure. She told me that I could give it a try. These words of encouragement from an experienced professional will surely inspire me to go ahead with it. [Participant 14]

Participants Highly Valued Their Family Members' Positive Opinions

The participants in the study highly valued the positive opinions of their family members and considered them to be crucial in their decision-making process. The unwavering support and encouragement they received from their loved ones played a significant role in shaping their inclination towards participating in the FMT trial. This support system provided by their family members served as a source of strength and conviction, particularly among the elderly participants.

My daughter's opinion mattered a lot. She strongly recommended FMT, assuring me that it is a good treatment option with no side effects. She instilled confidence in me and gave me the reassurance I needed to consider FMT. Without her recommendation, I would have been hesitant to undergo FMT. To be honest, my condition is not extremely severe, but with my daughter's unwavering support, I felt more at ease. [Participant 23]

Positive Encounters Inspire Hope in FMT Decision-Making

Several participants highlighted the significant impact of positive encounters with successful cases of FMT on their decision-making process. These encounters served as a source of inspiration and instilled a sense of hope among the participants, influencing their decision to pursue FMT as a potential treatment option for their rUTIs.

Hearing about the positive experience of an elderly lady who underwent FMT for rUTIs was truly uplifting. Knowing that she has been free from episodes for nine months and no longer needs medication is incredibly encouraging. It gave me hope and reassurance that FMT could potentially bring about positive changes in my own condition. [Participant 4]

The Patients' Perception of FMT as a Low-Risk Treatment Option

During the interviews, it became evident that some patients had varying levels of knowledge about FMT, with some reporting limited understanding of the procedure. Despite this, participants generally perceived FMT as a natural treatment option with low risk, which played a crucial role in their acceptance of the therapy. In addition to the information provided by the research team, participants and their family members actively sought information online about the potential side effects of FMT to assess any associated risks. This proactive approach demonstrated their commitment to making informed decisions regarding their participation in the treatment. The participants' perception of FMT as a natural treatment with low risk and minimal side effects significantly influenced their willingness to engage in the therapy.

In fact, I took the initiative to gather additional information and make judgments about FMT beyond what the physicians told me. By seeking information and evaluating the potential risks associated with FMT, I adopted a proactive mindset to understand the procedure and its possible consequences. This experience empowered me to make a well-informed assessment of the suitability of FMT for the treatment of rUTIs. It strengthened my belief that FMT is a safe and potentially effective option worth considering in my mother's case, given her age-related concerns. Making informed judgments regarding her health requires careful consideration. It is important to note that my positive perception of FMT was shaped by the information I collected and my thorough understanding of the procedure. [Participant 6]

Interestingly, while most participants in the study reported limited knowledge about FMT, they did not express concerns that the procedure would worsen their conditions. It appears that their hopes for improvement and relief from their current situation may have overshadowed their ability to fully perceive or consider potential risks associated with FMT.

During my visit, I admitted to being unfamiliar with FMT until the doctor provided me with a comprehensive explanation of the procedure as part of an ongoing trial. Following this discussion, the doctor asked if I would be willing to consider FMT as a potential treatment option. Expressing my eagerness for improvement, I confidently expressed my desire to give it a try, firmly believing that it would be a step towards better health. Additionally, after discussing the procedure and its associated risks, I am convinced that FMT carries a low risk and minimal side effects… [Participant 9]

The Dedication to the Advancement of Medical Treatments

The dedication to medicine and the desire to contribute to the advancement of medical knowledge emerged as motivating factors for some participants in the trial. The commitment to helping others and the belief that their participation in the trial could not only provide hope for their own cure but also contribute to the progress of medicine were expressed by three participants.

Moreover, my participation in clinical trials and support for the advancement of medicine allows me to play a role in improving the lives of others and shaping the future of healthcare. [Participant 5]

Reasons for Their Refusal

That Conventional Treatment Controls Disease Activity, While FMT Effects Remain Uncertain

Several participants who chose not to participate in the trial cited the effectiveness of conventional treatments, particularly antibiotics, in controlling their UTIs. They viewed UTIs as a common and uncomplicated ailment and perceived the risks associated with enrolling in a trial with uncertain efficacy as unnecessary. These individuals expressed a preference for the simplicity and convenience of antibiotic treatment.

I see UTIs as a common condition that can be effectively treated with antibiotics. I have found my current antibiotic treatment to be sufficient and successful in managing my UTI symptoms. The convenience and simplicity of antibiotic treatment are important factors for me. [Decliner 4]

That Safety Concerns Surrounding Over FMT

Some participants, particularly those with a background in healthcare-related industries, expressed safety concerns as a primary reason for refusing to participate in the trial. They perceived FMT as a technology without standardized procedures and were apprehensive about the potential risks associated with it. The difficulty in controlling the process and the introduction of unknown bacteria into the body raised concerns about potential side effects and the possibility of inducing other diseases. These individuals, having knowledge in the field, were aware of the challenges in standardizing and controlling such procedures.

The main factor influencing my decision to decline FMT is safety concerns. I am particularly worried about the potential side effects and long-term implications that could arise from undergoing the procedure. There is also a concern regarding the possibility of FMT triggering other health conditions. Given that my elderly mother, who is the patient, lacks knowledge about FMT, it is essential for me to prioritize her overall well-being. Moreover, considering my professional involvement with microbes, I am particularly concerned about the control and standardization of human-derived bacteria in FMT. [Decliner 1]

Similarly, another participant, involved in medical device research and development, emphasized the high requirements and complexities of FMT as a research technology. They recognized the difficulties in controlling the process and acknowledged the potential problems that could arise if not properly managed.

It's difficult to control the process, and that can lead to problems if not properly managed. My experience in the medical field has made me aware of the challenges in standardizing and controlling such procedures. [Decliner 4]

For some participants, their existing health conditions, such as rheumatoid arthritis or poor immunity, played a significant role in their decision to decline FMT participation. They were hesitant due to their pre-existing health conditions and concerns about the potential impact of FMT on their overall well-being.

I have been dealing with rheumatoid arthritis for 5–6 years and rely on continuous medication for management. Due to my poor immunity and fear of FMT, I am hesitant to participate in it. [Decliner 2]

Additionally, the conventional notion that participating in clinical trials is equivalent to being a "guinea pig" influenced some participants' decision to decline FMT treatment. They perceived clinical trial participation as potentially dangerous to their health and were apprehensive about the unknown consequences. This perception led them to refuse participation not only in FMT but also in all clinical trials.

I worry about the potential risks and side effects associated with clinical trials. This has led me to refuse participation not only in FMT but also in all clinical trials. [Decliner 5]

Discussion

This qualitative research provides a valuable contribution to existing knowledge concerning the decision-making process of patients with rUTIs considering participation in FMT. It not only adds to the qualitative evidence base but also has practical implications for patient education and future clinical research related to FMT.

One noteworthy finding of our study is that the decision-making process of participants was notably influenced by their perception of the severity of the disease and the effectiveness of conventional treatments. This aligns with previous research conducted on the decision-making processes of cancer patients regarding clinical trial participation.[30] In the case of cancer patients, who often face rapid disease progression, the primary motivation for engaging in clinical trials is the hope of extending their life. Conversely, patients with rUTIs, who generally experience a relatively uncomplicated and slow-progressing condition, may exhibit less urgency to participate in clinical trials. In our study, participants' perception of the severity of rUTIs primarily relied on urinary symptoms and the frequency of recurrence. Patients who did not view rUTIs as a serious health concern were less inclined to seek help, even if conventional treatments had limited efficacy. On the other hand, patients who endured long-term urinary symptoms showed a greater inclination to consider alternative treatments like FMT. When conventional treatments proved ineffective, their expectations for FMT increased, often driven by a "gambler's psychology" where they were willing to take risks in the hopes of finding a successful treatment. In cases where the patient's condition was well-managed through conventional treatments, the perceived risks associated with participating in a clinical trial with potentially inconclusive results outweighed the incentives to participate. Consequently, patients in such situations may refuse to take part.

Interestingly, our study revealed a conflict between the ideal decision-making process, characterized by a careful consideration of risks and benefits, and the reality of decision-making. In the context of dilemmas and frustrations with conventional treatments, patients tended to overshadow the potential side effects of FMT and were more accepting of the treatment.

Another important aspect highlighted in our study is the impact of patients' quality of life on their decision-making process regarding clinical trial participation. While the evaluation of treatment effectiveness often encompasses the consideration of quality of life,[31,32] few studies have explicitly explored its influence on the decision to participate in clinical trials. For patients with rUTIs, who generally experience a low quality of life due to urinary tract symptoms and mental health issues,[33] this factor becomes particularly relevant. Our study revealed that patients whose urinary symptoms severely affected their quality of life exhibited a greater interest in participating in clinical trials. This indicates that participants not only display a willingness to take risks in trials for life-threatening conditions but also consider the potential impact on their quality of life as a crucial factor in their decision-making process. This finding underscores the importance of considering quality of life outcomes when evaluating the benefits and risks of clinical trial participation. Furthermore, our study highlights the significant role of invisible emotional complications in the decision-making process. Patients with rUTIs who experienced frequent recurrence, poor response to conventional treatments, and severe disturbances were more likely to experience anxiety and depression. This emotional burden may increase their receptiveness to emerging treatments, as they were in a state of desperation to find effective solutions to improve their quality of life. These findings align with previous studies that have demonstrated how emotional and psychological factors can influence patients' decision-making processes.[34,35]

Our study also emphasizes the significant role of healthcare providers, family members, and friends in the decision-making processes of patients with rUTIs considering FMT as a treatment option. This finding aligns with previous studies that have highlighted the influence of patients' social networks on decision-making.[36,37] In our study, patients with rUTIs expressed a preference for seeking recommendations and involving their family members in the decision-making process, particularly among elderly patients. Patients who received support from their family members exhibited stronger conviction to participate in the clinical trial. Conversely, those without familial backing were more likely to experience decisional delay or regret, as they heavily relied on the opinions of their loved ones. The role of healthcare providers, especially team physicians, in influencing clinical trial enrollment has been underscored in previous studies.[38,39] Patients tend to place a great deal of trust in their healthcare providers and rely on their recommendations when making healthcare decisions. However, our study provides an interesting perspective by showing that participants did not perceive clinical trials as a treatment option solely based on the recommendation of team physicians. Instead, some participants evaluated the information independently, considering various factors, seeking multiple opinions, and placing confidence in advice from non-team doctors.

The assurance of security emerges as an important factor in the decision-making process for clinical trial participation.[40,41] The negative stereotype of being a "guinea pig" in clinical trials, particularly drug trials, has been

widely recognized as a deterrent to trial enrollment. The perception of being treated as an experimental subject can have a detrimental effect on participants' sense of security within the research environment. Concerns may arise about potential mishaps or inadequate support throughout the research process.[42] As a result, participants may feel anxious or uncertain about their well-being and the overall success of the study. It is crucial for researchers to address these concerns by ensuring clear communication, providing comprehensive information about the study, and demonstrating their expertise and commitment to participant safety and care. By establishing a supportive and trustworthy environment, researchers can help alleviate these fears and foster a sense of confidence and security among participants.

In our study, participants perceived FMT as a low-risk intervention compared to other drug trials, which contributed to their sense of relative safety and increased their willingness to participate. The Internet played a crucial role in our study, serving as the fastest and most convenient source of information, a finding supported by the research of De Lacey and co-authors.[43] Participants proactively utilized the Internet to access relevant information and explore the clinical applications of FMT. This allowed them to acquire a comprehensive understanding of the intervention's potential efficacy and safety. Additionally, the availability of information about previous successful cases of FMT served as a morale booster for patients considering participation in clinical trials. When patients learn about positive outcomes and success stories from previous FMT cases, it can instil confidence and optimism regarding the potential effectiveness of the treatment. This positive reinforcement can play a significant role in their decision-making process and increase their willingness to participate.

It is interesting to note that participants with family members in healthcare-related industries, who possessed a better understanding of microbial technology, held a negative attitude towards FMT techniques. Their concerns primarily revolved around the potential for disease transmission and the challenges in controlling the quality of FMT, which they perceived as increasing trial risks.

Implications for Future Research and Clinical Practice

Based on our findings, we propose the following recommendations for researchers conducting FMT studies:

Prioritize trial safety: Safety should be the foremost concern in any clinical trial involving FMT. Researchers must take necessary precautions and create a safe environment for patients. This includes implementing rigorous screening and quality control measures to minimize the potential risks of FMT.

Enhance patient and family comprehension: It is crucial to enhance patients' and their families' understanding of FMT, including its benefits and risks, while clarifying its value. By doing so, we empower patients and their families to make informed decisions confidently. Additionally, involving family members in the decision-making process can enhance patient support and engagement.

Improve education on FMT: Many participants expressed a lack of prior knowledge about FMT and a desire for greater understanding. Researchers should prioritize educating patients and the general public about FMT, its mechanism of action, and its potential benefits.

Utilize peer education: Peer education can be a valuable tool for promoting enrollment in FMT. Patients who have undergone FMT can share their experiences and knowledge with potential participants, helping to address concerns, provide realistic expectations, and increase awareness of the treatment.

Limitations

We acknowledge several limitations in our study that should be considered:

Selection bias: Our study primarily recruited patients from outpatient settings, which may have resulted in a skewed sample. The inclusion of severely ill patients may have limited the perspectives of those who are less severely affected by rUTIs and their perceptions of FMT. Future studies should aim to include a more diverse range of patients to obtain a comprehensive understanding of their attitudes and decision-making processes.

Limited insight into non-participating patients: The limited number of patients who declined participation in the study and their tendency to provide brief reasons for refusal posed challenges in assessing their genuine attitudes towards FMT. Further research should explore alternative methods to gather comprehensive perspectives from non-participating patients to gain a more complete understanding of their decision-making process.

Potential interviewer bias: There may be a selection bias in the recruitment of interviewers, leading to a sample that primarily consists of individuals with higher household incomes. This may limit the generalizability of our findings and overlook the impact of economic conditions on decision-making. Future studies should aim to recruit a more diverse group of interviewers to address this limitation and capture a broader range of perspectives.

Lacking of the perspective of male patients: Urinary tract infection is well known to affect both genders, however women are mostly vulnerable to the infection because of anatomy and reproductive physiology. We were unable to recruit male patients who met the inclusion criteria due to low prevalence.

Conclusions

The findings from our qualitative interviews conducted during the clinical trial of FMT for patients with rUTIs underscore the significance of providing comprehensive information to patients and their families regarding various aspects of FMT. This includes donor selection criteria, fecal sample processing procedures, microbiota transfer procedures, potential pain and discomfort experienced during FMT, and adherence to clinical protocols. By addressing these aspects, researchers can facilitate better patient understanding, improve decision-making processes, and ensure the safe and effective implementation of FMT in clinical practice.

Abbreviations

FMT, Fecal microbiota transplantation; rUTI, recurrent urinary tract infection; rUTIs, recurrent urinary tract infections; UTI, Urinary tract infection; UTIs, Urinary tract infections.

Data Sharing Statement

Due to the sensitive nature of the questions asked in this study, survey respondents were assured raw data would remain confidential and would not be shared, so supporting data is not available.

Ethics Approval and Consent to Participate

This study was approved from the Ethical Review Board of Wuxi No.2 People's Hospital (ref: 2021Y-8) and conducted in accordance with the principles of the Declaration of Helsinki. The consent to participate in the interview has been recorded as well as permission to record it. Participants were informed that the interviews will be analysed and used for write paper.

Acknowledgments

The authors would like to express their sincere gratitude to the Department of Urology for their valuable assistance during the data collection phase of this study. Additionally, the authors extend special thanks to all the individuals who generously shared their personal experiences and stories, as their contributions were essential to the success of this research.

The authors declare that this article was published in Research Square on September 17, 2023, and has not been published in any other journal except for the preprint. Preprint doi: doi:10.21203/rs.3.rs-3256940/v1.

Funding

This work was supported by the Wuxi "Taihu Talents Program" Medical and Health High-level Talents Project [THRCJH20200901]; Wuxi "key medical discipline construction" Municipal Clinical Medical Center (municipal public health center) Project [LCYXZX202103]; and the Wuxi Technological Project [N20192047].

Disclosure

Dr Alan Wolfe reports grants and/or personal fees for investigator initiated study and/or member of scientific advisory board from Pathnostics, Urobiome Therapeutics, anonymous donor, and Neilsen Foundation, outside the submitted work. The authors declare no other competing interests in this work.

References

1. Foxman B. The epidemiology of urinary tract infection. *Nat Rev Urol*. 2010;7(12):653–660. doi:10.1038/nrurol.2010.190
2. Kwok M, McGeorge S, Mayer-Coverdale J, et al. Guideline of guidelines: management of recurrent urinary tract infections in women. *BJU Int*. 2022;130 Suppl 3(Suppl 3):11–22. doi:10.1111/bju.15756
3. Wagenlehner F, Wullt B, Ballarini S, Zingg D, Naber KG. Social and economic burden of recurrent urinary tract infections and quality of life: a patient web-based study (GESPRIT). *Expert Rev Pharmacoecon Outcomes Res*. 2018;18(1):107–117. doi:10.1080/14737167.2017.1359543
4. Lyonga EE, Toukam M, Nkenfou C, et al. Resistance pattern of Enterobacteriaceae isolates from urinary tract infections to selected quinolones in Yaoundé. *Pan Afr Med J*. 2015;21:105. doi:10.11604/pamj.2015.21.105.5469
5. Valentine-King M, Laytner L, Hines-Munson C, et al. Qualitative Analysis of a Twitter-Disseminated Survey Reveals New Patient Perspectives on the Impact of Urinary Tract Infection. *Antibiotics (Basel)*. 2022;11(12). doi:10.3390/antibiotics11121687
6. Alanazi MQ. Evaluation of Health-Related Quality of Life in Women with Community-Acquired Urinary Tract Infections Using the EQ-5D-3L in Saudi Arabia. *Patient Preference Adherence*. 2020;14:2419–2426. doi:10.2147/ppa.S277367
7. Ioannou P, Plexousaki M, Dimogerontas K, et al. Characteristics of urinary tract infections in older patients in a tertiary hospital in Greece. *Geriatr Gerontol Int*. 2020;20(12):1228–1233. doi:10.1111/ggi.14080
8. Shaikh N, Craig JC, Rovers MM, et al. Identification of children and adolescents at risk for renal scarring after a first urinary tract infection: a meta-analysis with individual patient data. *JAMA Pediatr*. 2014;168(10):893–900. doi:10.1001/jamapediatrics.2014.637
9. Mathur P, Malpiedi P, Walia K, et al. Health-care-associated bloodstream and urinary tract infections in a network of hospitals in India: a multicentre, hospital-based, prospective surveillance study. *Lancet Glob Health*. 2022;10(9):e1317–e1325. doi:10.1016/s2214-109x(22)00274-1
10. Hsiao CY, Yang HY, Hsiao MC, Hung PH, Wang MC. Risk Factors for Development of Acute Kidney Injury in Patients with Urinary Tract Infection. *PLoS One*. 2015;10(7):e0133835. doi:10.1371/journal.pone.0133835
11. Li X, Fan H, Zi H, et al. Global and Regional Burden of Bacterial Antimicrobial Resistance in Urinary Tract Infections in 2019. *J Clin Med*. 2022;11(10):2817. doi:10.3390/jcm11102817
12. Gharbi M, Drysdale JH, Lishman H, et al. Antibiotic management of urinary tract infection in elderly patients in primary care and its association with bloodstream infections and all cause mortality: population based cohort study. *BMJ*. 2019;364:l525. doi:10.1136/bmj.l525
13. Antushevich H. Fecal microbiota transplantation in disease therapy. *Clin. Chim. Acta*. 2020;503:90–98. doi:10.1016/j.cca.2019.12.010
14. Magruder M, Edusei E, Zhang L, et al. Gut commensal microbiota and decreased risk for Enterobacteriaceae bacteriuria and urinary tract infection. *Gut Microbes*. 2020;12(1):1805281. doi:10.1080/19490976.2020.1805281
15. Paalanne N, Husso A, Salo J, et al. Intestinal microbiome as a risk factor for urinary tract infections in children. *Eur J Clin Microbiol Infect Dis*. 2018;37(10):1881–1891. doi:10.1007/s10096-018-3322-7
16. Magruder M, Sholi AN, Gong C, et al. Gut uropathogen abundance is a risk factor for development of bacteriuria and urinary tract infection. *Nat Commun*. 2019;10(1):5521. doi:10.1038/s41467-019-13467-w
17. Johnsen PH, Hilpüsch F, Cavanagh JP, et al. Faecal microbiota transplantation versus placebo for moderate-to-severe irritable bowel syndrome: a double-blind, randomised, placebo-controlled, parallel-group, single-centre trial. *Lancet Gastroenterol Hepatol*. 2018;3(1):17–24. doi:10.1016/s2468-1253(17)30338-2
18. Peyrin-Biroulet L, Pillot C, Oussalah A, et al. Urinary tract infections in hospitalized inflammatory bowel disease patients: a 10-year experience. *Inflamm Bowel Dis*. 2012;18(4):697–702. doi:10.1002/ibd.21777
19. Tariq R, Pardi DS, Tosh PK, Walker RC, Razonable RR, Khanna S. Fecal Microbiota Transplantation for Recurrent Clostridium difficile Infection Reduces Recurrent Urinary Tract Infection Frequency. *Clin Infect Dis*. 2017;65(10):1745–1747. doi:10.1093/cid/cix618
20. Biehl LM, Cruz Aguilar R, Farowski F, et al. Fecal microbiota transplantation in a kidney transplant recipient with recurrent urinary tract infection. *Infection*. 2018;46(6):871–874. doi:10.1007/s15010-018-1190-9
21. Jeney SES, Lane F, Oliver A, Whiteson K, Dutta S. Fecal Microbiota Transplantation for the Treatment of Refractory Recurrent Urinary Tract Infection. *Obstet Gynecol*. 2020;136(4):771–773. doi:10.1097/aog.0000000000004052
22. Aira A, Rubio E, Vergara Gómez A, et al. rUTI Resolution After FMT for Clostridioides difficile Infection: a Case Report. *Infect Dis Ther*. 2021;10(2):1065–1071. doi:10.1007/s40121-020-00365-8
23. Zhang Y, Xue X, Su S, et al. Patients and physicians' attitudes change on fecal microbiota transplantation for inflammatory bowel disease over the past 3 years. *Ann Transl Med*. 2021;9(21):1619. doi:10.21037/atm-21-3683
24. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Health Care*. 2007;19(6):349–357. doi:10.1093/intqhc/mzm042
25. Arnold JJ, Hehn LE, Klein DA. Common Questions About Recurrent Urinary Tract Infections in Women. *Am Fam Physician*. 2016;93(7):560–569.
26. Partington G. Qualitative Research Interviews: identifying Problems in Technique. *Issues in Educational*. 2001;11(2):32–44.
27. Kiger ME, Varpio L. Thematic analysis of qualitative data: AMEE Guide No. 131. *Med Teach*. 2020;42(8):846–854. doi:10.1080/0142159x.2020.1755030
28. Rowley J. Conducting research interviews. *Management Research Review*. 2012;35(3/4):260–271. doi:10.1108/01409171211210154
29. McNulty CA, Richards J, Livermore DM, et al. Clinical relevance of laboratory-reported antibiotic resistance in acute uncomplicated urinary tract infection in primary care. *J Antimicrob Chemother*. 2006;58(5):1000–1008. doi:10.1093/jac/dkl368
30. Bell JAH, Forcina V, Mitchell L, et al. Perceptions of and decision making about clinical trials in adolescent and young adults with Cancer: a qualitative analysis. *BMC Cancer*. 2018;18(1):629. doi:10.1186/s12885-018-4515-2
31. Parameswaran R, McNair A, Avery KN, et al. The role of health-related quality of life outcomes in clinical decision making in surgery for esophageal cancer: a systematic review. *Ann Surg Oncol*. 2008;15(9):2372–2379. doi:10.1245/s10434-008-0042-8
32. Efficace F, Kemmler G, Vignetti M, Mandelli F, Molica S, Holzner B. Health-related quality of life assessment and reported outcomes in leukaemia randomised controlled trials - A systematic review to evaluate the added value in supporting clinical decision making. *Eur J Cancer*. 2008;44(11):1497–1506. doi:10.1016/j.ejca.2008.03.017
33. Ennis SS, Guo H, Raman L, Tambyah PA, Chen SL, Tiong HY. Premenopausal women with recurrent urinary tract infections have lower quality of life. *Int J Urol*. 2018;25(7):684–689. doi:10.1111/iju.13698

34. Bishop SJ, Gagne C. Anxiety, Depression, and Decision Making: a Computational Perspective. *Annu Rev Neurosci*. 2018;41:371–388. doi:10.1146/annurev-neuro-080317-062007
35. Paulus MP, Yu AJ. Emotion and decision-making: affect-driven belief systems in anxiety and depression. *Trends Cognit Sci*. 2012;16(9):476–483. doi:10.1016/j.tics.2012.07.009
36. Cartmell KB, Bonilha HS, Simpson KN, Ford ME, Bryant DC, Alberg AJ. Patient barriers to cancer clinical trial participation and navigator activities to assist. *Adv Cancer Res*. 2020;146:139–166. doi:10.1016/bs.acr.2020.01.008
37. Houghton C, Dowling M, Meskell P, et al. Factors that impact on recruitment to randomised trials in health care: a qualitative evidence synthesis. *Cochrane Database Syst Rev*. 2020;10(10):Mr000045. doi:10.1002/14651858.MR000045.pub2
38. Jenkins V, Farewell V, Farewell D, et al. Drivers and barriers to patient participation in RCTs. *Br J Cancer*. 2013;108(7):1402–1407. doi:10.1038/bjc.2013.113
39. Keusch F, Rao R, Chang L, Lepkowski J, Reddy P, Choi SW. Participation in clinical research: perspectives of adult patients and parents of pediatric patients undergoing hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant*. 2014;20(10):1604–1611. doi:10.1016/j.bbmt.2014.06.020
40. Madsen SM, Holm S, Riis P. Attitudes towards clinical research among cancer trial participants and non-participants: an interview study using a Grounded Theory approach. *J Med Ethics*. 2007;33(4):234–240. doi:10.1136/jme.2005.015255
41. Bleidorn J, Bucak S, Gágyor I, Hummers-Pradier E, Dierks ML. Why do - or don't - patients with urinary tract infection participate in a clinical trial? A qualitative study in German family medicine. *Ger Med Sci*. 2015;13:Doc17. doi:10.3205/000221
42. Massett HA, Dilts DM, Bailey R, et al. Raising Public Awareness of Clinical Trials: development of Messages for a National Health Communication Campaign. *J Health Commun*. 2017;22(5):373–385. doi:10.1080/10810730.2017.1290715
43. de Lacey SL, Sanderman E, Smith CA. Acupuncture in reproductive medicine: the motivations of infertile women to participate in a randomised controlled trial. *J Psychosom Obstet Gynaecol*. 2018;39(2):112–120. doi:10.1080/0167482x.2017.1308349