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A Systematic Review of the Effects of Probiotics and Synbiotics on Infection Incidence after Liver Transplant Surgery

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ABSTRACT: Among organ transplant operations, liver transplantation (LTX) has one of the highest risks of postoperative infection. This study aimed to systematically review the current evidence on the use of probiotics and synbiotics in reducing the incidence of postoperative infections in liver transplant recipients. A systematic search was performed to identify studies that investigated the role of probiotics and synbiotics in reducing postoperative infection rates in liver transplant recipients. Eight studies that qualified were included in the review. The results showed that probiotics and synbiotics effectively reduced the overall infection rates in liver transplant patients compared with the placebo or control groups. This positive effect might be attributed to improved intestinal barrier function, gut microbiota restoration, and decreased inflammation. Furthermore, probiotic treatment was associated with shorter durations of antibiotic use and hospital stays. The use of probiotics and synbiotics after LTX holds promise in decreasing postoperative infections and providing substantial advantages for patients. Probiotics have been shown to boost the levels of beneficial bacterial, decrease inflammation, fortify the intestinal barrier, lessen oxidative stress, and improve the generation of anti-inflammatory short-chain fatty acids. However, more extensive research is needed to identify the most effective probiotic strains and evaluate their effectiveness in this specific patient demographic.

Keywords: infections, liver transplantation, probiotics, synbiotics

INTRODUCTION

The history of liver transplantation (LTX) dates back to 1955 when Welch proposed an ectopic LTX in the abdominal cavity for the first time (Welch, 1955). Starzl et al. (1963) performed the world's first LTX on a three-year-old boy with biliary atresia. However, the initial outcomes were not promising as no patients had survived more than 23 days in the first five LTX procedures (Starzl et al., 1963). Nonetheless, modern medicine has significantly benefited from solid organ transplantation, particularly LTX, which has extended the life expectancy and improved the quality of life for millions of patients with end-stage liver disease and liver cancer (Ma et al., 2021).

Since the widespread adoption of transplant surgery in the 1950s and 1960s, infection complications have remained a leading cause of morbidity and mortality (Garibaldi, 1983). Among all organ transplant procedures, LTX has one of the highest rates of postoperative infections (Linares et al., 2009). LTX recipients are more susceptible to bacterial infections than recipients of other transplants because of the procedure's complexity, which involves penetration of the hepatobiliary system (Bennett et al., 2019). The incidence of postoperative infections in LTX has been reported to range from 30% to 70% (Kitt, 2022), with specific infections (e.g., invasive aspergillosis) occurring in approximately 2.7% of cases and pneumonia in 22.2% of cases (Liu et al., 2009; Farahani et al., 2023). Other prevalent infections include deep intra-abdominal infections, bacteremia, catheter-related infections, urinary tract infections, and surgical site infections (SSIs) (Bennett et al., 2019).

The current strategies to address this issue include preventing postoperative hyperglycemia (Kang et al., 2020), implementing care bundle strategies to reduce SSIs (Wassef et al., 2022), early cessation of mechanical ventilation (Zhang et al., 2020), perioperative use of antibiotics (Paya and Hermans, 1989), and non-absorbable antibiotic-based selective bowel decontamination (SBD) protocols (Emre et al., 1999).

Probiotics and synbiotics (combinations of probiotics and prebiotics) play essential roles in human physiology,

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including nutritional pathways, vitamin synthesis, drug metabolism, protection against infections, and recovery from illness (Davison and Wischmeyer, 2019). Probiotics can promote human health by modulating gut microbial populations, preventing enteric pathogens, enhancing the immune response, and gut homeostasis (Kerry et al., 2018). Meanwhile, synbiotics work synergistically to provide additional benefits beyond their actions (Flesch et al., 2014). Bacterial translocation is considered a primary cause of illness post-LTX, with translocated bacteria primarily originating from the gut (Ren et al., 2011). Bacterial translocation can occur because of intestinal barrier breakdown, intestinal microbiota disruption, and weakened immune system (Levitsky, 2006). The gut microbiota are crucial for maintaining intestinal homeostasis in the host (Bäckhed et al., 2005). However, this balance can be disrupted under pathophysiological conditions (Ren et al., 2011). According to Yu et al. (2008), the imbalance is mainly because of the reduction in the counts of *Bifidobacterium* and *Lactobacillus*. Previous studies have shown the promising effects of probiotics in reducing bacterial infections after LTX (Ma et al., 2021).

The present study aimed to systematically review the current evidence on the use of probiotics and synbiotics in preventing postoperative infections after LTX and to provide insights into protecting patients undergoing LTX from the complications of infection.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Page et al., 2021).

Search strategies

A search was conducted to find research articles published from 2000 to May 2024 that investigated the role of probiotics and synbiotics in reducing the overall infection rate after LTX. Electronic databases, including PubMed, Scopus, Web of Science, Science Direct, and Google Scholar, were used to search for articles. Moreover, relevant keywords, including "Probiotics," "Synbiotics," "Liver transplantation," "Hepatic transplantation," "Postoperative," "Infection," "Overall infection rate," "Sepsis," "Pneumonia," "Microbiome," "Liver function tests," either alone or in combination with "OR" and/or "AND," were used in the search. The reference lists of the identified studies, related projects, dissertations, congress papers, and pertinent reviews were also searched as gray literature to ensure that all relevant studies were included.

Study selection

The inclusion criteria included studies written in English, involving patients/animals undergoing LTX, and having at least two groups—one receiving probiotics/synbiotics and the other not. Meanwhile, the exclusion criteria included studies using overlapping databases or the same population and congress abstracts, dissertations, and relevant reviews.

Quality assessment

The quality of the included randomized controlled trials was evaluated using the Cochrane Risk of Bias 2 tool (Higgins et al., 2019). To conduct this study, a number of criteria were examined, including the effectiveness of random sequence generation, blinding, allocation concealment, handling of missing outcome data, detection of selective outcome reporting, and other potential sources of bias. Following the guidelines of the Cochrane Handbook, each category was classified as having a "low," "high," or "unclear" risk of bias (Supplementary Table 1, Supplementary Fig. 1 and 2). All disputes regarding data extraction and bias evaluation were settled with the help of a third reviewer.

Data extraction

Two researchers independently extracted all available data using the aforementioned inclusion criteria. A third author engaged in discussion to resolve any disagreements that might have existed among the researchers. The collected data included the name, nation, study design, year of publication, sample size, length of probiotic treatment, and evaluated results.

Ethics statement

This study was approved by the Ethical Committee of the National Nutrition and Food Technology Research Institute of Shahid Beheshti University of Medical (IR.SBMU.RETECH.REC.1403.247).

RESULTS

Thirty articles were initially identified from the specified databases in accordance with the PRISMA guidelines. Thereafter, four duplicates were eliminated. Out of the 26 titles and abstracts that were screened, six studies were excluded. This resulted in 20 studies. Among them, 12 studies were excluded because of the absence of the necessary factors, resulting in eight studies that met the criteria for evaluation in the current review (Fig. 1). Characteristics of the eligible studies, including author, country, study design, sample size, and intervention details, are summarized in Table 1.

Mallick et al. (2022) observed the use of Prowel® (*Lactobacillus acidophilus*, *Bifidobacterium longum*, *Bifidobacterium bifidum*, *Bifidobacterium lactis*, fructooligosaccharide, and

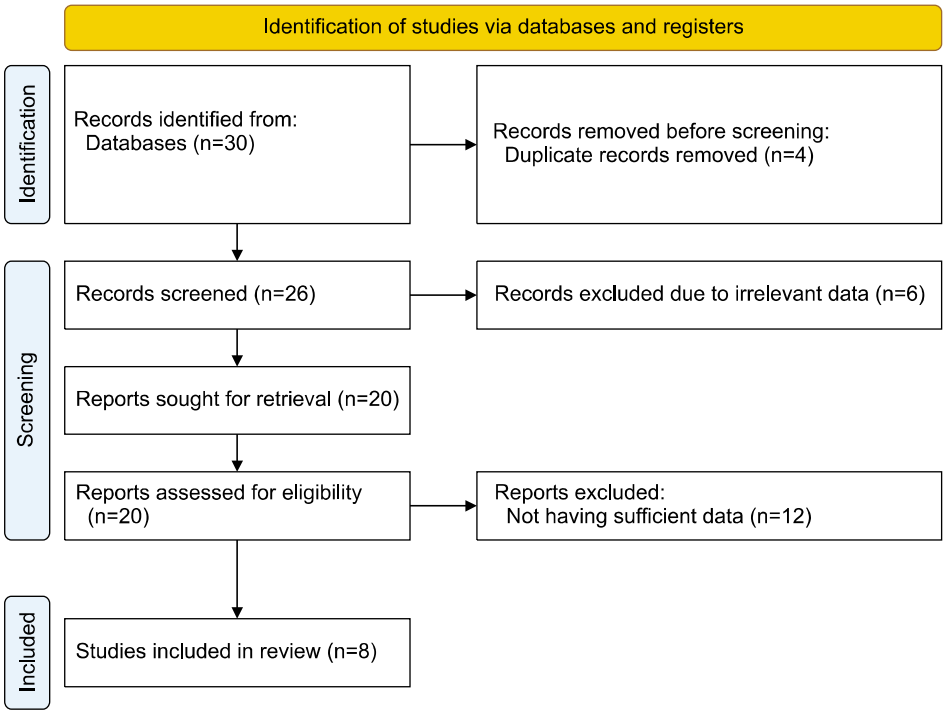

Fig. 1. Diagram illustrating the included studies, detailing the processes of identification, screening, eligibility assessment, and final sample selection.

inulin) in 16 days double-blind, investigator-initiated, placebo-controlled experiment including 100 patients. Based on their findings, the PREPRO arm experienced a substantial reduction in total infectious complications [44% vs. 22%, *P*=0.019, odds ratio (OR) 0.359, 95% confidence interval (CI) 0.150–0.858] compared with the placebo arm. The incidence rates of urinary tract and intra-abdominal infections were similar, whereas those of bloodstream infections were considerably lower in the study arm (21.7% vs. 53.3%, *P*=0.020, OR: 0.243, 95% CI: 0.072–0.826) (Mallick et al., 2022).

Grąt et al. (2017) performed a randomized, double-blind, placebo-controlled trial with the daily administration of a four-strain probiotic (*Lactococcus lactis* PB411, *Lactobacillus casei* PB121, *L. acidophilus* PB111, and *B. bifidum* PB211) preparation until LTX in 50 patients. They concluded that the probiotics significantly reduced the infection rates (30-day: 4.8% vs. 34.8%, 90-day: 4.8% vs. 47.8%) and improved the liver function after LTX, but did not affect the mortality. However, this study was limited by the refusal rate to take part in the study (Grąt et al., 2017).

Zhang et al. (2013) conducted a pre- and post-study on 34 patients who received fiber (prebiotics) and probiotics [*L. acidophilus* (LA-14), *Lactobacillus plantarum* (LP-115), *B. lactis* (BL-04), *L. casei* (LC-11), *Lactobacillus rhamnosus*, *Lactobacillus brevis*] after LTX for seven days compared with 33 patients who received only fiber (retrospective study). They reported that the fiber and probiotics group had significantly lower infection rates (8.8% vs. 30.3%) and shorter use of antibiotics, with minimal side effects, compared with the fiber only group (Zhang et al., 2013).

Eguchi et al. (2011) conducted a prospective randomized control study for two-day pre-surgery and two-week post-surgery synbiotic therapy (*B. breve*, *L. casei*, and galactooligosaccharides) in 55 patients undergoing living donor LTX (LDLTX). They found that synbiotic therapy significantly reduced infectious complications (4% vs. 24%) after LDLTX (Eguchi et al., 2011).

Ren et al. (2011) conducted a study on rats in 2011. They selected 12 Lewis rats as the donor group and 12 Brown Norway (BN) rats as recipients who were semi-starved and malnourished for four to five weeks. The recipients were divided into two random groups: one for the probiotics (*Bifidobacterium* and *Lactobacillus*) and one for the control (phosphate-buffered saline). Intramuscular imipenem and subcutaneous cyclosporine A were administered to each rat. Moreover, a normal group comprising six BN rats that had not received any medication or surgery was used. All rats were euthanized eight days after the procedure to analyze their blood. The weight of malnourished rats decreased by 20% and they lived for an additional eight days following the procedure. On the eighth postoperative day, all recipients had higher amounts of translocated microorganisms, serum endotoxin, and tumor necrosis factor (TNF)-α compared with the normal group. Meanwhile, the counts of *Bifidobacterium* and *Lactobacillus* in the ileocecum, secretory immunoglobulin A (sIgA) concentration, and lymphocytes in Peyer's patches all decreased. The increased ratios of CD8+ and γδTCR+ cells further demonstrated a partial change in the lymphocyte phenotypes. Compared with the control group, probiotic supplementation increased

Table 1. Characteristics of the eligible studies

Author's name (year)	Country	Study design	Sample size (female/male)	Duration of probiotics/synbiotics therapy	Dose of probiotics	Outcome
Mallick et al. (2022)	India	PREPRO trial	n=100 (N/A)	16 days of Fructooligosacccharide inulin, *Bifidobacterium lactis*, *Bifidobacterium longum*, *Bifidobacterium bifidum*, and *Lactobacillus acidophilus*	2.0 billion, 0.25 billion, 0.25 billion, and 2.5 billion, respectively (CFUs)	Synbiotic administration significantly decreased the early postoperative bloodstream and overall infection problems
Grąt et al. (2017)	Poland	Randomized Clinical Trial	n=50 (12/38)	90 days of *Bifidobacterium bifidum* PB211 (12.5%), *Lactobacillus casei PB121* (25.0%), *Lactococcus lactis PB411* (50.0%), and *Lactobacillus acidophilus PB111* (12.5%)	3×10^9 CFUs	Probiotic administration effectively protects against surgical site infections
Zhang et al. (2013)	Australia	Retrospective Control Study	n=67 (31/36)	7 days of prebiotics, *Bifidobacterium lactis* (BL-04), *Lactobacillus acidophilus* (LA-14), *Lactobacillus plantarum* (LP-115), *Lactobacillus casei* (LC-11), *Lactobacillus rhamnosus* (LR-32), and *Lactobacillus brevis* (LBr-35)	2.0 billion, 15.5 billion, 5.0 billion, 1.5 billion, 1.5 billion, and 1.5 billion, respectively (CFUs)	Taking probiotics and fiber together can decrease the risk of bacterial infections and shorten the course of antibiotic therapy following liver donation
Eguchi et al. (2011)	Japan	A prospective randomized study	n=25 (21/29)	16 days of *Lactobacillus casei* strain Shirota, live *Bifidobacterium breve* strain Yakult, and galactooligosaccharides	20 mg and 15 mg, respectively	After an elective living donor liver transplant, the preoperative use of synbiotic therapy dramatically decreased the incidence of infections
Ren et al. (2011)	China	Animal trial	n=12 (N/A)	14 days of *Bifidobacterium* and *Lactobacillus*	4×10^9 CFUs	Probiotic treatment with *Bifidobacterium* and *Lactobacillus* improved the intestinal barrier function and partially restored the intestinal microbiota in malnourished rats following liver transplantation with prolonged antibiotic usage
Rayes et al. (2005)	Germany	Randomized, Double-Blind Trial	n=66 (28/38)	14 days of *Pediacoccus pentosaceus*, *Leuconostoc mesenteroides*, *Lactobacillus paracasei* ssp., *L. plantarum*, and as prebiotics 2.5 g of each beta-glucan, inulin, pectin and resistant starch	10^{10} CFUs	After liver transplantation, the combination of lactic acid bacteria and fibers decreased the risk of bacterial infections
Rayes et al. (2002)	Germany	Controlled Trial	n=95 (46/49)	12 days of *Lactobacillus* and fibers	10^9 CFUs	It significantly reduced the incidence of surgical site infections
Rammohan et al. (2014)	India	Single-blind placebo-controlled prospective randomized control trial	n=70 (N/A)	*Bacillus mesentericus*, *Lactobacillus sporogenes*, *Streptococcus faecalis*, *Clostridium butyricum*, and fructooligosaccharides for 15 days	2 million, 100 million, 60 million, and 4 million, respectively (CFUs)	Perioperative synbiotic therapy had the potential to reduce postoperative infectious complications

All of the individuals included in the studies were adults (>18-year-old).
N/A, not applicable; CFU, colony-forming unit.

the counts of *Bifidobacterium* and *Lactobacillus*; decreased the levels of serum endotoxin, TNF-α, and bacterial translocation; increased the concentration of sIgA and lymphocytes in Peyer's patches; and partially restored the altered phenotypes of lymphocytes. The authors concluded that probiotic supplements, including *Bifidobacterium* and *Lactobacillus*, enhanced the intestinal barrier function and partially restored the intestinal microbiota in malnourished rats undergoing LTX with prolonged antibiotic usage (Ren et al., 2011).

Rayes et al. (2005) conducted a prospective randomized double-blind experiment with 66 liver transplant recipients. All patients received enteral nutrition shortly after surgery. The study compared one group (Group A) receiving a combination of four lactic acid bacteria (LAB) (*Pediococcus pentosaceus*, *Leuconostoc mesenteroides*, *Lactobacillus paracasei* ssp., and *L. plantarum*) and four fibers and prebiotics (2.5 g of each beta-glucan, inulin, pectin, and resistant starch) and another group (Group B) receiving only fibers. The 14-day treatment course began the day before the operation. The 30-day infection rate, length of hospital stay, length of antibiotic therapy, noninfectious issues, and enteral feeding side effects were also recorded in the study. Group A exhibited a substantial decrease in the occurrence of postoperative bacterial infections (3%) compared with Group B (48%). Additionally, Group A required less antibiotic medication. Both groups experienced mostly mild or severe infections, and the fibers and LAB were well tolerated (Rayes et al., 2005).

Rayes et al. (2002) conducted a prospective, randomized, placebo-controlled study involving 95 liver transplant patients to compare the incidence of complications and postoperative infections between three groups receiving early enteral nutrition: (a) standard formula plus SBD, (b) fiber-containing formula (15 g/L of fiber, divided into 0.6 g/L of soluble and 14.4 g/L of nonsoluble fibers) plus live *L. plantarum* 299, and (c) fiber-containing formula plus heat-killed *L. plantarum*. According to the Child-Pugh classification system, amount of immunosuppression, operative data, and preoperative American Society of Anesthesiologists classification, the groups were identical. Bacterial infections were reduced in patients who received fiber and live lactobacilli (13% vs. 48% in SBD). The infection rate was 34% in the group that received fiber and inactivated lactobacilli. The two most common illnesses were cholera and pneumonia, with *Enterococci* being the most commonly isolated bacterium. Compared with patients in the inactivated lactobacilli, fiber, and SBD groups, individuals in the living *Lactobacillus* group required fewer antibiotic prescriptions and spent less time in the hospital (Rayes et al., 2002).

Rammohan et al. (2014) conducted a prospective, single-blind, randomized, monocentric trial on patients undergoing major liver and pancreatic resections, including Whipple procedure, distal pancreatectomy, and Frey procedure. Group A received a specific synbiotic composition (*Streptococcus faecalis* T-110, 60 million; *Clostridium butyricum* TO-A, 4 million; *Bacillus mesentericus* TO-A, 2 million; *Lactobacillus sporogenes*, 100 million; fructooligosaccharides) five days before and 10 days after surgery, whereas Group B was given a placebo. A 10% dropout rate was estimated for each group and a sample size of 35 patients was calculated with an alpha of 0.05 and power of 80%. The study's secondary outcomes included death, bowel movement, days in the intensive care unit, length of hospital stay, and duration of antibiotic medication. Moreover, the study examined the potential side effects of probiotics. The researchers expected that perioperative synbiotics would decrease the proportion of patients with infection issues from 50% to 12% based on previous research. Moreover, the study aimed to explore the effects of perioperative synbiotic therapy on mortality, morbidity, and postoperative infections in patients undergoing major hepatic and pancreatic procedures (Rammohan et al., 2014).

DISCUSSION

Infectious complications remain a significant cause of morbidity and mortality in LTX recipients, despite advancements in surgical techniques, posttransplant care, hospital settings, immunosuppression, infectious disease treatment, infection prevention, and prophylaxis (Fishman, 2007). LTX recipients are more vulnerable to bacterial infections than other transplant recipients because of the complex surgical procedure, which involves penetration of the hepatobiliary system (Bennett et al., 2019). Infection is the primary cause of death three months post-LTX, with an incidence ranging from 30% to 86%. This is a much higher rate compared with that in kidney and heart transplant recipients (Rayes et al., 2005).

In this study, a systematic review using the PRISMA guidelines was conducted, making it the largest systematic review done on the topic to date. Previous systematic reviews have included fewer studies. However, the present study reviewed a broader range of studies to assess the effects of probiotics and synbiotics on the incidence of infection after LTX more comprehensively. Ma et al. (2021) conducted a systematic review that included six studies. By contrast, Sawas et al. (2015) conducted a systematic review in 2015 that included only four studies.

The gut-liver axis, which demonstrates circular causation, is the result of the liver's bidirectional link with the gut and its microbiota given their respective positions. Thus, the liver serves as the body's first line of defense

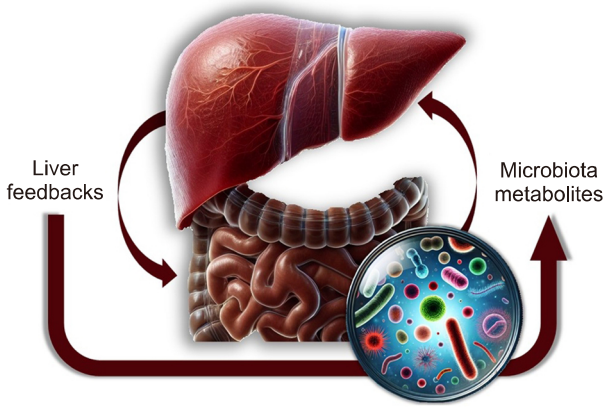

Fig. 2. Visual representation of the gut-liver axis.

against toxins and antigens produced from the gut (Giannelli et al., 2014) (Fig. 2 illustrates the interplay between liver feedback mechanisms, gut microbiota, and their metabolites in the context of post-LTX infections. Probiotics and synbiotics may modulate these interactions to reduce the incidence of infections).

The results of the studies showed that probiotics and synbiotics can decrease infectious complications after LTX, although the main mechanisms remain unclear. The proposed mechanisms of action include bacterial translocation, inflammation reduction, immune system modulations, and liver function improvements.

Bacterial translocation

Bacterial translocation is a leading cause of infection following LTX, with bacteria primarily originating from the intestine. This phenomenon occurs when bacteria from the colon traverse the intestinal epithelium to reach the mesenteric lymph nodes, abdominal organs (e.g., liver, spleen, and lungs), and the bloodstream, potentially resulting in infections (Ren et al., 2011). According to Ren et al. (2011), the changes in the microflora predominantly involve a significant decline in anaerobic bacteria, including *Lactobacillus* and *Bifidobacterium*. The majority of translocated bacteria are *Enterococci*, *Klebsiella*, and *Escherichia coli* (Yu et al., 2008; Ren et al., 2011). Under pathophysiological conditions, the disruption of the intestinal microflora may adversely affect the infectious status of patients who underwent LTX. Generally, three primary factors are considered responsible for the incidence of bacterial translocation: (i) intestinal barrier breakdown, (ii) intestinal microbiota disruption, and (iii) weakened immune system (Levitsky, 2006). Antibiotic use, abdominal surgeries, gastrointestinal disorders, and hepatic injuries are thought to be the main contributors to alterations in the normal microflora of the human intestine (Noverr et al., 2004; Sartor, 2004; Rayes et al., 2005; Xing et al., 2006). Probiotic administration has been shown to increase the counts of *Bifidobacterium* and *Lactobacillus*, partially reversing the effects of alterations in the gut microbiota.

Inflammation

According to literature, the first month following LTX is characterized by increased inflammation, which significantly increases the risk of infection (Lease, 2017; Figiel et al., 2020). The administration of probiotics and synbiotics downregulates intestinal inflammation through several mechanisms, as discussed below (Fig. 3):

***Inhibiting signaling pathways*:** Through blocking signaling pathways including NF-κB, probiotics and synbiotics may have anti-inflammatory effects by lowering the amounts of proinflammatory cytokines [e.g., TNF-α, interleukin (IL)-1β, and IL-6] in the intestine (Komano et al., 2023).

***Enhancing anti-inflammatory cytokines*:** These medications can reduce excessive inflammatory reactions in the intestine by increasing the levels of anti-inflammatory cytokines such as IL-10 (Komano et al., 2023).

***Enhancing intestinal barrier function*:** Strengthening the expression of tight junction proteins (e.g., occludin and claudin-1) helps maintain intestinal barrier integrity (Ashique et al., 2023). For this reason, synbiotic administration can thus prevent inflammation and bacterial translocation.

***Reducing oxidative stress*:** Reactive oxygen species can be reduced by increasing the activity of enzymes, such as glutathione peroxidase and superoxide dismutase (Ashique

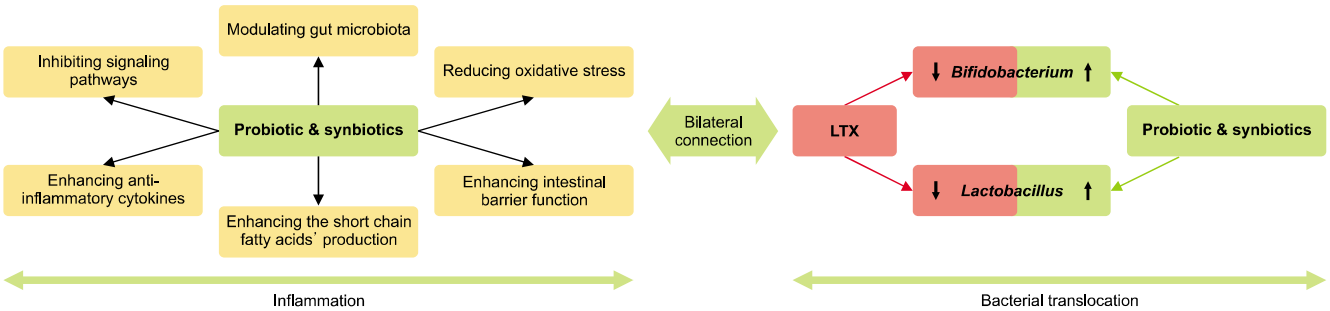

Fig. 3. Downregulation of intestinal inflammation by probiotics and synbiotics. LTX, liver transplantation.

Table 2. Interconnection of bacterial translocation and inflammation

Bacterial translocation	Reduced inflammation	Reference
Fewer bacteria and bacterial products entering the circulation lead to less stimulation of the immune system	Inflammation in the intestinal tract can disrupt the gut barrier integrity, allowing bacteria to translocate more easily	Rodríguez-Laiz et al. (2019), Wong et al. (2022)
This results in lower levels of proinflammatory cytokines, including tumor necrosis factor-α and interlukin-6, which further reduce systemic inflammation	As inflammation decreases posttransplant, the gut barrier function improves, reducing bacterial translocation into the bloodstream and liver	

et al., 2023).

***Modulating the gut microbiota*:** Synbiotic administration promotes the growth of beneficial bacteria, bifidobacteria and lactobacilli, favorably altering the gut microbiota composition and reducing inflammation (Jadhav et al., 2023; Roy and Dhaneshwar, 2023).

***Enhancing the production of short-chain fatty acids (SCFAs)*:** As synbiotics include prebiotics, they encourage the gut flora to produce anti-inflammatory SCFAs, including butyrate (Jadhav et al., 2023).

As shown in Table 2 (Rodríguez-Laiz et al., 2019; Wong et al., 2022), bacterial translocation and reduced inflammation are interconnected, both contributing to a decrease in postoperative infections in liver transplant recipients.

In addition to the previously discussed mechanisms, probiotics and synbiotics may reduce the incidence of infections after LTX through other pathways.

***Immune system modulations*:** The innate and adaptive immune systems may be influenced by the use of probiotics and synbiotics. Therefore, these treatments can improve the overall immunological tolerance and reduce graft rejection by boosting the production of anti-inflammatory cytokines while decreasing the production of proinflammatory cytokines (Zhang et al., 2013; Jorgenson et al., 2018).

***Liver function and graft health*:** Although probiotics and synbiotics have not shown any discernible negative effects on liver function and graft health, data suggest potential benefits in reducing acute liver rejection and improving overall liver function metrics (Cooper et al., 2022).

Safety concerns

Although probiotics and synbiotics offer numerous potential health benefits, safety concerns remain, particularly for patients with compromised immune systems. Most documented adverse effects are associated with products containing *Saccharomyces* species, which were not included in efficacy studies involving liver transplant recipients (Jorgenson et al., 2018).

Based on the findings of this systematic review, probiotic and synbiotic administration following LTX may effectively reduce the overall infection rate, a significant complication faced by liver transplant recipients. The potential mechanisms by which probiotics and synbiotics could decrease infection rates include minimizing bacterial translocation, enhancing gut barrier integrity, reducing inflammation through various pathways, and modulating the immune system to foster tolerance. Collectively, these results highlight a promising strategy for mitigating postoperative infections in liver transplant recipients.

Despite these encouraging findings, further research is needed to definitively evaluate the efficacy of probiotics and synbiotics and to identify the optimal strains for this specific population. The use of probiotics has been associated with an increase in beneficial bacterial counts, the downregulation of inflammation, the reinforcement of the intestinal barrier, the reduction of oxidative stress, and the enhancement of anti-inflammatory SCFA production.

Although probiotics and synbiotics demonstrate potential benefits in decreasing the incidence of infections post-LTX, safety concerns should be considered, particularly for patients with compromised immune systems. Further research is needed to fully elucidate the mechanisms and effects of probiotics and synbiotics in liver transplant recipients.

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AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Concept and design: BA, GE. Analysis and interpretation: BA. Data collection: BA, MM. Writing the article: All authors. Critical revision of the article: BA, GE. Final approval of the article: All authors.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.3746/pnf.2025.30.2.101

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