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The Role of Probiotics and Prebiotics in the Management of MASLD: A Clinical Perspective

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ABSTRACT

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a global health burden linked to metabolic syndrome and gut microbiota dysbiosis. Recent studies suggest that probiotics and prebiotics may play a pivotal role in modifying gut microbiota and improving liver outcomes in MASLD. Gut microbiota modulation with probiotics and prebiotics is emerging as a promising intervention.

Objective: To assess the clinical impact of probiotic-prebiotic therapy on liver function in MASLD patients.

Methods: A prospective observational study was conducted on 85 patients with MASLD. Participants received a standardized combination of probiotics (*Lactobacillus rhamnosus GG* and *Bifidobacterium longum*) and prebiotics (inulin and fructooligosaccharides) for 12 weeks. Liver function tests (LFTs) including ALT, AST, and GGT were measured before and after treatment.

Results: After 12 weeks, significant reductions were observed in ALT (mean reduction: 18.5 U/L, $p<0.001$), AST (mean reduction: 12.3 U/L, $p=0.002$), and GGT (mean reduction: 15.2 U/L, $p=0.005$). 64.7% of patients achieved normalization of at least one elevated liver enzyme. No serious adverse events were reported.

Conclusion: This study provides evidence that short-term probiotic-prebiotic therapy improves liver biochemistry in MASLD patients, supporting gut microbiota modulation as an adjunctive strategy in MASLD management.

Keywords: MASLD, probiotics, prebiotics, liver function, dysbiosis, gut-liver axis

INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD) is defined by the accumulation of fat—specifically triglycerides—in more than 5% of liver cells (hepatocytes), occurring independently of significant alcohol intake. MASLD encompasses a continuum of liver conditions, ranging from simple steatosis without inflammation to more advanced stages, including metabolic dysfunction-associated steatohepatitis (MASH) [17]. MASH is characterized by hepatic inflammation and fibrosis that can progress to cirrhosis. It is estimated that MASLD affects about one-third of the global population, with a higher prevalence in men than women [17]. Many individuals with MASLD remain asymptomatic until the disease reaches more advanced stages, making it a potentially silent but serious threat to public health. This liver condition is closely associated with several metabolic disorders, such as type 2 diabetes, central obesity, dyslipidemia, hypertension, and elevated liver enzymes [7,17]. MASLD has become a leading cause of chronic liver disease and cirrhosis, alongside alcohol-related liver disease and viral hepatitis [7].

Pathogenesis of MASLD and the Role of Gut Microbiota

The underlying mechanisms driving MASLD are not yet fully clarified. While fat accumulation in the liver is a hallmark, other factors such as oxidative stress from lipids, insulin resistance, gut microbial composition, microbial metabolites, and compromised intestinal barrier function are all closely linked to its initiation and progression [6,7]. The liver and intestine are functionally and anatomically connected through what is known as the gut-liver axis. Notably, around 75% of the liver's blood flow is derived from the portal vein, positioning the liver as the primary organ exposed to gut-derived microbes and their metabolites [10].

A healthy intestinal barrier plays a critical role in restricting the movement of microbes, toxins, and byproducts beyond the gut lumen. However, an imbalance in gut microbiota—referred to as dysbiosis—can disrupt this barrier, increase permeability, and alter the metabolic landscape [11,12]. These disruptions facilitate microbial migration into the bloodstream, heighten immune responses, and contribute to liver inflammation and disease progression [10,11,12].

Alterations in Gut Microbiota Associated with MASLD

The human gut hosts a highly diverse microbial ecosystem consisting of approximately 1,000 to 1,500 species and between 10 and 100 trillion bacteria—about ten times more than human cells. The two predominant bacterial groups, Bacteroidetes and Firmicutes, are strongly linked to the development of hepatic steatosis [11].

Research has shown that higher levels of Bacteroidetes are independently associated with MASH, whereas elevated Ruminococcus is linked to liver fibrosis [13,14]. Compared to individuals without the disease, those with MASLD tend to show significantly decreased microbial diversity, notable shifts in microbial community structure, an increased presence of gram-negative species, and reduced levels of Firmicutes [13,14]. Metagenomic analyses have further demonstrated a positive correlation between liver fibrosis and increased

amounts of Bacteroides and E. coli [4,5]. Moreover, a higher presence of Escherichia, Shigella, and other Enterobacteriaceae members has been observed in more severe cases of fibrosis [4,5].

However, findings regarding Bacteroidetes levels in MASH patients have been inconsistent, with some studies showing no difference compared to healthy controls [5,6]. Such discrepancies may stem from variables including diet, geography, age, and differences in study populations. Consequently, further research is necessary to uncover the precise interactions between gut microbes and liver inflammation.

Dietary habits and lifestyle choices have a substantial impact on gut flora. Prolonged consumption of high-fat and high-sugar diets can disrupt microbial balance, weaken the intestinal barrier, and disturb immune equilibrium [18,19]. An overload of bacteria, their metabolic products, and cytokines reaching the liver via the portal vein can overwhelm hepatic macrophages [6,19], triggering inflammatory cascades and immune hyperactivation. This response can result in the release of inflammatory mediators, aggravating hepatic inflammation, fibrosis, and the advancement of MASLD. Thus, the gut microbiota plays a central role in the disease's development [6,7,8].

Restoring gut microbial balance using probiotics and prebiotics has shown promise in reducing hepatic steatosis, improving insulin sensitivity, and lowering inflammatory responses [2,3,15]. This study aimed to clinically evaluate the effect of probiotic-prebiotic therapy on liver function in MASLD patients.

Mechanisms and Evidence for Probiotic and Prebiotic Use in MASLD

Probiotics are live microorganisms which, when administered in adequate amounts, confer a health benefit to the host. Prebiotics are non-digestible dietary components—primarily fibers—that selectively stimulate the growth and/or activity of beneficial gut bacteria [15]. Together, probiotics and prebiotics work synergistically to restore gut microbial balance, enhance intestinal barrier integrity, and suppress inflammation, making them a promising adjunctive approach in the management of MASLD [2,3,15,20].

Mechanisms of Action

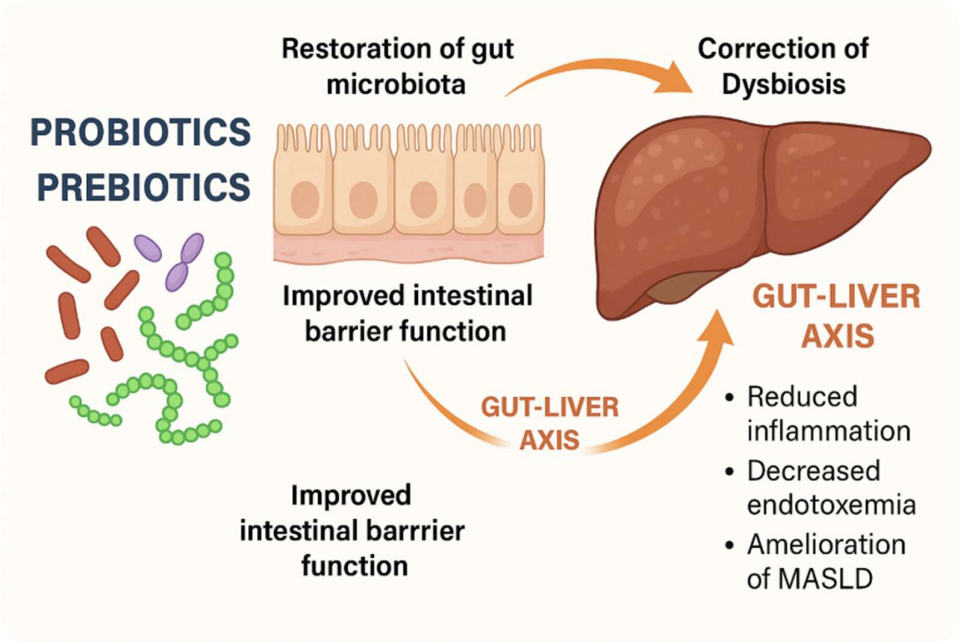
Restoration of microbial diversity: Probiotics help repopulate beneficial bacteria such as Lactobacillus and Bifidobacterium, while prebiotics selectively promote their growth [2,3].

Reduction of endotoxemia: By reducing populations of gram-negative bacteria, these agents' lower lipopolysaccharide (LPS) production, a key driver of hepatic inflammation via the TLR4 pathway [7,8].

Improvement in intestinal barrier function: Probiotics strengthen tight junction proteins (e.g., occludin, claudins), decreasing gut permeability and systemic inflammation [10,11].

Modulation of bile acid metabolism: Certain probiotic strains influence bile acid composition, which can impact lipid and glucose metabolism [6,8].

Suppression of pro-inflammatory cytokines: Both probiotics and prebiotics have been shown to reduce serum levels of TNF-α, IL-6, and CRP—key inflammatory mediators in MASLD [2,12,16].



Clinical Evidence

Multiple clinical studies and meta-analyses have reported improvements in liver enzyme levels, hepatic steatosis, and metabolic parameters with probiotic or synbiotic supplementation in NAFLD/MASLD patients:

A meta-analysis of 18 randomized controlled trials showed significant reductions in ALT and AST with various probiotic combinations [2].

Inulin and fructooligosaccharides (FOS), common prebiotics, have been shown to increase butyrate-producing bacteria and improve insulin sensitivity [16].

Some studies using Lactobacillus rhamnosus GG or Bifidobacterium longum reported histologic improvements in hepatic steatosis and inflammation [21,22].

However, strain-specific effects are highly variable, and few trials have used standardized formulations. The combination of multi-strain probiotics and targeted prebiotics—termed synbiotics—may offer synergistic benefits by both introducing beneficial bacteria and enhancing their survival and colonization [3,15].

These findings provided the rationale for selecting a multi-strain probiotic and a prebiotic blend in this study to evaluate their combined impact on liver function in patients with MASLD.

METHODS

Study Design and Population

This prospective observational study enrolled 85 adult MASLD patients (mean age 46.2 ± 8.7 years; 54% male) at three clinics affiliated with Tbilisi State Medical University between January and November 2024. MASLD diagnosis was confirmed by ultrasound and elevated

ALT/AST levels, in the absence of alcohol abuse or viral hepatitis. Dysbiosis was confirmed via fecal microbiological analysis, including stool culture and specific dysbiosis markers."

Intervention

Participants received:

- **Probiotic**: 2 capsules t.i.d. Each capsule containing Lactobacillus delbrueckii ssp. lactis LL 82 – 1 billion, Lactobacillus acidophilus LA 3 – 1 billion, Lactobacillus delbrueckii ssp. bulgaricus SP 5 - 1 billion, Bifidobacterium animalis ssp. lactis BLC01 – 1 billion, Bacillus clausii DSM 8716 – 1 1 billion, Streptococcus thermophilus SP4 – 1 1 billion,
- **Prebiotic**: 5g inulin + 5g fructooligosaccharides daily

Duration: **12 weeks**

All patients were advised lifestyle modifications in the form of control of various risk factors like hypertension, hyperlipidaemia (with statins or fibrates) and overweight/obesity. All patients were advised regular exercise like brisk walking, jogging, running, swimming, cycling, etc for at least 30–45 min/day, for at least 5 days in a week. Patients with overweight/obesity, in addition, were advised 5%–10% of weight reduction from baseline (not more than 1.6 kg/week) with the help of hypocaloric diet (30% reduction in calorie intake) by reducing the intake of both carbohydrates and fats.

Inclusion Criteria

- Age 18–70
- Confirmed MASLD with elevated liver enzymes and abdominal ultrasound
- No antibiotics, corticosteroids, or probiotic use in prior 6 weeks

Exclusion Criteria

- Cirrhosis, hepatitis B/C, alcohol use >40g/week
- Immunosuppressive therapy or recent gastrointestinal surgery

Outcome Measures

Liver function tests (ALT, AST, GGT) were recorded at baseline and after 8 weeks. Primary endpoint: absolute change in ALT. Secondary endpoints: AST and GGT changes, safety, and tolerance.

RESULTS

Baseline Characteristics

- Mean BMI: 29.8 ± 3.4 kg/m²
- Mean ALT: 58.7 ± 14.5 U/L
- Mean AST: 42.1 ± 11.2 U/L
- Mean GGT: 76.3 ± 23.4 U/L

Table 1. Baseline and Post-Treatment Liver Function Test (LFT) Results in MASLD Patients

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	Mean Change	p-value
ALT (U/L)	58.7 ± 14.5	40.2 ± 11.3	–18.5	< 0.001
AST (U/L)	42.1 ± 11.2	29.8 ± 10.7	–12.3	0.002
GGT (U/L)	76.3 ± 23.4	61.1 ± 20.9	–15.2	0.005
% Normalized at Least 1 LFT	—	64.7%	—	—
Adverse Events	—	Mild bloating (8.2%)	—	—

- **Normalization**: 55 patients (64.7%) had normalization of at least one elevated LFT
- **No worsening**: No patient showed worsening of LFT values

Safety

- Mild bloating in 8.2% of participants
- No serious adverse events reported

DISCUSSION

The results confirm the therapeutic potential of probiotics and prebiotics in MASLD through measurable improvements in liver biochemistry. The mechanisms likely include:

- Reduction in endotoxemia and hepatic inflammation [2,3,6,8,10]
- Strengthened intestinal barrier [10,11,12]

1. Favorable shifts in gut microbial composition [3,6,13,15,20]

The study supports microbiota modulation as a practical adjunctive therapy in the clinical management of MASLD. Notably, the intervention was well-tolerated, and adherence was high.

However, limitations include the lack of a placebo control group and absence of gut microbiota profiling. Future RCTs with microbiome sequencing are needed to validate these findings [2,3,14].

CONCLUSION

This study demonstrates that a 12-week course of targeted probiotic and prebiotic supplementation significantly improves liver function markers in patients with MASLD. Gut microbiota modulation should be considered a valuable non-pharmacologic approach in MASLD management strategies.

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პრობიოტიკებისა და პრებიოტიკების როლი მეტაბოლურ დისფუნქციასთან ასოცირებული სტეატოზული ღვიძლის დაავადების (MASLD) მართვაში: კლინიკური პერსპექტივა

თათია ხაჩიძე, გელა სულაბერიძე, გოჩა ბარბაქაძე

რეზიუმე

შესავალი: მეტაბოლურ დისფუნქციასთან ასოცირებული ღვიძლის სტეატოზური დაავადება (MASLD) წარმოადგენს გლობალურ ჯანმრთელობის პრობლემას და იგი ღვიძლის ყველაზე გავრცელებული ქრონიკული დაავადებაა, რომელსაც შეუძლია პროგრესირდეს ციროზში და ჰეპატოცელულარულ კარცინომაში. დაავადება მჭიდრო კავშირშია მეტაბოლურ სინდრომთან და ნაწლავის მიკრობიოტის დისბიოზთან. ბოლო კვლევებმა დაადასტურა, რომ პრობიოტიკებისა და პრებიოტიკების გამოყენება მნიშვნელოვან როლს თამაშობს ნაწლავის მიკრობიოტის მოდულირებაში და ღვიძლის ფუნქციის გაუმჯობესებაში MASLD-ის მქონე პაციენტებში. აქედან გამომდინარე ნაწლავის მიკრობიოტის მოდულაცია პრობიოტიკებითა და პრებიოტიკებით წარმოადგენს პერსპექტიულ თერაპიას.

მიზანი: კვლევის მიზანია შეფასდეს პრობიოტიკების და პრებიოტიკების თერაპიის კლინიკური გავლენა ღვიძლის ფუნქციებზე MASLD-ის მქონე პაციენტებში.

მეთოდები: კვლევაში ჩართული იყო 85 MASLD-ით დიაგნოზირებული პაციენტი. მონაწილეები იღებდნენ პრობიოტიკებისა (Lactobacillus rhamnosus GG და Bifidobacterium longum) და პრებიოტიკების (ინულინი და ფრუქტოოლიგოსაქარიდები) სტანდარტიზებულ კომბინაციას 12 კვირის განმავლობაში. ღვიძლის ფუნქციის ტესტები (ALT, AST და GGT) შეფასდა თერაპიის დაწყებამდე და შემდეგ.

შედეგები: კვლევის შედეგად 12 კვირის შემდეგ აღინიშნა მნიშვნელოვანი კლება ALT-ში (საშუალო კლება: 18.5 U/L, $p<0.001$), AST-ში (საშუალო კლება: 12.3 U/L, $p=0.002$) და GGT-ში (საშუალო კლება: 15.2 U/L, $p=0.005$). პაციენტების 64.7%-მა მიაღწია ერთი ან მეტი მომატებული ღვიძლის ფერმენტის ნორმალიზებას. კვლევის პროცესში სერიოზული გვერდითი ეფექტები არ დაფიქსირებულა.

დასკვნა: კვლევამ აჩვენა, რომ მოკლევადიანი პრობიოტიკებითა და პრებიოტიკებით თერაპია აუმჯობესებს ღვიძლის ბიოქიმიურ მაჩვენებლებს MASLD-ის მქონე პაციენტებში, რაც ამყარებს ნაწლავის მიკრობიოტის მოდულაციის თერაპიულ პოტენციალს MASLD-ის მართვაში.

საკვანძო სიტყვები: მეტაბოლურ დისფუნქციასთან ასოცირებული ღვიძლის სტეატოზური დაავადება, პრობიოტიკები, პრებიოტიკენი, დისბიოზი.