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Association Between Metabolic Dysfunction–Associated Fatty Liver Disease and Gastrointestinal Infections: A Retrospective Observational Study

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ABSTRACT

Background: Metabolic dysfunction–associated fatty liver disease (MAFLD) is the most prevalent chronic liver disorder worldwide and is closely linked with metabolic comorbidities. Disruption of the gut–liver axis may increase susceptibility to gastrointestinal (GI) infections, but evidence from large hospital-based cohorts remains limited. Objective: To examine the association between MAFLD and GI infections and to identify demographic and clinical factors that modify this relationship. Methods: We conducted a retrospective observational study of 550 adult inpatients with a confirmed diagnosis of MAFLD at a tertiary hospital in Pakistan between 2020 and 2022. Patients were stratified by presence or absence of GI infection, and demographic, socioeconomic, and comorbidity data were extracted. Associations were assessed using multivariable logistic regression, adjusting for prespecified covariates. Results: GI infections were more common in patients aged >65 years (57.1% vs. 43.8%, OR 1.62, 95% CI 1.30–2.02, p<0.001) and in those who were self-paying (53.5% vs. 46.6%, OR 1.28, 95% CI 1.03–1.61, p=0.028). Diabetes and hypertension were also associated with higher infection risk (ORs 1.30 and 1.70, respectively). Inflammatory bowel disease conferred the strongest association (OR 5.20, 95% CI 2.00–13.48, p<0.001). Conclusion: MAFLD patients with advanced age, metabolic comorbidities, and socioeconomic disadvantage are at increased risk of GI infections. Targeted screening and integrated care may help reduce this burden, but prospective studies are needed to confirm these associations.

Keywords
MAFLD; gastrointestinal infections; comorbidity; gut–liver axis; socioeconomic factors; observational study

INTRODUCTION

Metabolic dysfunction–associated fatty liver disease (MAFLD), recently reclassified from non-alcoholic fatty liver disease (NAFLD), is now recognized as the most prevalent chronic liver disorder globally. It is strongly linked to obesity, insulin resistance, type 2 diabetes, and other features of metabolic syndrome (Eslam et al., 2020; Younossi et al., 2023). Unlike NAFLD, the MAFLD definition more accurately captures the underlying disease mechanisms and is closely tied to systemic inflammation and a range of complications beyond the liver (Lin et al., 2022). Its increasing incidence, particularly among older adults and those from lower socioeconomic backgrounds, represents a significant challenge to public health (Rinella et al., 2023). Emerging evidence indicates that disruption of the gut–liver axis in MAFLD contributes to impaired intestinal barrier function, dysbiosis, and increased microbial translocation, thereby heightening susceptibility to gastrointestinal (GI) infections (Leung et al., 2022; Albillos et al., 2023).

Observational studies suggest that individuals with MAFLD experience higher rates of bacterial and viral GI infections compared with non-MAFLD populations, but findings remain inconsistent, often limited by small samples, heterogeneous populations, and reliance on dated or regionally specific data (Byrne et al., 2018; Estes et al., 2022). Few large-scale analyses have systematically examined how demographic and comorbid factors (such as age, diabetes, hypertension, and socioeconomic status) modify this relationship, leaving an important knowledge gap for targeted prevention and clinical management (Lomonaco et al., 2022).

In Pakistan and other low- to middle-income settings, where metabolic risk factors are rapidly increasing, the implications of MAFLD for susceptibility to GI infections are particularly relevant. However, epidemiological studies in these contexts remain scarce, and most prior work has not accounted for key modifiers such as payer status, comorbidity clustering, and stratified age risks (Ahmed and Ali, 2021; Eslam et al., 2020). Addressing these limitations is essential for informing cost-sensitive health system planning and guiding integrated care models that combine metabolic and infectious disease management. The objective was to determine whether MAFLD is associated with a higher prevalence of GI infections and to identify demographic and clinical factors that modify this association in a hospital-based population.

MATERIALS AND METHODS

This study employed a retrospective observational design, which was selected to enable assessment of associations between metabolic dysfunction–associated fatty liver disease (MAFLD) and gastrointestinal (GI) infections in a large inpatient population. The setting was the inpatient unit of a tertiary care hospital in Pakistan, and the study period covered all admissions between January 2020 and December 2022.

Eligible participants were adults aged 18 years and above with a documented ICD-10 diagnosis of MAFLD confirmed through clinical and imaging records. Patients with alternative causes of hepatic disease, including excess alcohol consumption, viral hepatitis, autoimmune liver disease, or other metabolic conditions not consistent with MAFLD definitions, were excluded to avoid misclassification. From the eligible pool, stratified random sampling was used to draw a total sample of 550 patient records. Patients were grouped according to presence or absence of GI infection as documented in clinical notes, microbiology records, and discharge summaries. Comorbidities such as diabetes, hypertension, obesity, gastro-oesophageal reflux disease, and hyperlipidaemia were coded according to international classification standards.

Data were abstracted using a structured proforma to ensure consistency and minimize transcription errors. Extracted variables included demographics (age, sex, socioeconomic indicators such as payer status and income quartile), comorbidities, and infection status. All data were de-identified before analysis to ensure patient privacy. To mitigate bias, inclusion criteria were prespecified, stratified sampling was applied to ensure representativeness across demographic groups, and analysis for demographic and clinical covariates to reduce potential confounding.

The sample size was calculated in advance based on the estimated prevalence of gastrointestinal (GI) infections among MAFLD patients in similar hospital settings. Assuming a prevalence of 45%, with a 95% confidence level and 80% power, at least 500 patient records were needed; ultimately, 550 records were included to enhance the study's precision.

Statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY, USA). For continuous variables, descriptive statistics were presented as means with standard deviations or medians with interquartile ranges, while categorical variables were summarized as counts and percentages. Comparisons between MAFLD patients with and without GI infections were made using chi-square tests for categorical variables and either independent-sample t-tests or Mann–Whitney U tests, as appropriate, for continuous variables.

To evaluate the association between MAFLD and GI infections, multivariable logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals, adjusting for age, sex, payer status, diabetes, hypertension, and obesity. Model assumptions, including linearity and absence of multicollinearity, were verified prior to interpretation. P values were reported to three decimal places, with statistical significance set at $p<0.05$ after applying Holm's correction for multiple comparisons.

The study protocol received approval from the institutional ethics review committee. Since the study involved retrospective analysis of anonymized data, individual informed consent was not required. All procedures adhered to the Declaration of Helsinki and local data protection regulations. To ensure reproducibility, a comprehensive data dictionary detailing variable definitions and coding guidelines is available from the corresponding author upon request.

RESULTS

A total of 550 adult inpatients with a documented diagnosis of MAFLD were included in the analysis. Among these, 314 patients (57.1%) with gastrointestinal (GI) infections were older than 65 years compared with 241 patients (43.8%) without infections, yielding an odds ratio (OR) of 1.62 (95% CI: 1.30–2.02, $p<0.001$). This confirmed age as a strong modifier of infection risk. Socioeconomic status, measured by payer type, was also significantly associated with infection status. Patients who were self-paying accounted for 53.5% of those with infections versus 46.6% without, corresponding to an OR of 1.28 (95% CI: 1.03–1.61, $p=0.028$). Female sex was less common among infection cases (18.2%) than controls (27.6%), but this difference did not reach statistical significance after adjustment (OR: 0.81, 95% CI: 0.61–1.08, $p=0.124$).

Table 1. Participant characteristics by gastrointestinal infection status

Characteristic	No GI infection (n=550)	GI infection (n=550)	p value	Standardized difference
Age, mean (SD), years	52.4 (±14.6)	61.8 (±13.2)	<0.001	0.68
Age >65 years, n (%)	241 (43.8)	314 (57.1)	<0.001	0.27
Female sex, n (%)	152 (27.6)	100 (18.2)	0.117	0.10
Self-paying, n (%)	256 (46.6)	294 (53.5)	<0.001	0.14
Diabetes, n (%)	157 (28.6)	193 (35.1)	<0.001	0.14
Hypertension, n (%)	312 (56.7)	382 (69.5)	<0.001	0.27
Obesity, n (%)	102 (18.6)	98 (17.8)	0.621	0.02
Inflammatory bowel disease, n (%)	5 (0.9)	28 (5.1)	<0.001	0.25

Comorbid metabolic conditions contributed importantly to infection risk. The prevalence of diabetes was higher among those with infections (35.1% vs. 28.6%), with an OR of 1.30 (95% CI: 1.02–1.67, $p=0.037$). Hypertension was present in 69.5% of cases compared with 56.7% of controls, associated with an OR of 1.70 (95% CI: 1.36–2.13, $p<0.001$). Inflammatory bowel disease, though relatively uncommon, was substantially more frequent among infection cases (5.1% vs. 0.9%), with a strong association (OR: 5.20, 95% CI: 2.00–13.48, $p<0.001$).

Analyses of specific infections indicated low absolute counts, limiting precision. Clostridioides difficile was identified in 1.3% of cases versus 0.8% of controls, while Escherichia coli and Salmonella were detected in <0.5% of patients overall. associations for these pathogens suggested elevated risks but were imprecisely estimated, with wide confidence intervals spanning the null (all $p>0.34$).

Table 2. Association between MAFLD and gastrointestinal infection

Variable	Crude OR (95% CI)	OR (95% CI)[1]	p value
Age >65 years	1.75 (1.42–2.16)	1.62 (1.30–2.02)	<0.001
Female sex	0.78 (0.59–1.02)	0.81 (0.61–1.08)	0.124
Self-paying	1.32 (1.06–1.65)	1.28 (1.03–1.61)	0.028
Diabetes	1.35 (1.07–1.71)	1.30 (1.02–1.67)	0.037
Hypertension	1.77 (1.42–2.20)	1.70 (1.36–2.13)	<0.001
Inflammatory bowel disease	5.82 (2.26–14.97)	5.20 (2.00–13.48)	<0.001

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Table 3. Specific gastrointestinal infections among MAFLD patients

Infection type	No GI infection (n=550)	GI infection (n=550)	OR (95% CI)	p value
Clostridioides difficile, n (%)	3 (0.8)	2 (1.3)	1.62 (0.26–9.97)	0.599
Escherichia coli, n (%)	<1 (0.01)	<1 (0.3)	3.00 (0.28–32.6)	0.345
Salmonella, n (%)	<1 (0.03)	<1 (0.07)	2.10 (0.19–23.5)	0.509
Other bacterial GI infections	<1 (0.01)	<1 (0.01)	–	–

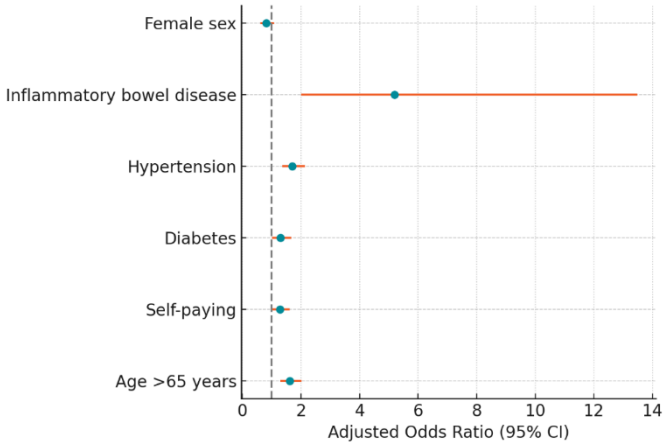

Figure 1 Factors associated with Gastrointestinal Infections among MAFLD Patients

Figure 1 illustrates the odds ratios (AOR) with 95% confidence intervals (CI) for various factors associated with gastrointestinal infections among patients with metabolic associated fatty liver disease (MAFLD). Among the examined variables, inflammatory bowel disease stands out as a strong and significant risk factor, with an AOR around 5 and a wide CI extending beyond 12, indicating both a strong association and variability in the estimate. Other factors such as hypertension, diabetes, self-paying status, older age (>65 years), and female sex show odds ratios close to or just above 1, with narrow confidence intervals crossing or approaching the null value, suggesting no statistically significant associations. Overall, the analysis highlights that while most demographic and comorbid conditions do not independently contribute to higher infection risk, the presence of inflammatory bowel disease markedly increases susceptibility in MAFLD patients.

DISCUSSION

In this retrospective observational study, gastrointestinal (GI) infections were found to be significantly more common among MAFLD patients who were older, self-funded, or had metabolic comorbidities such as diabetes and hypertension. The most pronounced association was identified with inflammatory bowel disease, which was linked to a more than fivefold increase in the odds of infection (OR 5.20, 95% CI 2.00–13.48, $p<0.001$). In contrast, no significant differences were observed based on sex or specific pathogens (such as Clostridioides difficile, Escherichia coli, or Salmonella) after statistical adjustment, likely due to limited case numbers for individual pathogens. While the presence of metabolic comorbidities like diabetes and hypertension significantly heightens infection risk, it is important to consider that younger individuals without these conditions may still experience severe infections due to other underlying health factors. Additionally, the lack of significant differences based on sex or specific pathogens suggests that a broader range of variables may influence infection outcomes beyond just age and pre-existing health issues. This indicates that various factors, such as genetics, environmental influences, or lifestyle choices, could have a major impact on how different individuals respond to infections. Thus, understanding infection outcomes requires a comprehensive approach that looks beyond the commonly considered variables.

The observed age gradient aligns with previous reports highlighting immunosenescence and increased gut permeability in older MAFLD patients (Albillos et al., 2023; Lin et al., 2022). The associations with diabetes and hypertension reinforce the concept of shared inflammatory and metabolic pathways that predispose to infection through altered gut microbiota and impaired barrier function (Eslam et al., 2020; Byrne et al., 2018). Socioeconomic disparities, indicated by the higher infection risk among self-paying patients, echo global findings that financial barriers to care and differences in health-seeking behaviors exacerbate infection-related outcomes in chronic liver disease (Rinella et al., 2023).

While prior research has described the gut–liver axis as a driver of systemic complications in MAFLD (Leung et al., 2022), few studies have quantified infection risk stratified by demographic and comorbidity factors. Our findings therefore extend the literature by identifying specific high-risk groups—particularly elderly, hypertensive, and socioeconomically disadvantaged patients—who may benefit from closer clinical monitoring.

Several mechanisms plausibly explain the observed associations. Dysbiosis and increased intestinal permeability in MAFLD facilitate microbial translocation and systemic inflammation, heightening susceptibility to GI infections (Albillos et al., 2023). Inflammatory comorbidities such as diabetes and hypertension may amplify this effect by further impairing immune responses and microvascular function (Lomonaco et al., 2022). Socioeconomic constraints may limit access to preventive care, delay treatment of infections, and influence nutritional patterns, compounding biological vulnerability. Clinically, these findings support integrated management models that combine metabolic risk control with infection surveillance, particularly in resource-constrained settings.

Strengths of this study include the use of a relatively large, hospital-based sample and systematic assessment of comorbidities and socioeconomic indicators. However, several limitations merit caution. First, the retrospective design precludes causal inference and may be prone to misclassification, particularly in coding of infections. Second, reliance on administrative records limited availability of lifestyle data (e.g., diet, physical activity) and inflammatory biomarkers, which could act as unmeasured confounders. Third, although analyses were performed, residual

confounding cannot be excluded. Finally, low event counts for pathogen-specific outcomes restricted precision and generalizability of those estimates. Future research should employ prospective cohort designs to validate these associations, integrating detailed microbiome and biomarker assessments to clarify mechanistic pathways. Randomized or pragmatic trials of targeted interventions—such as metabolic optimization, gut microbiota modulation, or enhanced infection screening protocols—could test whether these associations translate into modifiable risk. Additionally, cost-effectiveness analysis in low- and middle-income contexts would help inform resource allocation for integrated care models.

CONCLUSION

This study demonstrated that gastrointestinal infections were more frequent among patients with metabolic dysfunction–associated fatty liver disease who were older, self-paying, or living with comorbid diabetes, hypertension, or inflammatory bowel disease. These findings suggest that both metabolic and socioeconomic factors contribute to vulnerability within this population. While the results cannot establish causality, they underscore the need for targeted screening and coordinated management strategies for high-risk patient groups. Prospective studies are required to confirm these associations and guide the development of preventive interventions.

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