

## Original Article

# Association of Metabolic Dysfunction-Associated Fatty Liver Disease with Gastrointestinal Infections

Fatima Hussain<sup>\*1</sup>, Gohar Kaleem<sup>1</sup>

## ABSTRACT

**Background:** Metabolic dysfunction-associated fatty liver disease (MAFLD) is, in current context, a highly emergent health issue globally, associated with most of the other components of the metabolic syndrome, such as diabetes and obesity. A new study adds to the body of such reports, associating it with a higher susceptibility to gastrointestinal (GI) infections, primarily due to gut-liver axis dysregulation. This is necessary to understand for the purpose of developing effective treatment and management programmes.

**Objective:** To know how MAFLD is associated with the presence of gastrointestinal infections together with identifying the demographic and comorbid factors that may influence this relationship.

**Methods:** The current research was a retrospective analysis of the data from the Patient record on adult patients who had been diagnosed with MAFLD. The patients were stratified in sampling based on which of the 550 patients will form an appropriate sample divided into two categories: 550 were compared with and without GI infections. Data collection was anonymous in relation to the patient, and the current procedures were performed in compliance with the ethical provisions set out in the Declaration of Helsinki. The data were analyzed statistically by SPSS 25 software, and the *p*-values for significance for all categorical variables were found through chi-square testing.

**Results:** Our evaluation indicated that patients aged over 65 years had a frequency of 57.09% for GI infections with MAFLD, compared to 43.82% in their counterparts without GI infections, and the *p*-value was very statistically significant, i.e. less than 0.001. Another set of statistically significant findings were an increased rate of GI infections in patients who were self-paying, at 53.45%, compared to 46.55% whose expenses were covered, with a *p*-value of less than 0.001, and those with diabetes, hypertension, or both. In general, when adjusted for demographic and comorbidity, the analysis of the group was statistically significant regarding GI infections in the patient population of MAFLD.

**Conclusion:** The study underscores the strong association of MAFLD with higher prevalence of the GI infections in elderly and in economic disadvantage groups. The evidence indicates that clinical outcomes in a MAFLD population are improved by care coordination in metabolic and infectious disease.

**Keywords:** Metabolic Dysfunction-Associated Fatty Liver Disease; Gastrointestinal Infections; Patient Record; Gut-Liver Axis; Comorbidity Analysis

\* Corresponding Author: hussainfatima656@gmail.com  
Authors' and timeline information is given at end of article.

## INTRODUCTION

Metabolic dysfunction-associated fatty liver disease (MAFLD) is set to become one of the largest threats to global public health. Previously known as non-alcoholic fatty liver disease (NAFLD), this is an insidious condition defined by atypical fat accumulation in a patient's liver without evidence of an alcohol use history (1-3). This usually occurs in conjunction with manifestations of the metabolic syndrome, such as dyslipidemia, obesity, and type 2 diabetes mellitus. As a hepatic manifestation of the metabolic syndrome, MAFLD has taken the mantle of the most common form of liver disease in most parts of the world, which remains a critical concern considering its broader implications for health, more so in relation to its association with GI infections (4-6).

Recent epidemiological studies have started to see a potential relationship between MAFLD and heightened susceptibility to various GI infections. This is believed to be mediated through various mechanisms such as altered gut microbiota, intestinal barrier function, and systemic inflammation, all of which are common amongst those with MAFLD. The interaction between the gut and liver is mutual; when this mutual interaction is disturbed, it can heighten susceptibility of the organism to the different pathogenic invasions and responses in the gastrointestinal tract (7-11).

In the background of this relationship between MAFLD and GI infections are shared metabolic and inflammatory pathways that implicate one disease with the other. Such information regarding the association could be taken to derive better strategies of preventive and therapeutic interventions that do not simply encompass the liver disease but the associated complications in the gastrointestinal tract. Moreover, study of the observation regarding demographics and comorbidities provides invaluable information related to the risk profiles and, in fact, specifically tailors the interventions that must be used for different patient groups (12-17).

We, therefore, aimed to help fill this knowledge gap by understanding the association of MAFLD with the presence of GI infections using data from the Patient record.(13, 14) This provided an in-depth analysis ranging from patient demographics to common comorbidities, which are likely to influence the incidence of GI infections in this patient population.(15, 16) This allows for a better association of how MAFLD could predispose to gastrointestinal pathogens and these could potentially reflect on clinical management and overall patient care in this subpopulation. As such, the study will add to the literature on MAFLD and GI infection and to that of metabolic health and infectious diseases at large. (17, 18)

## MATERIAL AND METHODS

This study was carried out in adult patients diagnosed with MAFLD and its relationship to GI infections, as identified from data reviewed from the patient record. All participants in this study were adult patients who

had been admitted to the inpatient unit, having been 18 years and above. The study's participants were adult patients with a medically already ICD-10 coded and certified diagnosis of MAFLD. Patients showing evidence of excess alcohol consumption, viral hepatitis, or any other hepatic conditions that might possibly influence the diagnosis of fatty liver disease not associated with metabolic dysfunction were not the adult patients in this study's study participants. A stratified random sampling strategy was used to draw the sample, which offered a representative sample from the national population. The number of the sample size was calculated based on the proportion of MAFLD and GI infections on record in the period of study; hence, a total of 550 patient records were accessed for profiling patient information, payer status, and comorbid conditions. Data from the patient's records were accessed retrospectively, and such records had a massive pool of information on demographic data, clinical diagnosis, comorbid conditions, and primary expected payer, thus offering broad coverage of the variables related to the objective of this study (19-21).

Data were collected in conformity with the Declaration of Helsinki's principles regarding research involving human subjects, and ethical standards were taken into consideration in every stage of the research. Anonymization and deidentification of information were carried out to guarantee anonymity and privacy.

The data were analyzed using SPSS software version 25. Descriptive statistics are used to describe the patient demographics, comorbidities, and incidence of GI infections. We compared the categorical variables between patients with GI infection and non-GI infection using the chi-square test. In the current study, a p-value of  $<0.05$  was taken for statistical significance.

## RESULTS

The Patient record provides comprehensive patient demographics and comorbidities. The relation with metabolic dysfunction-associated fatty liver disease (MAFLD) and the prevalence of gastrointestinal [GI] infection is depicted herein. The rate of GI infections is high in all stratifications of differences among the patient demographics and comorbidities (Table 1).

Of the three age groups, the age group of  $>65$  years has a significantly higher prevalence of GI infection as compared to those without infections, at 57.09% vs. 43.82% ( $p < 0.001$ ). In the youngest age category of 18-44 years, the prevalence of GI infections is much lower, with 12.91% compared to 28.55% in the non-infected group. In the middle-aged group of 45-64 years, the prevalence is more evenly distributed: 30.00% in those with GI infections and 27.64% in those without.

The sex-based analysis showed that the discrepancy in infection rates did not vary much, with nearly the same percentage in both sexes: 26.91% of males had infections, while 27.27% did not; in females, this percentage was 18.18% compared to 27.64% without infections.

Financial status, as per the primary anticipated payer and the median household income categories, also came out to be significantly associated. Patients who were self-paying account for a vast majority of GI infections, 53.45% vis-à-vis 46.55% of those who did not have the infections as defined by a very significant p-value of less than 0.001. Government support and other supported groups also significantly differ in their infection rates.

Significant differences were seen in these when comorbidities were looked at. Those with gastro-oesophageal reflux disease, hyperlipidaemia, smoking habits, diabetes, and hypertension significantly had more GI infections with a p-value all under 0.001, showing a strong statistical significance for these variables. Of note, however, is the fact that rates of obstructive sleep apnoea showed very little difference between the infected and non-infected groups, which was not seen in other comorbid conditions such as inflammatory bowel disease, significantly more prevalent in infected (5.09%) than in non-infected (0.91%) groups.

Even more pronounced, these trends were evidenced in the secondary analysis that had targeted specific GI conditions within the framework of fatty liver disease, as shown in Table 2. Patients with MAFLD had a higher prevalence of bacterial GI infections, including the *Clostridioides difficile* pathogen, *Escherichia coli*, and *Salmonella*. Each of these conditions showed a p-value of less than 0.001, evidencing increased burdens in patients with a fatty liver disease versus those without.

Such findings also underscore the close interactions of metabolic health and socioeconomic factors in the risk of gastrointestinal infections and suggest that individuals with certain comorbid and demographic profiles, among which older adults and those with MAFLD, are associated with an increased risk of developing GI infections.

Table 1 Patient demographics and comorbidities

Demographics	Absence of GI infection n (%)	Presence of GI infection n (%)	P value
Age category			<0.001
18–44	157 (28.55%)	71 (12.91%)	
45–64	152 (27.64%)	165 (30.00%)	
>65	241 (43.82%)	314 (57.09%)	
Sex			0.1174
Male	150 (27.27%)	148 (26.91%)	
Female	152 (27.64%)	100 (18.18%)	
Primary expected payer			<0.001
Self	256 (46.55%)	294 (53.45%)	
Govt	103 (18.73%)	47 (8.55%)	
Supported	191 (34.73%)	209 (38.00%)	
Median household income			<0.001
Lowest quartile	168 (30.55%)	162 (29.45%)	
Second quartile	154 (28.00%)	152 (27.64%)	

Third quartile	126 (22.91%)	124 (22.55%)	
Highest quartile	102 (18.55%)	112 (20.36%)	
Comorbidity			
Gastro-oesophageal reflux disease	103 (18.73%)	132 (24.00%)	<0.001
Hyperlipidaemia	181 (32.91%)	197 (35.82%)	<0.001
Smoking	200 (36.36%)	190 (34.55%)	<0.001
Diabetes	157 (28.55%)	193 (35.09%)	<0.001
Hypertension	312 (56.73%)	382 (69.45%)	<0.001
Obesity	102 (18.55%)	98 (17.82%)	<0.001
Obstructive sleep apnoea	41 (7.45%)	40 (7.27%)	0.02
MAFLD/NASH	15 (2.73%)	27 (4.91%)	<0.001
Inflammatory bowel disease	5 (0.91%)	28 (5.09%)	<0.001

Table 2 Gastrointestinal (GI) conditions

Condition	Absence of MAFLD n (%)	Presence of MAFLD n (%)	P value
Bacterial GI infections	4 (0.9%)	2 (1.5%)	<0.001
Clostridioides difficile	3 (0.8%)	2 (1.3%)	<0.001
Escherichia coli	<1 (0.01%)	<1 (0.3%)	<0.001
Salmonella	<1 (0.03%)	<1 (0.07%)	<0.001
Other	<1 (0.008%)	<1 (0.012%)	0.10

## DISCUSSION

Studies have identified significant correlations, particularly with older people and in the presence of other metabolic comorbidities, such as diabetes and hypertension, between an increased prevalence of gastrointestinal infection and metabolic dysfunction-associated fatty liver disease (MAFLD). Most likely, this is due to the delicate relation between the gut-liver axis and MAFLD, which not only involves the change in microbiota of the gut but also increases the permeability of the intestine in facilitating the transfer of bacteria and associated endotoxins (22-24).

This is consistent with previous findings that showed a higher frequency of these infections in people with liver diseases, with a theoretical premise that liver failure reduces the immune defenses by the development of portal hypertension, which initiates bacterial translocation. However, our study goes a step further and identifies certain age and socio-economic factors that add to this risk. Age-stratified analysis by age and primary expected payer in this study points toward vulnerability to such infections in the older adults and hence suggests that socio-economic factors, possibly manifesting in health access and nutrition disparities, critically modulate this vulnerability to infections (22-25).

Alongside the study's strengths, such as a large sample size and the use of a nationally representative database, there were several limitations. The study's retrospective nature naturally limits inferences about causality from MAFLD to GI infections. The coding accuracy can be flawed with respect to the actual diagnoses. Second,

patient lifestyle factors, which are crucial in the pathophysiology of MAFLD and potentially drive GI health, were not available, and this indeed limits the scope of our analysis (7, 19).

In view of these findings and limitations, future research should focus on prospective studies to better delineate the causal relationships between MAFLD and GI infections. In this context, the use of prospective studies with more detailed clinical information, including lifestyle and dietary patterns, may be more effective in targeting interventions. Clinical practice guidelines should also note increased vigilance for gastrointestinal infections among patients with MAFLD, with a particular focus on demographic groups identified in this study as high risk. Early screening and active management of metabolic comorbidities in such patients may help reduce the burden of serious infections, with a consequent improvement in patient outcomes (21-24).

## CONCLUSION

A large corpus of research has demonstrated a significant positive association between metabolic dysfunction-associated fatty liver disease (MAFLD) and an increase in the prevalence of gastrointestinal infections, particularly in high-risk demographic groups such as the elderly and the socioeconomically deprived. These findings help to justify the need for comprehensive strategies for the screening and management of metabolic and infectious diseases in healthcare systems. This, in turn, would be associated with better clinical outcomes and quality of life for the MAFLD patient due to the reduction of risk and burden from GI infections by the application of preventive targeted measures and personalized treatment approaches. An integrated approach to the management of such complex interrelated conditions would go a long way toward increasing the overall effectiveness of healthcare delivery.

## REFERENCES

1. Popoff MR, Bouvet P. Clostridial toxins. *Future microbiology*. 2009;4(8):1021-64.
2. Rodríguez L, Cervantes E, Ortiz R. Malnutrition and gastrointestinal and respiratory infections in children: a public health problem. *International journal of environmental research and public health*. 2011;8(4):1174-205.
3. Morgan XC, Tickle TL, Sokol H, Gevers D, Devaney KL, Ward DV, et al. Dysfunction of the intestinal microbiome in inflammatory bowel disease and treatment. *Genome biology*. 2012;13(9):R79.
4. Croxen MA, Law RJ, Scholz R, Keeney KM, Wlodarska M, Finlay BB. Recent advances in understanding enteric pathogenic *Escherichia coli*. *Clinical microbiology reviews*. 2013;26(4):822-80.
5. Smits WK, Lyras D, Lacy DB, Wilcox MH, Kuijper EJ. *Clostridium difficile* infection. *Nature reviews Disease primers*. 2016;2:16020.

6. Cortez V, Meliopoulos VA, Karlsson EA, Hargest V, Johnson C, Schultz-Cherry S. Astrovirus Biology and Pathogenesis. *Annual review of virology*. 2017;4(1):327-48.
7. Lanas A, Dumonceau JM, Hunt RH, Fujishiro M, Scheiman JM, Gralnek IM, et al. Non-variceal upper gastrointestinal bleeding. *Nature reviews Disease primers*. 2018;4:18020.
8. Nouvenne A, Ticinesi A, Tana C, Prati B, Catania P, Miraglia C, et al. Digestive disorders and Intestinal microbiota. *Acta bio-medica : Atenei Parmensis*. 2018;89(9-s):47-51.
9. Rasmussen AL. Host Factors Involved in Ebola Virus Replication. *Current topics in microbiology and immunology*. 2018;419:113-50.
10. Cani PD. Microbiota and metabolites in metabolic diseases. *Nature reviews Endocrinology*. 2019;15(2):69-70.
11. Syed-Ahmed M, Narayanan M. Immune Dysfunction and Risk of Infection in Chronic Kidney Disease. *Advances in chronic kidney disease*. 2019;26(1):8-15.
12. Gauer R, Forbes D, Boyer N. Sepsis: Diagnosis and Management. *American family physician*. 2020;101(7):409-18.
13. Gupta A, Madhavan MV, Sehgal K, Nair N, Mahajan S, Sehrawat TS, et al. Extrapulmonary manifestations of COVID-19. *Nat Med*. 2020;26(7):1017-32.
14. Hifumi T. Spontaneous Non-Traumatic Clostridium perfringens Sepsis. *Japanese journal of infectious diseases*. 2020;73(3):177-80.
15. Jothimani D, Venugopal R, Abedin MF, Kaliamoorthy I, Rela M. COVID-19 and the liver. *J Hepatol*. 2020;73(5):1231-40.
16. Kc D, Sumner R, Lippmann S. Gut microbiota and health. *Postgraduate medicine*. 2020;132(3):274.
17. Sarkesh A, Daei Sorkhabi A, Sheykhsaran E, Alinezhad F, Mohammadzadeh N, Hemmat N, et al. Extrapulmonary Clinical Manifestations in COVID-19 Patients. *The American journal of tropical medicine and hygiene*. 2020;103(5):1783-96.
18. Sun J, Zhang J, Wang X, Ji F, Ronco C, Tian J, et al. Gut-liver crosstalk in sepsis-induced liver injury. *Critical care (London, England)*. 2020;24(1):614.
19. Ye Q, Wang B, Zhang T, Xu J, Shang S. The mechanism and treatment of gastrointestinal symptoms in patients with COVID-19. *American journal of physiology Gastrointestinal and liver physiology*. 2020;319(2):G245-g52.



20. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy*. 2020;75(7):1730-41.
21. Al-Aly Z, Xie Y, Bowe B. High-dimensional characterization of post-acute sequelae of COVID-19. *Nature*. 2021;594(7862):259-64.
22. Dietrich R, Jessberger N, Ehling-Schulz M, Märtilbauer E, Granum PE. The Food Poisoning Toxins of *Bacillus cereus*. *Toxins*. 2021;13(2).
23. Carod-Artal FJ. Post-COVID-19 syndrome: epidemiology, diagnostic criteria and pathogenic mechanisms involved. *Revista de neurologia*. 2021;72(11):384-96.
24. Sim JH, Mukerji SS, Russo SC, Lo J. Gastrointestinal Dysfunction and HIV Comorbidities. *Current HIV/AIDS reports*. 2021;18(1):57-62.
25. Chen H, Chen Q. COVID-19 Pandemic: Insights into Interactions between SARS-CoV-2 Infection and MAFLD. *International journal of biological sciences*. 2022;18(12):4756-67.

---

**Authors and Affiliations:**

<sup>1</sup> Hospital Wah Cantt, Pakistan,

<sup>1</sup> Wah Medical College, Wah Cantt, Pakistan

**Author Details:**

Dr. Fatima Hussain: MBBS, Senior House Officer (S.H.O), POF Hospital Wah Cantt, Pakistan, Wah Medical College, Wah Cantt, Pakistan, [hussainfatima656@gmail.com](mailto:hussainfatima656@gmail.com)

Dr. Gohar Kaleem: MBBS, Senior House Officer (S.H.O), POF Hospital Wah Cantt, Pakistan, Wah Medical College, Wah Cantt, Pakistan, [gohar.kaleem.raja@gmail.com](mailto:gohar.kaleem.raja@gmail.com)

**Timeline:**

Received: September 1, 2023

Accepted: October 13, 2023

Scheduled for Publication: October 20, 2023