ORIGINAL ARTICLE

CONTENTS

Frequency and features of cholelithiasis in patients with metabolic-associated fatty liver disease

Yelyzaveta S. Sirchak, Dmitro O. Dubovenko, Mykhailo M. Havrylec, Tetyana F. Rosola, Habriella E. Reyti, Valentina Yu. Koval

UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE

ABSTRACT

Aim: to determine the frequency and peculiarities of the clinical course of GD in patients with MAFLD depending on body mass index (BMI).

Materials and Methods: 324 patients with MAFLD were examined. At the first stage of the study, the frequency of GD in patients with MAFLD was determined. At the second stage of the study, the features of the clinical course of GD in patients with MAFLD were assessed.

Results: The analysis of the results of ultrasound examination of the abdominal cavity indicates a high incidence of GD in patients with MAFLD, namely in 117 (36.1 %) patients. In accordance with the aim of our study, patients were divided into 2 groups: group I (n=117) included patients with MAFLD and GD; group II included patients with MAFLD without GD (n=207). In patients with MAFLD and grade II obesity, mainly calculi larger than 10.0 mm were diagnosed. In patients with normal body weight, as well as with excessive body weight, calculi up to 5.0 mm in size are more often detected.

Conclusions: In 36.1 % of patients with MAFLD, gallbladder disease was detected. In patients with MAFLD, with the progression of obesity, a decrease in the size of gallstones was found.

KEY WORDS: metabolic (dysfunction) associated fatty liver disease, gallstone disease, body mass index, obesity.

Wiad Lek. 2025;78(7):1356-1360. doi: 10.36740/WLek/208995 DOI

INTRODUCTION

Metabolic (dysfunction) associated fatty liver disease (MAFLD) is one of the most common chronic liver diseases with an estimated prevalence of 25-40% in the adult population, rising to 62-84% in high-risk individuals [1-3].

Gallstone disease (GD), including gallstones detected by ultrasound or a history of cholecystectomy, occurs in approximately 5-25% of adults in Western countries. The risk factors for gallstones include hyperlipidemia, obesity, sedentary lifestyle and diabetes. The global prevalence of gallstones is highest in geographical regions with high levels of obesity (North America) [4]. Gallstone disease is also associated with the development of cardiovascular disease, which can be partially explained by changes in the enterohepatic circulation of bile acids and related signalling pathways. Consequently, gallstone disease is associated with increased mortality from all causes, mainly cardiovascular disease and cancer-related mortality [5, 6].

Gallstone disease is also highly prevalent, especially among women of reproductive age, and has similar risk factors to MAFLD, such as obesity, diabetes, high blood pressure, dyslipidaemia and multiple births [1, 7].

Metabolic (dysfunction) associated fatty liver disease shares many risk factors with GD, including hyperlipidemia, obesity, sedentary lifestyle, and diabetes [7], especially in women of reproductive age [1]. Unhealthy and irrational diet has been identified as a risk factor for both MAFLD and GD [8]. The prevalence of both MAFLD and gallstones is increasing in developed countries and correlates with the epidemic of obesity and metabolic syndrome [9].

Therefore, due to the alarming trajectory of these two pathological conditions, further research is needed to better understand the relationship between gallstones and MAFLD.

AIM

The aim of the research to determine the frequency and peculiarities of the clinical course of GD in patients with MAFLD depending on body mass index (BMI).

MATERIALS AND METHODS

At the clinical base of the Department of Procedure of Internal Diseases, 324 patients with MAFLD were

examined. The examined patients with MAFLD for the period 2020 to 2025 were treated in the gastroenterological and endocrinological departments of the Municipal Non-Profit Enterprise «Andriy Novak Transcarpathian Regional Clinical Hospital» of the Transcarpathian Regional Council.

Among the examined patients, there were 186 (57.4 %) men, with an average age of 42.3±4.1 years; there were 138 (42.6 %) women, with an average age of 40.6±3.7 years. The control group included 30 healthy individuals (17 (56.7 %) men and 13 (43.3 %) women). The average age was 41.5±4.5 years.

The examinations were performed with the consent of the patients (written consent for appropriate diagnosis and treatment was obtained from all patients and control subjects) with all measures taken to ensure the anonymity of the information obtained. The methodology of the studies was in line with the Helsinki Declaration of Human Rights of 1975 and its revision of 1983, the Council of Europe Convention on Human Rights and Biomedicine, and the legislation of Ukraine.

The exclusion criteria were as follows: age under 18 years and over 70 years, liver damage due to viral (hepatitis B, C, D viruses), alcohol etiology; haemochromatosis; Wilson-Conovalov disease; history of cholecystectomy; systemic autoimmune diseases; oncological diseases; pulmonary tuberculosis; psychiatric diseases that do not allow adequate assessment of the patient's health status and signing an informed consent for diagnosis and treatment; pregnancy and lactation; acute myocardial infarction, stroke (in the history of up to 6 months);

The diagnosis of MAFLD was made in accordance with the criteria of the unified clinical protocol (Order of the Ministry of Health of Ukraine of 06.11.2014 No. 826) and the EASL-EASD-EASO clinical guidelines for the diagnosis and treatment of these patients. The degree of liver damage was determined using online calculators NAFLD fibrosis score (NFS), Fibrosis 4 calculator (FIB-4), fibrotest, FibroIndex, Forns, APRI, and liver elastometry results.

All examined patients were subjected to examination by general clinical, anthropometric, instrumental and laboratory methods. To verify the diagnosis, the nature of complaints and medical history were detailed. During the anthropometric examination, height, weight, waist circumference were determined, and BMI was calculated. In accordance with WHO recommendations, patients were divided according to BMI, with BMI of 16.0 or less corresponding to severe underweight; 16.0-18.5 - to underweight; 18.0-24.9 - to normal weight; 25.0-29.9 - to overweight; 30.0-34.9 - to obesity of the first degree; 35.0-39.9 - to obesity of the second degree; 40.0 and more - to obesity of the third degree.

All patients underwent an ultrasound examination of the abdominal cavity according to the generally accepted methodology, with an emphasis on the organs of the hepatobiliary and biliary systems. The size of the gallbladder and common bile duct, as well as the presence and absence of calculi in the gallbladder were determined.

At the first stage of the study, the frequency of GD in patients with MAFLD was determined. At the second stage of the study, the features of the clinical course of GD in patients with MAFLD were assessed.

The analysis and processing of the results of the examined patients were performed with the help of the computer program STATISTICA 10.0 (StatSoft Inc, USA) using parametric and non-parametric methods of evaluation of the results.

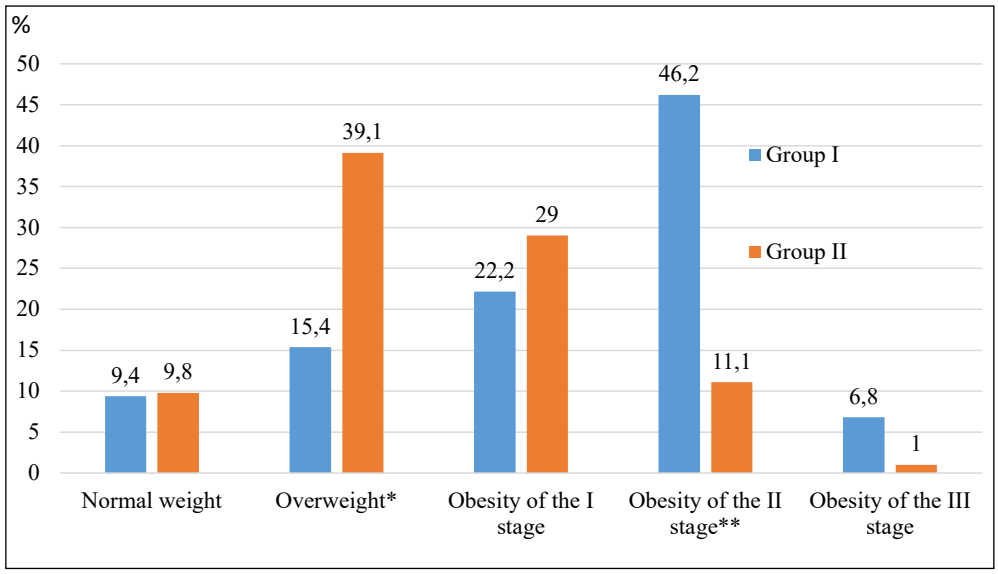

Fig. 1. Changes in BMI in patients with GD with MAFLD
Note: the difference between the indicators in patients is significant: * - $p<0.05$; ** - $p<0.01$

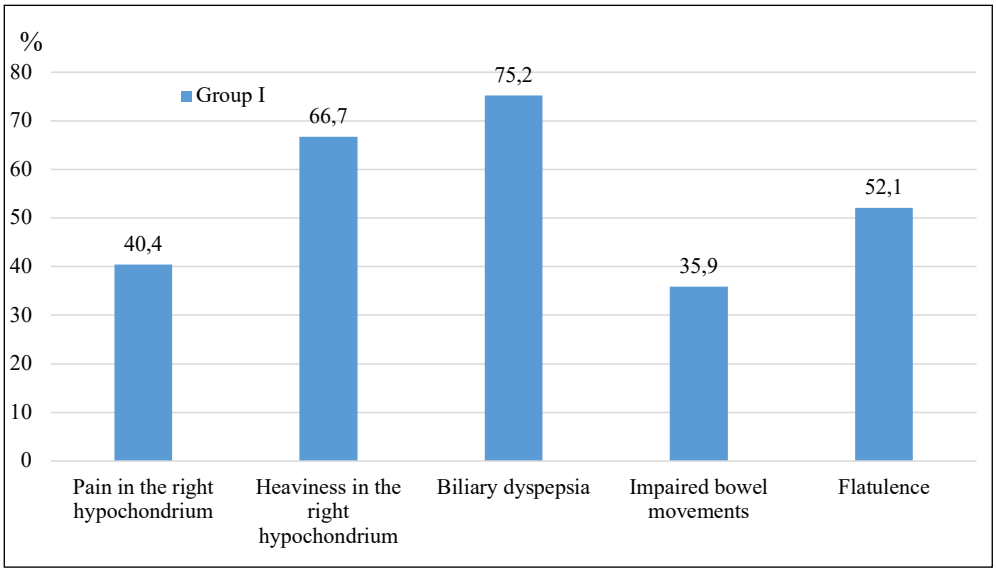

Fig. 2. Frequency of clinical manifestations of GD in patients with MAFLD

Table 1. Changes in the size of gallstones in patients with GD and MAFLD depending on body mass index

Distribution of patients depending on BMI	Size of calculi		
	to 5 mm	5-10 mm	more 10 mm
Normal weight (n=11)	81.8 %	18.2 %	_
Overweight (n=18)	77.8 %	22.2 %	_
Obesity I st. (n=26)	23.1 %	53.8 %	23.1 %
Obesity II st. (n=54)	11.1 %	31.5 %	57.4 %
Obesity III st. (n=8)	_	25.0 %	75.0 %

RESULTS

The analysis of the results of ultrasound examination of the abdominal cavity indicates a high incidence of GD in patients with MAFLD, namely in 117 (36.1 %) patients. In accordance with the aim of our study, patients were divided into 2 groups: group I (n=117) included patients with MAFLD and GD; group II included patients with MAFLD without GD (n=207).

The assessment of anthropometric parameters indicates the prevalence of obesity of varying severity in patients with MAFLD and GD (Fig. 1).

At the second stage of the study in patients with MAFLD (group I), the features of clinical symptoms of GD were assessed.

According to the results obtained, the vast majority of patients with MAFLD GD manifested with heaviness in the right hypochondrium (66.7% of cases), biliary dyspepsia (75.2% of patients), flatulence (52.1% of patients), and impaired defecation (mainly a tendency to constipation). It should be noted that the symptoms occur more often after eating fatty and fried foods (Fig. 2).

An analysis of the size of gallstones is shown in Table 1.

According to the results obtained, with an increase in BMI, an increase in the size of calculi was diagnosed. In patients with MAFLD and grade II obesity, mainly calculi larger than 10.0 mm were diagnosed. The same trend was found among patients with grade II obesity - large calculi greater than 1.0 cm were detected in 57.4% of patients. In patients with normal body weight, as well as with excessive body weight, calculi up to 5.0 mm in size are more often detected.

Thus, our studies allow us to establish a high incidence of GD in patients with MAFLD, which has distinct clinical symptoms. At the same time, the signs of GD in MAFLD are more pronounced in patients with obesity of II-III degree. Further studies are needed to develop effective methods of correction and prevention of GD in patients with MAFLD.

DISCUSSION

Current evidence suggests that metabolic dysfunction is not only the cause of MAFLD, but also a contributing factor to a number of disorders, such as obesity, diabetes and cardiovascular disease. At the same time, cholelithiasis, in particular gallstones, is becoming one of the most important global health issues. The growing prevalence of this disease, which currently affects 5-25% of adults in the US and Europe, combined with

the significant economic burden associated with more than 700,000 cholecystectomies performed annually in the USA, indicates an urgent need to understand its etiology and risk factors [10, 11].

There is a critical intersection of their pathogenetic mechanisms between MAFLD and GD. A meta-analysis conducted from 2005 to 2019 found a 1.71-fold increase in the risk of gallstones in patients with MAFLD, indicating a complex relationship that is not yet fully understood. Various results from international studies, including those from China, South Korea and Turkey, emphasise the need for targeted studies in different demographic populations to clarify this relationship [10, 12]. A study by Arrese M. at al. (2018) found an independent association between MAFLD and gallstone disease [13].

The results of our studies also indicate a high incidence of gallstones in patients with MAFLD. At the same time, our results also indicate a higher incidence of gallstone in patients with MAFLD and obesity of varying severity.

Thus, the common risk factors between MAFLD and gallstone disease, such as obesity, insulin resistance and metabolic syndrome, highlight the common metabolic basis linking these two conditions. However, the high level of comorbidity of MAFLD and cholelithiasis poses challenges for clinical management, especially in patients with metabolic disorders. Studying this relationship is of clinical importance, as it may facilitate early identification of high-risk patients and enable targeted interventions, such as lifestyle modification and lipid control, to prevent the development of gallstones [10].

Given the close relationship between GD and metabolic disorders, many studies have been conducted to investigate the association between GD and the development of metabolic syndrome/MAFLD. However, these relationships are still controversial and differ between studies. Further in-depth analyses are needed to show the consistent risk of quantitative metabolic variables on the risk of developing metabolic syndrome, obesity in MAFLD [14].

CONCLUSIONS

In 36.1 % of patients with MAFLD, gallbladder disease was detected. In patients with MAFLD, with the progression of obesity, a decrease in the size of gallstones was found.

REFERENCES

1. Roesch-Dietlen F, Pérez-Morales AG, Grube-Pagola P et al. Prevalence of metabolic associated fatty liver disease (MAFLD) in patients with gallstone disease. Study on a cohort of cases in South-Southeastern Mexico. Rev Gastroenterol Mex (Engl Ed). 2023;88 (3): 225-231. doi: 10.1016/j.rgmxen.2021.09.006. DOI
2. Miwa T, Tajirika S, Imamura N et al. Usefulness of health checkup-based indices in identifying metabolic dysfunction-associated steatotic liver disease. JGH Open. 2024;8(6):e13110. doi: 10.1002/jgh3.13110. DOI
3. Miao L, Targher G, Byrne CD et al. Current status and future trends of the global burden of MASLD. Trends Endocrinol Metab. 2024;35(8):697-707. doi: 10.1016/j.tem.2024.02.007. DOI
4. Konyn P, Alshuwaykh O, Dennis BB et al. Gallstone Disease and Its Association With Nonalcoholic Fatty Liver Disease, All-Cause and Cause-Specific Mortality. Clin Gastroenterol Hepatol. 2023;21(4):940-948.e2. doi: 10.1016/j.cgh.2022.04.043. DOI
5. Di Ciaula A, Garruti G, Wang DQ, Portincasa P. Cholecystectomy and risk of metabolic syndrome. Eur J Intern Med. 2018;53:3-11. doi: 10.1016/j.ejim.2018.04.019. DOI
6. Zheng Y, Xu M, Heianza Y et al. Gallstone disease and increased risk of mortality: Two large prospective studies in US men and women. J Gastroenterol Hepatol. 2018;33(11):1925-1931. doi: 10.1111/jgh.14264. DOI
7. Jarvis H, Craig D, Barker R et al. Metabolic risk factors and incident advanced liver disease in nonalcoholic fatty liver disease (NAFLD): A systematic review and meta-analysis of population-based observational studies. PLoS Med. 2020;17(4):e1003100. doi:10.1371/journal.pmed.1003100. DOI
8. Yoo ER, Kim D, Vazquez-Montesino LM et al. Diet quality and its association with nonalcoholic fatty liver disease and all-cause and cause-specific mortality. Liver Int. 2020;40(4):815-824. doi: 10.1111/liv.14374. DOI
9. Murag S, Ahmed A, Kim D. Recent Epidemiology of Nonalcoholic Fatty Liver Disease. Gut Liver. 2021;15(2):206-216. doi: 10.5009/gnl20127. DOI
10. Zhang Y, Zhang J, Yu D et al. Association between metabolic dysfunction associated steatotic liver disease and gallstones in the US population using propensity score matching. Sci Rep. 2025;15:910. doi:10.1038/s41598-025-85218-5. DOI
11. Figueiredo JC, Haiman C, Porcel J et al. Sex and ethnic/racial-specific risk factors for gallbladder disease. BMC Gastroenterol. 2017;17(1):153. doi: 10.1186/s12876-017-0678-6. DOI
12. Gu S, Hu S, Wang S et al. Bidirectional association between NAFLD and gallstone disease: a systematic review and meta-analysis of observational studies. Expert Rev Gastroenterol Hepatol. 2023;17(3):283-293. doi: 10.1080/17474124.2023.2175671. DOI
13. Arrese M, Cortés V, Barrera F, Nervi F. Nonalcoholic fatty liver disease, cholesterol gallstones, and cholecystectomy: new insights on a complex relationship. Curr Opin Gastroenterol. 2018;34(2):90-96.doi: 10.1097/MOG.0000000000000416.

14. Lyu J, Lin Q, Fang Z et al. Complex impacts of gallstone disease on metabolic syndrome and nonalcoholic fatty liver disease. Front. Endocrinol. 2022;13:1032557. doi: 10.3389/fendo.2022.1032557. DOI

The study was performed within the framework of the scientific topics "Clinical and Pathogenetic Features of Polymorbid Diseases in the Digestive System and Development of Differentiated Therapy Scheme in the Conditions of the COVID-19 Pandemic" (state registration number 0121U110177) researched by the Department of Propedeutics of Internal Diseases of State University "Uzhhorod National University".

CONFLICT OF INTEREST
The Authors declare no conflict of interest

CORRESPONDING AUTHOR
Yelyzaveta S. Sirchak
Uzhhorod national university
1 Narodna Sqr., 88000 Uzhhorod, Ukraine
e-mail: sirchakliza777@gmail.com

ORCID AND CONTRIBUTIONSHIP
Yelyzaveta S. Sirchak: 0000-0001-6738-0843 A F
Dmitro O. Dubovenko: 0009-0000-3242-8026 B C D
Mykhailo M. Havrylec: 0000-0002-5995-4576 B C D
Tetyana F. Rosola: 0000-0001-5323-8678 B E
Habriella E. Reyti: 0009-0009-0380-1894 B C
Valentina Yu. Koval: 0000-0001-8423-9534 B C

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 14.01.2025
ACCEPTED: 25.06.2025

CREATIVE COMMONS 4.0