Research Square

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Significant Impact of Polypharmacy on Metabolic Dysfunction–Associated Steatotic Liver Disease: Experience from Family Medicine Practice

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Abstract

1.1 Background

Steatotic liver disease (SLD) has emerged as a major public health problem due to its rapidly increasing prevalence and associated disease burden. Metabolic dysfunction–associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), represents a newly adopted nomenclature. In some regions, the term metabolic associated fatty liver disease (MAFLD) is also used, based on slightly different diagnostic criteria. This study aimed to determine the prevalence of NAFLD, MAFLD, and MASLD among adult patients presenting to family medicine outpatient clinics and to evaluate the association of MASLD and polypharmacy.

1.2 Methods

In this cross-sectional study, a total of 1,159 patients who presented to our tertiary care outpatient clinic between 2023 and 2024 were initially screened. After applying the predefined inclusion and exclusion criteria, 408 patients were ultimately included in the final analysis. NAFLD, MAFLD and MASLD were diagnosed according to diagnostic criteria defined by guidelines. Polypharmacy was defined as the concurrent use of more than 5 medications.

1.3 Results

Among the 408 participants, 51.7% met the criteria for NAFLD (N = 211), 52.2% for MAFLD (N = 213), and 50.5% for MASLD (N = 206). Patients with SLD were older and had significantly higher prevalences of hypertension, diabetes mellitus, dyslipidemia, and polypharmacy ($P < 0.005$ for each). In univariable analyses, NAFLD, MAFLD, and MASLD were all associated with increased odds of polypharmacy, with MAFLD showing the strongest association (OR: 2.34; 95% CI: 1.30–4.24). After adjustment for age and sex, only MAFLD remained significantly associated with polypharmacy (OR: 1.63; 95% CI: 1.01–2.65). This association persisted after further adjustment for cardiometabolic risk factors (OR: 1.58; 95% CI: 1.02–2.46), whereas NAFLD and MASLD were no longer significant. The combined presence of NAFLD, MAFLD, and MASLD was associated with polypharmacy in univariable analysis (OR: 2.19; 95% CI: 1.21–3.96) but not after full adjustment.

1.4 Conclusion

The prevalence of NAFLD, MAFLD, and MASLD was significantly high and these conditions were significantly associated with advanced age, metabolic comorbidities, and polypharmacy. Future multicenter, prospective studies are needed to further elucidate the impact of polypharmacy on disease severity.

1.5 Trial registration

Not applicable.

Background

Steatotic liver disease (SLD) became a major public health concern due to its rapidly increasing prevalence. In an analysis of 21,034 individuals from the National Health and Nutrition Examination Survey (NHANES) conducted between 1999 and 2018, the reported prevalence of non-alcoholic fatty liver disease (NAFLD), metabolic associated fatty liver disease (MAFLD), and metabolic dysfunction–associated steatotic liver disease (MASLD) was 27.6%, 29.9%, and 27.7%, respectively, underscoring an epidemiological burden affecting nearly one-third of the population (1). Its prevalence in apparently healthy individuals has been shown to exceed 20% in recent years (2, 3). Additionally, patients

in hepatology practice have been shown to have a higher prevalence of MASLD (4). Moreover, the burden associated with liver transplantation has been shown to increase (5).

In the current literature, although an increasing number of studies examined the associations of the newly proposed nomenclatures (MAFLD and MASLD) with clinical outcomes, metabolic parameters, and cardiovascular risk, the population-level implications of these definitions remained unclear (6). Epidemiological investigations using different diagnostic criteria indicated that disease prevalences are relatively similar, yet the clinical profiles of affected individuals may vary considerably (1, 7, 8). The limited availability of large-scale data incorporating the newly adopted terminologies constitutes an important unmet need in current research.

Meanwhile, medication use and the concept of polypharmacy have gained growing importance in the context of liver health. Polypharmacy may exert direct or indirect effects on hepatic metabolism and potentially influence hepatic steatosis by triggering inflammatory pathways (9). However, studies evaluating the impact of polypharmacy on NAFLD, MAFLD, and MASLD remain scarce. On the other hand, previous studies have consistently shown that patients with a high disease burden—such as those with psoriasis or kidney transplant recipients requiring continuous immunosuppressive therapy—also have significantly higher prevalences of MASLD (10–12).

This study aims to compare the prevalence of NAFLD, MAFLD, and MASLD in a population-based sample and to evaluate the potential impact of polypharmacy on these conditions. The findings are expected to inform clinical risk assessment and provide a scientific basis for the development of early diagnostic and preventive strategies.

Methods

4.1 Study Population

This descriptive cross-sectional study was conducted through a retrospective review of medical records from 1,159 patients aged ≥ 18 years who presented to the Family Medicine Outpatient Clinic of Recep Tayyip Erdogan University Training and Research Hospital, Rize, between April 18, 2023 and June 27, 2024. Pregnant women and patients who were bedridden or wheelchair-dependent and therefore unable to undergo standing height and weight measurements were not included in the study. Additionally, 165 patients with incomplete laboratory data and 586 patients in whom hepatic steatosis could not be assessed using ultrasonography, computed tomography, magnetic resonance imaging, or fibroscan were excluded from the analysis.

Patients who met the inclusion criteria were stratified into two groups according to the availability of imaging data suitable for the assessment of hepatic steatosis. For patients with available imaging, reports from ultrasonography (USG), computed tomography (CT), or magnetic resonance imaging (MRI) were reviewed. Individuals with documented hepatic steatosis on imaging were directly assigned to the diagnostic classification stage, whereas those without evidence of hepatic steatosis were designated as the reference group (13, 14). For patients without available imaging data, hepatic steatosis was assessed using FibroScan measurements. Controlled attenuation parameter (CAP) values were evaluated, with a CAP value ≥ 248 dB/m considered indicative of hepatic steatosis. Prior to FibroScan examination, Fibrosis-4 (FIB-4) scores were calculated, and patients with a FIB-4 score ≥ 1.3 subsequently underwent FibroScan assessment. FIB- score was calculated as follows: FIB 4 = (Age x AST) / (Platelet count x √ALT) (15).

In the final step, patients with hepatic steatosis confirmed through imaging modalities or Fibroscan assessment were combined, and NAFLD, MAFLD, and MASLD groups were formed according to the guideline-based diagnostic criteria. Following diagnostic classification, polypharmacy status was evaluated within these groups (Fig. 1).

4.2 Classification of Steatotic Liver Disease

In this study, individuals with hepatic steatosis were evaluated according to the NAFLD, MASLD, and MAFLD terminologies defined in the contemporary literature. Secondary causes of hepatic steatosis, including significant alcohol consumption greater than 20 g/day for women and 30 g/day for men, viral hepatitis, autoimmune hepatitis, and the use of hepatotoxic medications, were excluded, and patients with hepatic steatosis were classified into the NAFLD group (6, 16). MAFLD classification considered the presence of hepatic steatosis in addition to diabetes, overweight/obesity, or metabolic risk factors (17). In the definition of MASLD, the metabolic approach was applied with simpler criteria, and the presence of at least one cardiometabolic risk factor (e.g., obesity, hypertension, dyslipidemia, or glucose metabolism disorder) accompanying hepatic steatosis was considered sufficient for diagnosis (18, 19).

4.3 Definition of Polypharmacy

Polypharmacy was defined as the concurrent use of five or more medications, in accordance with the widely accepted definition in the literature (20). Information on patients' medication use was recorded during outpatient clinic visits by reviewing detailed medical history and the national electronic healthcare record system.

4.4 Statistical Analysis

Statistical analyses were performed using SPSS software version 26.0. The normality of data distribution was assessed using the Kolmogorov–Smirnov or Shapiro–Wilk tests. Descriptive statistics were presented as mean ± standard deviation for normally distributed continuous variables and as frequencies and percentages for categorical variables.

For comparisons between groups, the independent-samples t test was used when parametric assumptions were satisfied. Categorical variables were analyzed using the Pearson chi-square test or Fisher's exact test, as appropriate.

Additionally, the association between polypharmacy and diagnostic groups was evaluated using univariable and multivariable logistic regression analyses. Variables included in the multivariable logistic regression model were selected based on the results of univariable analyses and their observed associations with polypharmacy within the study population. A p-value < 0.05 was considered statistically significant for all analyses.

Results

A total of 408 individuals were included in the study. Hepatic steatosis was detected in 220 participants. In the subclassification of this group, NAFLD, MAFLD, and MASLD were identified in 211 (51.7%), 213 (52.2%), and 206 (50.5%) patients, respectively. A substantial overlap was observed among the three definitions; 205 (50.2%) participants simultaneously met the diagnostic criteria for NAFLD, MAFLD, and MASLD. In contrast, 5 (1.2%) participants fulfilled only the NAFLD definition, 8 (2%) fulfilled only the MAFLD definition, and 1 (0.2%) participant met both NAFLD and MASLD definitions. Additionally, 188 (46.1%) individuals were classified as the reference group (Fig. 2).

Table 1
Comparison of Characteristics among NAFLD, MAFLD, MASLD, and the Reference Group

	REFERENCE Group (N = 188)	**NAFLD Group (N = 211)**	**p**	**MAFLD Group (N = 213)**	**p**	**MASLD Group (N = 206)**	**p**
Age (years), mean (SD)[1]	50,15 (18, 21)	58.83 (13.72)	**< 0,001**	59,50 (13, 13)	**< 0,001**	59,36 (13, 29)	**< 0,001**
Sex, n (%)[2]			0,874		0,996		0,982
Female	135 (%71,8)	150 (%71,1)		153 (%71,8)		147 (%71,4)	
Male	53 (%28,2)	61 (%28,9)		60 (%28,2)		59 (%28,6)	
Hypertension, n (%)[2]			**0,005**		**0,002**		**0,003**
Absent	113 (%60,1)	97 (%46,0)		95 (%44,6)		93 (%45,1)	
Present	75 (%39,9)	114 (%54,0)		118 (%55,4)		113 (%54,9)	
Diabetes Mellitus, n(%)[2]			**< 0,001**		**< 0,001**		**< 0,001**
Absent	167 (%88,8)	158 (%74,9)		160 (%75,1)		153 (%74,3)	
Present	21 (%11,2)	53 (%25,1)		53 (%24,9)		53 (%25,7)	
Use of Lipid-Lowering Medication, n (%)[2]			0,115		0,057		0,091
Absent	167 (%88,8)	175 (%83,3)		174 (%82,1)		170 (%82,9)	
Present	21 (%11,2)	35 (%16,7)		38 (%17,9)		35 (%17,1)	
Number of Regularly Used Medications, Mean (SD)[1]	1.67 (1,95)	2,42 (2, 18)	**< 0,001**	2,53 (2, 19)	**< 0,001**	2,47 (2, 18)	**< 0,001**
Polypharmacy, n (%)[2]			**0,015**		**0,006**		**0,011**
Absent	170 (%90,4)	173 (%82,0)		172 (%80,8)		168 (%81,6)	

* [1]Independent Samples T-Test [2] Pearson's Chi-Square Test [3] Fisher's Exact test

	REFERENCE Group (N = 188)	NAFLD Group (N = 211)	p	MAFLD Group (N = 213)	p	MASLD Group (N = 206)	p
Present	18 (%9,6)	38 (%18,0)		41 (%19,2)		38 (%18,4)	
Smoking status, n (%)[2]			0,756		0,776		0,692
Never smoker	165 (%87,8)	180 (%85,3)		182 (%85,4)		175 (%85,0)	
Current smoker	18 (%9,6)	25 (%11,8)		25 (%11,7)		25 (%12,1)	
Former smoker	5 (%2,7)	6 (%2,8)		6 (%2,8)		6 (%2,9)	
Alcohol use, n (%)[3]			0,347		0,669		0,353
Non-user	185 (%98,4)	210 (%99,5)		211 (%99,1)		205 (%99,5)	
Alcohol user	3 (%1,6)	1 (%0,5)		2 (%0,9)		1 (%0,5)	
Former alcohol user	-	-		-		-	
* [1]Independent Samples T-Test [2] Pearson's Chi-Square Test [3] Fisher's Exact test							

* P values indicated the comparison of a steatotic liver disease group to the reference group. Patients in the NAFLD group had an alcohol consumption below the significant alcohol consumption limit.

In Table 1, the mean age of participants in the reference group was 50.15 ± 18.21 years, whereas it was significantly higher in the NAFLD, MAFLD, and MASLD groups ($P < 0.001$). The prevalence of hypertension and diabetes mellitus was also significantly greater in all hepatic steatosis groups compared with the reference group ($P < 0.01$). In addition, the mean number of regularly used medications was higher among patients with hepatic steatosis. Consistently, the prevalence of polypharmacy was markedly increased across all hepatic steatosis groups relative to the reference group ($P < 0.05$).

Table 2
Comparison of Laboratory and Anthropometric Parameters Among Reference, NAFLD, MAFLD, and MASLD Groups

	REFERENCE Group (N = 188)	**NAFLD Group (N = 211)**	**p**	**MAFLD Group (N = 213)**	**p**	**MASLD Group (N = 206)**	**p**
Weight, kg, mean (SD)	74,21 (15,40)	85,06 (14, 27)	**< 0,001**	85,31 (13,92)	**< 0,001**	85,64 (13,98)	**< 0,001**
Height, cm, mean (SD)	163,12 (8.67)	162,70 (9.30)	0,646	162,35 (9, 31)	0,394	162,49 (9, 28)	0,492
Waist circumference, cm, mean (SD)	90,23 (13,74)	101,95 (12,93)	**< 0,001**	102,31 (12,56)	**< 0,001**	102,49 (12,68)	**< 0,001**
BMI, kg/m², mean (SD)	28,00 (6, 15)	32,21 (5, 21)	**< 0,001**	32,42 (4,95)	**< 0,001**	32,50 (5,00)	**< 0,001**
Blood pressure ≥ 130/85 mmHg, n (%)	78 (%41,5)	108 (%51,4)	**0,047***	111 (%52,4)	**0,030***	106 (%51,5)	**0,038***
ALT, U/L, mean (SD)	22,27 (26,43)	31,20 (42,96)	**0,012**	31,42 (42,94)	**0,010**	31,67 (43,49)	**0,009**
AST, U/L, mean (SD)	23,32 (16,02)	26,94 (26,70)	0,107	27,08 (26,74)	0,094	27,21 (27,02)	0,087
PLT, 10^3/uL, mean (SD)	256,38 (105,62)	243,60 (105,62)	0,134	245,32 (61,18)	0,194	243,72 (60,76)	0,142
Glucose, mg/dL, mean (SD)	97,98 (31,84)	104,80 (28,62)	**0,025**	105,61 (30, 23)	**0,014**	105,30 (28,85)	**0,017**
HbA1C, %, mean (SD)	5,84 (0,74)	6,22 (0,87)	**< 0,001**	6,25 (0,86)	**< 0,001**	6,24 (0,87)	**< 0,001**
LDL, mg/dL, mean (SD)	131,12 (44,58)	136,23 (45,14)	0,257	137,45 (44,83)	0,158	136,13 (45,09)	0,270
Non-HDL, mg/dL, mean (SD)	155,29 (49,41)	166,14 (45,14)	**0,027**	167,95 (48,15)	**0,010**	166,44 (48,25)	**0,024**
HDL, mg/dL, mean (SD)	56,72 (13, 11)	53,43 (12,55)	**0,011**	53,48 (12,67)	**0,012**	53,20 (12,62)	**0,007**
Triglycerides, mg/dL, mean (SD)	124,90 (68,59)	155,47 (78,67)	**< 0,001**	159,91 (85,68)	**< 0,001**	157,58 (78,75)	**< 0,001**
GGT, U/L, mean (SD)	25,75 (24,82)	36,98 (50,46)	**0,005**	37,27 (50,21)	**0,003**	37,46 (51,08)	**0,004**

	REFERENCE Group (N = 188)	NAFLD Group (N = 211)	p	MAFLD Group (N = 213)	p	MASLD Group (N = 206)	p
FIB-4 Score, mean (SD)	1,15 (0,68)	1,35 (0,75)	**0,005**	1,35 (0,74)	**0,004**	1,36 (0,75)	**0,003**

* Pearson's Chi-Square Test was used for the analysis of the marked categorical variables, whereas the Independent Samples T-Test was applied for all other numerical variables.

As shown in Table 2, the NAFLD, MAFLD, and MASLD groups exhibited significantly higher values for body weight, waist circumference, body mass index, blood pressure, alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), glucose, HbA1c, non–HDL cholesterol, triglycerides, and the FIB-4 score compared with the reference group. In contrast, high-density lipoprotein (HDL) cholesterol levels were significantly lower across all three hepatic steatosis groups.

Table 3
Association Between NAFLD, MAFLD, MASLD and Polypharmacy: Univariable and Multivariable Logistic Regression Analyses

Disease status	N	n (polypharmacy)	Univariable OR (95% CI)	p-value	Multivariable Model 1 OR (95% CI)*	p-value	Multivariable Model 2 OR (95% CI)**	p-value
No NAFLD	–	–	1	–	1	–	1	–
NAFLD	211	38	**1.84 (1.04–3.26)**	**0.037**	1.21 (0.68–2.15)	0.51	1.09 (0.61–1.94)	0.77
No MAFLD	–	–	1	–	1	–	1	–
MAFLD	213	41	**2.34 (1.30–4.24)**	**0.005**	**1.63 (1.01–2.65)**	0.046	**1.58 (1.02–2.46)**	**0.041**
No MASLD	–	–	1	–	1	–	1	–
MASLD	206	38	**1.95 (1.10–3.46)**	**0.022**	1.32 (0.78–2.22)	0.3	1.23 (0.62–2.44)	0.56
NAFLD − / MAFLD − / MASLD −	188	18	1	–	1	–	1	–
NAFLD + / MAFLD + / MASLD +	205	38	**2.19 (1.21–3.96)**	**0.013**	**1.45 (1.02–2.07)**	0.038	1.12 (0.97–1.29)	0.124

Note: Univariable and multivariable logistic regression models were used to evaluate the association between steatotic liver disease definitions and polypharmacy. Multivariable Model 1 was adjusted for age and sex. Multivariable Model 2 included all covariates in Model 1 and was further adjusted for hypertension, diabetes mellitus, body mass index, and lipid-lowering medication use. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Disease combination categories with very small sample sizes or zero polypharmacy events were excluded from multivariable analyses due to unstable estimates.

As shown in Table 3, in univariable analyses, NAFLD, MAFLD, and MASLD were all significantly associated with an increased likelihood of polypharmacy compared with individuals without hepatic steatosis. Among these definitions, MAFLD demonstrated the strongest unadjusted association (OR: 2.34; 95% CI: 1.30–4.24).

After adjustment for age and sex (Multivariable Model 1), the association between MAFLD and polypharmacy remained statistically significant (OR: 1.63; 95% CI: 1.01–2.65), whereas the associations for NAFLD and MASLD were attenuated and no longer significant.

In the fully adjusted model (Multivariable Model 2), which additionally accounted for hypertension, diabetes mellitus, body mass index, and lipid-lowering medication use, MAFLD continued to be independently associated with polypharmacy (OR: 1.58; 95% CI: 1.02–2.46). In contrast, NAFLD and MASLD did not show an independent association with polypharmacy after full adjustment.

When disease combinations were evaluated, individuals meeting the criteria for NAFLD, MAFLD, and MASLD simultaneously exhibited a significantly higher odds of polypharmacy in univariable analysis (OR: 2.19; 95% CI: 1.21–3.96). This association persisted after adjustment for age and sex but was no longer statistically significant in the fully adjusted model.

Table 4
Multivariable Logistic Regression Model for Polypharmacy

Variable	Adjusted OR	p-value	95% CI for OR	Effect Size (β)
Age (per year)	1.09	**< 0.001**	1.056–1.125	0.086
Sex (Male)	1.1	0.789	0.547–2.211	0.095
Hypertension	1.053	0.893	0.496–2.234	0.052
Diabetes Mellitus	4.625	**< 0.001**	2.339–9.144	1.531
BMI (kg/m²)	0.989	0.716	0.930–1.051	−0.011
Lipid-lowering medication use	2.423	**0.017**	1.172–5.009	0.885

Adjusted odds ratios with 95% confidence intervals (CIs) were obtained using multivariable logistic regression analysis. Effect size was reported as the regression coefficient (β, log odds). Polypharmacy was defined as the concurrent use of ≥ 5 medications.

In the multivariable logistic regression model presented in Table 4, age, diabetes mellitus, and lipid-lowering therapy emerged as independent determinants of polypharmacy. Increasing age was significantly associated with a higher likelihood of polypharmacy (adjusted OR per year: 1.09; 95% CI: 1.06–1.13; $p < 0.001$). Diabetes mellitus remained a strong and independent predictor of polypharmacy (adjusted OR: 3.87; 95% CI: 1.93–7.77; $p < 0.001$). Use of lipid-lowering medication was also independently associated with polypharmacy (adjusted OR: 2.42; 95% CI: 1.17–5.01; $p = 0.017$). Sex, hypertension, and body mass index were not independently associated with polypharmacy in the fully adjusted model.

Discussion

Our study represents the first prevalence investigation of NAFLD, MAFLD, and MASLD conducted within primary care settings in Türkiye, with prevalences of 51.7%, 52.2%, and 50.5%, respectively. In comparison, Pan et al. reported prevalences of 27.6%, 29.9%, and 27.7% in a U.S. cohort of 21,034 individuals using data collected between 1999 and 2018 (1). Population aging, increasing rates of metabolic syndrome, changes in dietary habits, and rising social stress levels may collectively explain the higher prevalences of NAFLD, MAFLD, and MASLD both in our study and in the broader literature. Moreover, previous studies from Türkiye have reported prevalence rates reaching up to 50%, highlighting the substantial burden of the disease (21–24)

In addition, we investigated the relationship between polypharmacy and MASLD in Türkiye for the first time. We found that both the number of regularly used medications and the prevalence of polypharmacy were significantly lower among individuals without hepatic steatosis. In univariable analyses, NAFLD, MAFLD, and MASLD were all associated with increased odds of polypharmacy, with MAFLD demonstrating the strongest association (OR: 2.34; 95% CI: 1.30–4.24). After adjustment for age and sex, only MAFLD remained significantly associated with polypharmacy (OR: 1.63; 95% CI: 1.01–2.65). This association persisted after further adjustment for cardiometabolic risk factors, including

hypertension, diabetes mellitus, body mass index, and lipid-lowering medication use (OR: 1.58; 95% CI: 1.02–2.46), whereas NAFLD and MASLD were no longer significantly associated with polypharmacy.

The combined presence of NAFLD, MAFLD, and MASLD was associated with an increased likelihood of polypharmacy in univariable analysis (OR: 2.19; 95% CI: 1.21–3.96); however, this association was no longer significant after full adjustment. In contrast to systematic reviews reporting a high prevalence of polypharmacy among MASLD populationsreaching up to 81% the prevalence observed in our cohort was substantially lower (25). The findings of the present study may differ due to sample characteristics and regional limitations. In this context, the restriction of the study population to Rize province limits the generalizability of the results, highlighting the need for larger, multicenter studies conducted in diverse populations to further elucidate this association. Similarly, among patients with NAFLD and diabetes mellitus, polypharmacy has been reported in 59% of cases, while hyperpolypharmacy (≥ 10 medications) has been observed in up to 31% (26).

The bidirectional relationship between polypharmacy and metabolic liver disease represents a complex clinical challenge. On one hand, the high burden of metabolic comorbidities including hypertension, diabetes mellitus, dyslipidemia, cardiovascular disease, and sleep apnea necessitates multiple medications to manage these conditions (25, 26). On the other hand, polypharmacy itself may contribute to liver injury through multiple pathophysiological mechanisms. Therefore, the management of polypharmacy in MASLD requires a multidisciplinary and individualized approach. In a systematic review and meta-analysis by Li et al., the incidence of drug-induced liver injury was reported as 4.94 per 100,000 person-years, with an upward trend over time (27). Furthermore, Stine et al. emphasized that polypharmacy is an important risk factor for drug-induced liver injury (28).

Polypharmacy has emerged as an increasingly important clinical concern worldwide. In a large-scale meta-analysis including 295 studies from 41 countries and a total of 59,552,762 participants, the prevalence of polypharmacy was reported as 37%, rising to 45% among older adults (29). Similarly, a comprehensive study evaluating the prevalence and temporal trends of polypharmacy in the adult population of the United States reported an overall prevalence of 17.1%, which increased to 44.1% among older adults, 61.7% among individuals with cardiovascular disease, and 57.7% among those with diabetes mellitus (30). In our study, the prevalence of polypharmacy was 9.6% among individuals without hepatic steatosis and 18.4% in the MASLD group. Consistent with previous reports, advancing age was significantly associated with an increased likelihood of polypharmacy, with each one-year increase in age corresponding to a 9% rise in risk. In addition, individuals with diabetes mellitus exhibited a 4.625-fold higher risk of polypharmacy, while those receiving lipid-lowering therapy had a 2.423-fold increased risk. The wide variation in reported prevalence rates across studies may be attributed to differences in age distribution, burden of comorbidities, prescribing practices across healthcare systems, and methodological heterogeneity among data sources. Collectively, these findings align with existing literature and indicate that the growing burden of age-related chronic diseases and the increasing need for pharmacological management render polypharmacy an increasingly unavoidable clinical phenomenon.

In our study, the prevalences of hypertension, diabetes mellitus, and dyslipidemia were significantly higher in the NAFLD, MAFLD, and MASLD groups compared with individuals without hepatic steatosis. Ballestri et al. reported that the incidence of type 2 diabetes mellitus is approximately two-fold higher in individuals diagnosed with NAFLD (31). Similarly, a meta-analytic evaluation by Younossi et al. identified hypertension as one of the major comorbidities associated with NAFLD (32). Our findings further support the strong link between metabolic dysfunction and hepatic steatosis described in the literature (33). With respect to lipid parameters, HDL levels were lower, while triglyceride and non-HDL cholesterol levels were higher in our cohort. These results are consistent with the findings of Song et al., who demonstrated that dyslipidemia plays an important role in the development of hepatic steatosis in a U.S. population (34). Kawano and Cohen also emphasized that triglyceride accumulation is one of the key pathophysiological mechanisms leading to hepatocellular steatosis (35). Furthermore, the significantly higher values of weight, waist

circumference, and BMI in the NAFLD, MAFLD, and MASLD groups underscore the role of obesity as a major determinant of hepatic steatosis. In a 2022 study, Xue et al. similarly found that BMI values were significantly higher in patients with NAFLD and MAFLD, with an average BMI of 31.3 among affected individuals (36). These findings collectively highlight that overweight and obese individuals are at elevated risk for hepatic steatosis and emphasize the importance of targeted disease management strategies. Additionally, our study contributes to the limited but growing body of literature examining polypharmacy within the context of the newly defined MASLD and MAFLD terminologies. The key finding of our study is the substantial overlap among the different nomenclatures within our study population, consistent with previous reports, supporting their interchangeable use (37) Future research should evaluate the effectiveness of deprescribing interventions on clinical outcomes and focus on the development of individualized dosing approaches that promote rational medication use in the general population.

Our study should be interpreted in light of its strengths and limitations. It adds to the limited existing literature by evaluating the newer definitions of MAFLD and MASLD alongside NAFLD and by examining their associations with polypharmacy. Nonetheless, several limitations warrant consideration. The single-center design may restrict generalizability and introduce potential selection bias. In addition, laboratory parameters were derived from a single measurement, which may not adequately reflect long-term biological variability.

Conclusion

Our study demonstrates that NAFLD, MAFLD, and MASLD are highly prevalent among adult patients and are strongly associated with older age, hypertension, diabetes mellitus, and polypharmacy. As the first study from Türkiye to specifically examine the relationship between MASLD and polypharmacy, our findings make a meaningful contribution to the evolving literature on this emerging terminology. Future multicenter and longitudinal studies are warranted to better elucidate the independent impact of polypharmacy on MASLD progression and clinical outcomes.

Abbreviations

SLD: Steatotic liver disease

MASLD: Metabolic dysfunction–associated steatotic liver disease

NAFLD: Non-alcoholic fatty liver disease

MAFLD: Metabolic associated fatty liver disease

NHANES: National health and nutrition examination survey

USG: Ultrasonography

CT: Computed tomography

MRI: Magnetic resonance imaging

CAP: Controlled attenuation parameter

FIB-4: Fibrosis-4

ALT: Alanine aminotransferase

AST: Aspartate aminotransferase

GGT: Gamma-glutamyl transferase

HDL: High-density lipoprotein

PLT: Platelet count

BMI: Body mass ındex

HbA1c: Glycated hemoglobin

Declarations

9. Ethics approval and consent to participate

This study was approved by the Clinical Research Ethics Committee of the Faculty of Medicine at Recep Tayyip Erdoğan University (Decision No: 2024/294, dated December 5, 2024) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

10. Consent for publication

Not applicable

11. Availability of data and materials

Data that support the results of this study are available from the corresponding author upon request.

12. Competing interests

All authors have declared no conflicts of interest.

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14. Authors' contributions

CA conceptualized and designed the study, contributed to the interpretation of the data, and critically revised the manuscript for important intellectual content. HÖ collected the data, performed the analyses, and drafted the manuscript. All authors read and approved the final manuscript.

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Figures

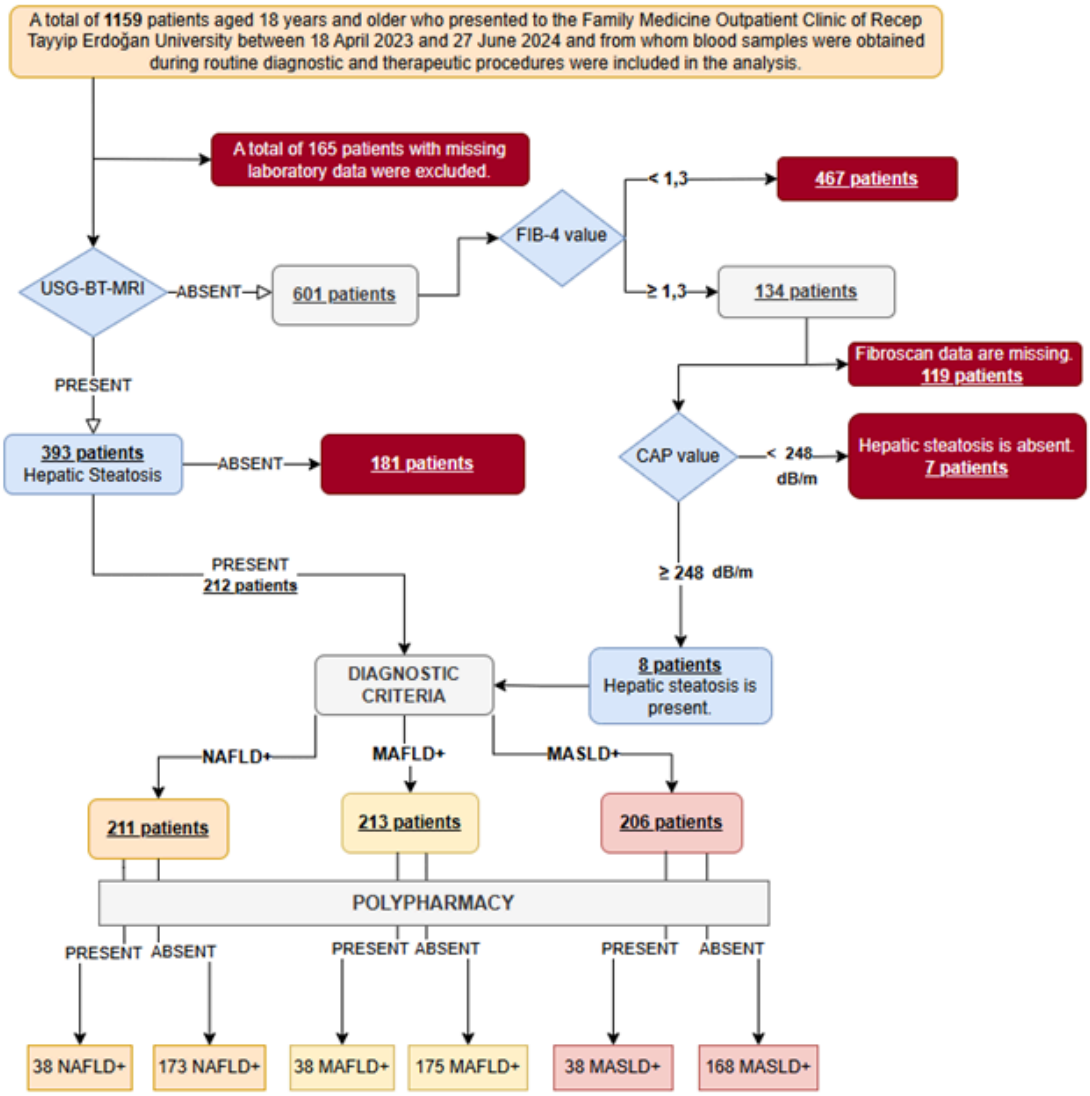


Figure 1

Flow Diagram

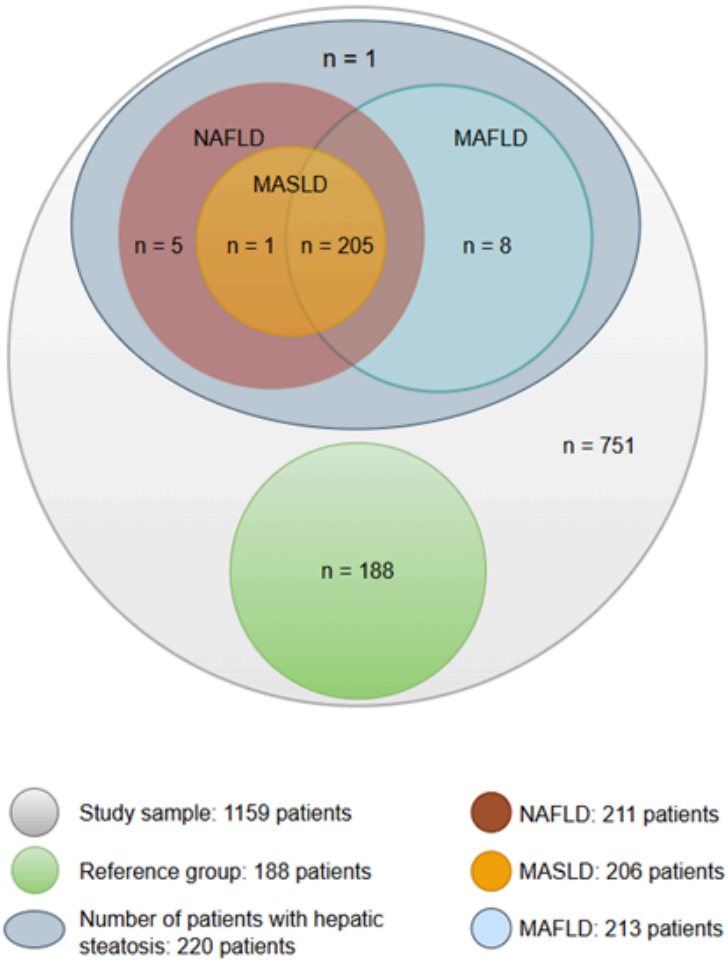


Figure 2

Venn Diagram showing the distrubution of MASLD, MAFLD, NAFLD and patients without hepatic steatosis