

Vitamin D deficiency as a risk factor for metabolic dysfunction-associated steatotic liver disease

Niedobór witaminy D jako czynnik ryzyka stłuszczeniowej choroby wątroby związanej z dysfunkcją metaboliczną

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Słowa kluczowe: stłuszczeniowa choroba wątroby związana z dysfunkcją metaboliczną, witamina D, czynniki ryzyka.

Abstract

Introduction: Vitamin D deficiency is an important health problem. Numerous studies reported a link between vitamin D deficiency and cancer as well as autoimmune and metabolic diseases. However, there are limited data on the association between vitamin D deficiency and metabolic dysfunction-associated steatotic liver disease (MASLD).

Aim of the research: To assess the association between vitamin D deficiency and MASLD.

Material and methods: This was a retrospective, single-centre study assessing the medical data of patients hospitalised at an internal medicine unit from January 2021 to December 2022. All patients were examined for vitamin D levels and the presence of MASLD.

Results: The study included 446 patients, of whom 41% were diagnosed with MASLD. To determine if serum vitamin D levels can be used to differentiate between patients with and without MASLD, the area under the receiver operating characteristic curve was estimated, and the optimal cutoff value was identified by maximising the Youden index. The cutoff value based on the Youden index for vitamin D levels was 27.6 ng/ml. Vitamin D levels of 27.6 ng/ml or lower were reported in 79.8% of patients with MASLD ($p = 0.0160$). In a multivariable regression analysis, male sex, diabetes mellitus, obesity or overweight, and vitamin D levels of 27.6 ng/ml or lower predicted MASLD.

Conclusions: The study confirmed that vitamin D deficiency is common among patients with MASLD. Vitamin D deficiency defined as vitamin D levels of 27.6 ng/ml or lower predicts MASLD. Vitamin D supplementation has the potential to become a therapeutic intervention aimed at reducing the risk of MASLD.

Streszczenie

Wprowadzenie: Niedobór witaminy D jest ważnym problemem zdrowia publicznego. Wiele badań potwierdza związek niedoboru witaminy D z chorobami nowotworowymi, autoimmunologicznymi oraz metabolicznymi. Poszukuje się powiązań niedoboru witaminy D ze stłuszczeniową chorobą wątroby związaną z dysfunkcją metaboliczną (MASLD).

Cel pracy: Ocena związku między niedoborem witaminy D a MASLD.

Materiał i metody: Przeprowadzono retrospektywną, jednośrodkową analizę danych medycznych pacjentów hospitalizowanych na oddziale chorób wewnętrznych od stycznia 2021 do grudnia 2022 roku. U pacjentów oznaczano stężenie witaminy D oraz oceniano występowanie MASLD.

Wyniki: Do badania włączono 446 pacjentów, wśród których u 41% rozpoznano MASLD. Aby ocenić, czy stężenie witaminy D w surowicy można wykorzystać do rozróżnienia pacjentów z MASLD i tych bez MASLD, oszacowano obszar pod krzywą ROC i określono optymalną wartość odcięcia poprzez maksymalizację wskaźnika Youdena. Punkt odcięcia na podstawie kryterium Youdena dla stężenia witaminy D wyniósł 27,6 ng/ml. Stężenie witaminy D $\leq 27,6$ ng/ml uzyskało 79,8% pacjentów z MASLD ($p = 0,0160$). Na podstawie analizy regresji wieloczynnikowej ustalono, że płeć męska, cukrzyca, otyłość lub nadwaga, stężenie witaminy D $\leq 27,6$ ng/ml stanowiły czynniki predykcyjne MASLD.

Wnioski: W przedstawionym badaniu potwierdzono częste występowanie niedoboru witaminy D. Niedobór tej witaminy określany jako stężenie witaminy D $\leq 27,6$ ng/ml jest predyktorem występowania MASLD. Możliwe, że uzupełnianie stężenia witaminy D będzie interwencją mającą na celu zmniejszenie ryzyka wystąpienia MASLD.

Introduction

Vitamin D deficiency is an important health problem that affects 50% to 70% of the European population [1]. Inactive vitamin D undergoes 2 metabolic processes: 25-hydroxylation in the liver and 1 α -hydroxylation in the kidneys. This conversion results in 1 α ,25-dihydroxyvitamin D (1,25(OH) $_2$ D), an active form that serves as the high-affinity ligand for the vitamin D receptor (VDR) [2]. The presence of VDR was confirmed not only in musculoskeletal cells, kidney tubules, or enterocytes, but also in immune cells, myocytes, and pancreatic and fatty tissue cells. 25-dihydroxyvitamin D, 25(OH)D, is a metabolite of vitamin D $_2$ and D $_3$ hydroxylation in the liver. The 25(OH)D level is used to determine the vitamin D status in the body. Vitamin D has been shown to have numerous pleiotropic effects in addition to regulating calcium metabolism. The deficiency of 25(OH)D was linked to cancer as well as autoimmune, cardiovascular, and metabolic diseases [3, 4].

Metabolic dysfunction-associated steatotic liver disease (MASLD) occurs in one-fourth of the population and is linked to underlying metabolic abnormalities. Recently, there have been changes in the diagnostic criteria of steatotic liver disease (SLD). So far, classification based on alcohol consumption has been used: non-alcoholic fatty liver disease (NAFLD) and alcohol-related liver disease (ALD). NAFLD was replaced by the term “metabolic dysfunction-associated fatty liver disease” (MAFLD) and then “metabolic dysfunction-associated steatotic liver disease” (MASLD). MASLD defines patients with SLD and at least one of 5 cardiometabolic risk factors, e.g. the presence of impaired glucose regulation, type 2 diabetes, hypertension or dyslipidaemia, overweight or obesity [5, 6]. Patients with MASLD have a higher risk of cardiovascular events, diabetes mellitus, and hypertension [7, 8]. MASLD is becoming the leading indication for liver transplantation [9]. It was reported that the vitamin D/VDR axis affects the inflammatory state, immune response, and lipogenic gene expression. Thus, there is an ongoing search for the links between the vitamin D/VDR axis and MASLD. VDR activation has been shown to inhibit hepatic lipid accumulation and inflammation. Moreover, vitamin D affects insulin sensitivity, which is important in the pathogenesis of MASLD [10]. Available studies suggest that VDR gene polymorphisms are associated with the severity of steatosis and progression to fibrosis by affecting insulin secretion, insulin resistance, and visceral fat activity [11–18].

Aim of the research

The aim of the study was to assess the association between vitamin D deficiency and MASLD.

Material and methods

Study group

This retrospective study included patients hospitalised at an internal medicine unit from 1 January 2021, to 31 December 2022, in whom vitamin D levels were measured during hospitalisation. Data on medical history, laboratory findings, and imaging tests were assessed. Patients with hepatitis type B and C and those with alcohol- and drug-induced liver damage were excluded.

Covariates

Data retrieved from patients' medical records included body mass index (BMI) and the occurrence of comorbidities. General morphological and biochemical parameters were determined, such as white blood cell count, platelet count, and the serum levels of haemoglobin, C-reactive protein (CRP), triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), γ -glutamyl transpeptidase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, and bilirubin.

Blood samples for laboratory testing were obtained by venipuncture on admission to the hospital. Overweight was defined as a BMI of 25 kg/m 2 or higher, and obesity as a BMI of 30 kg/m 2 or higher.

Serum 25(OH)D concentrations were assessed by electrochemiluminescence.

The following ranges of serum vitamin D levels were assumed: < 10, 10–30, 31–50, and > 50 ng/ml. In line with the current recommendations, vitamin D deficiency was defined as a vitamin D level of 30 ng/ml or lower, while the level of 31 to 50 ng/ml was considered optimal [2–4].

MASLD was diagnosed according to the current definition based on liver steatosis on imaging (abdominal ultrasound or computed tomography) and/or elevated liver enzymes, with the simultaneous presence of one of the following metabolic criteria: overweight, obesity, or abdominal obesity; type 2 diabetes mellitus or prediabetes; and hypertension, hypertriglyceridaemia, or low HDL-C level [5].

Statistical analysis

Categorical data were described as absolute numbers and percentages. Continuous variables were presented using means with standard deviations or medians and quartiles.

Categorical data were compared by the χ^2 or Fisher exact test. Quantitative variables with normal distribution were compared using the *t*-test or one-way analysis of variance, while those with nonnormal distribution were compared with the Mann-Whitney or

Kruskal-Wallis test. The normality of distribution was checked by the Shapiro-Wilk test.

Univariate and multivariate analyses according to factors associated with MASLD were done using logistic regression models. Odds ratios with 95% confidence intervals were calculated to assess the strength and statistical significance of the associations. Additionally, the receiver operating characteristic (ROC) curve analysis was performed to evaluate whether serum vitamin D levels can be used to distinguish between patients with and without MASLD. In this framework, the area under the ROC curve with 95% CIs was estimated, and the optimal cutoff value was determined by maximising the Youden index.

A two-tailed p -value of less than 0.05 was considered significant. All statistical analyses were performed using the R software package version 4.3.1.

Results

Characteristic of study group

The study included 446 patients (57% women). MASLD was diagnosed in 41% of patients (20.6% women). The mean age of patients with MASLD was 65.8 ± 14.4 years and that of patients without MASLD was 70.6 ± 16.8 years. Optimal vitamin D levels were noted in 13.1% of patients with MASLD vs. 21.7% of those without MASLD ($p = 0.0211$). Patients with MASLD more often had diabetes (59.1% vs. 31.8%, respectively, $p < 0.0001$) and overweight or obesity (34.4% vs. 15.2%, respectively, $p < 0.0001$). Patients with MASLD also had higher levels of total cholesterol (159.3 mg/dl vs. 145.3 mg/dl, $p = 0.0361$), triglycerides (145.8 mg/dl vs. 107.2 mg/dl, $p < 0.0001$), uric acid (6.1 mg/dl vs. 5.8 mg/dl, $p = 0.0422$), AST (69.8 U/l vs. 41.5 U/l, $p < 0.0001$), and ALT (50.2 U/l vs. 32.8 U/l, $p < 0.0001$). The characteristics of patients with and without MASLD are presented in Table 1. The characteristics of patients according to vitamin D levels are presented in Table 2.

We compared the clinical characteristics between men and women according to the different ranges of vitamin D levels. The results are presented in Supplementary Table S1.

Analyses of predictors of MASLD

The ROC curve analysis did not show a significant association between vitamin D levels in any of the ranges and the presence of MASLD. Based on the Youden index, the cutoff value for vitamin D of 27.6 ng/ml was determined and considered in the statistical analyses (Figure 1). In 79.8% of patients with MASLD, vitamin D levels were 27.6 ng/ml or lower, while 20.2% of patients had vitamin D levels higher than 27.6 ng/ml. Among patients without MASLD, 69.6% had a vitamin D level of 27.6 ng/ml

or lower, and 30.4% had levels higher than 27.6 ng/ml ($p = 0.0160$).

A univariable analysis of the predictors for MASLD was performed. The results are presented in Supplementary Table S2. The predictors of MASLD according to the multivariable analysis are shown in Table 3. The multivariable regression analysis revealed the following predictors of MASLD: male sex, diabetes, obesity or overweight, and vitamin D levels of 27.6 ng/ml or lower. The age of 80 years or older was associated with a lower risk of MASLD.

Discussion

Numerous studies investigated the association between MASLD and vitamin D levels. Moreover, investigators have been searching for the links between liver disease and the severity of vitamin D deficiency. The major findings of the present study are discussed below.

First, our registry data showed that vitamin D deficiency occurs in most hospitalised patients. Second, the predictors of MASLD were identified and the association between MASLD and vitamin D deficiency was confirmed.

Previous studies showed that vitamin D deficiency is a common problem with significant clinical consequences. As shown in the National Health and Nutrition Examination Survey (NHANES) including adults from the United States, patients with a low level of 25(OH)D (< 21 ng/ml) have an increased risk of hypertension, diabetes, and obesity [19, 20]. Dziedzic *et al.* [21] reported vitamin D deficiency in 94% of patients from central Poland with angiographically confirmed coronary artery disease. Severe vitamin D deficiency was noted in 22% of these patients. In our study, vitamin D deficiency was revealed in 76.4% of patients hospitalised at the internal medicine unit.

It was suggested that vitamin D, a hormone involved in calcium-phosphate metabolism, influences numerous metabolic processes, and vitamin D deficiency may be closely associated with MASLD. Moreover, the deficiency was linked to the pathogenesis of insulin resistance, the main factor in the development of MASLD. Vitamin D receptors are widely expressed in the liver and participate in various biological processes, including glucose and lipid metabolism, inflammation, cellular proliferation, differentiation, and apoptosis. Considering that these processes are often impaired in patients with MASLD, some studies have explored the relationship between vitamin D and MAFLD. Three cross-sectional studies reported that lower serum vitamin D levels were associated with a higher prevalence of MAFLD [22–24]. A cross-sectional study found that serum vitamin D levels were inversely related to liver fat content among patients with MAFLD [25].

Table 1. Characteristics of patients with and without metabolic dysfunction-associated steatotic liver disease

Parameter	MASLD		All patients N = 446	P-value
	No (N = 263)	Yes (N = 183)		
Age				0.0002
Mean (SD)	70.6 (16.8)	65.8 (14.4)	68.6 (16.1)	
Median (Q1, Q3)	74.0 (62.0, 84.0)	69.0 (56.0, 75.0)	71.0 (60.0, 80.8)	
Age groups (years), n (%)				< 0.0001
> 79	94 (35.7)	25 (13.7)	119 (26.7)	
65–79	90 (34.2)	85 (46.4)	175 (39.2)	
50–64	46 (17.5)	44 (24.0)	90 (20.2)	
< 50	33 (12.5)	29 (15.8)	62 (13.9)	
Sex, n (%)				0.0175
Female	162 (61.6)	92 (50.3)	254 (57.0)	
Male	101 (38.4)	91 (47.1)	192 (43.0)	
Diabetes, n (%)	N = 261 83 (31.8)	N = 181 107 (59.1)	N = 442 190 (43.0)	< 0.0001
Hypertension, n (%)	N = 262 159 (60.7)	N = 183 110 (60.1)	N = 445 269 (60.4)	0.9024
Overweight or obesity, n (%)	40 (15.2)	63 (34.4)	103 (23.1)	< 0.0001
Vitamin D [ng/ml]				0.2475
Mean (SD)	23.3 (22.0)	21.1 (18.2)	22.4 (20.5)	
Median (Q1, Q3)	19.2 (10.2, 31.5)	16.7 (9.6, 26.4)	18.7 (9.9, 29.3)	
Vitamin D ranges (ng/ml), n (%)				0.1445
>50	13 (4.9)	11 (6.0)	24 (5.4)	
31–50	57 (21.7)	24 (13.1)	81 (18.2)	
10–30	136 (51.7)	103 (56.3)	239 (53.6)	
< 10	57 (21.7)	45 (24.6)	102 (22.9)	
Vitamin D ≤ 27.6 ng/ml, ROC cutoff point, n (%)	183 (69.6)	146 (79.8)	329 (73.8)	0.0160
Total cholesterol [mg/dl]	N = 261	N = 183	N = 444	0.0361
Mean (SD)	145.3 (42.2)	159.3 (58.6)	151.0 (50.0)	
Median (Q1, Q3)	142.0 (114.0, 172.0)	154.0 (118.0, 194.0)	145.0 (115.8, 183.2)	
LDL-C [mg/dl]	N = 260	N = 182	N = 442	0.2493
Mean (SD)	80.6 (33.4)	88.7 (46.7)	84.0 (39.5)	
Median (Q1, Q3)	74.0 (56.0, 100.2)	83.0 (52.2, 111.0)	76.0 (55.0, 105.8)	
HDL-C [mg/dl]	N = 260	N = 182	N = 442	0.1598
Mean (SD)	43.4 (16.9)	41.4 (19.7)	42.6 (18.1)	
Median (Q1, Q3)	43.0 (30.0, 54.0)	41.0 (28.0, 50.8)	42.0 (29.0, 53.0)	
Triglycerides [mg/dl]	N = 260	N = 181	N = 441	< 0.0001
Mean (SD)	107.2 (56.7)	145.8 (90.7)	123.0 (75.0)	
Median (Q1, Q3)	91.5 (72.0, 127.0)	122.0 (89.0, 177.0)	103.0 (78.0, 148.0)	

Table 1. Cont.

Parameter	MASLD		All patients N = 446	P-value
	No (N = 263)	Yes (N = 183)		
Uric acid [mg/dl]	N = 260	N = 178	N = 441	0.0422
Mean (SD)	5.8 (2.5)	6.1 (2.6)	5.9 (2.5)	
Median (Q1, Q3)	5.3 (3.9, 6.9)	5.8 (4.6, 7.3)	5.5 (4.2, 7.0)	
HbA _{1c} (%)	N = 98	N = 110	N = 208	< 0.0001
Mean (SD)	7.1 (2.4)	8.3 (2.7)	7.7 (2.6)	
Median (Q1, Q3)	6.5 (5.8, 7.8)	7.7 (6.3, 9.9)	6.9 (6.0, 9.1)	
AST [U/l]	N = 262	N = 183	N = 445	< 0.0001
Mean (SD)	41.5 (62.8)	69.8 (98.2)	53.2 (80.4)	
Median (Q1, Q3)	28.0 (21.0, 40.0)	38.0 (25.5, 77.5)	31.0 (22.0, 50.0)	
ALT [U/l]	N = 262	N = 183	N = 445	< 0.0001
Mean (SD)	32.8 (57.2)	50.0 (54.4)	39.9 (56.6)	
Median (Q1, Q3)	20.0 (14.0, 32.8)	33.0 (20.0, 60.0)	25.0 (16.0, 41.0)	
Creatinine [mg/dl]				0.1270
Mean (SD)	1.3 (1.1)	1.2 (2.0)	1.3 (1.5)	
Median (Q1, Q3)	1.0 (0.8, 1.4)	0.9 (0.7, 1.2)	1.0 (0.8, 1.4)	
ALT [U/l], n (%)	N = 262	N = 183	N = 445	< 0.0001
< 5 U/l	1 (0.4)	0 (0.0)	1 (0.2)	
5–50 U/l	236 (90.1)	129 (70.5)	365 (82.0)	
> 50 U/l	25 (9.5)	54 (29.5)	79 (17.8)	
AST [U/l], n (%)	N = 262	N = 183	N = 445	< 0.0001
5–50 U/l	219 (83.6)	116 (63.4)	335 (75.3)	
> 50 U/l	43 (16.4)	67 (36.6)	110 (24.7)	

LDL-C – low-density lipoprotein cholesterol, HDL-C – high-density lipoprotein cholesterol, HbA_{1c} – glycated haemoglobin A_{1c}, AST – aspartate aminotransferase, ALT – alanine aminotransferase.

In our study, vitamin D levels of less than 27.6 ng/ml predicted MASLD in addition to male sex, type 2 diabetes, overweight, or obesity. Our results are in line with other observational studies that indicate an inverse correlation between vitamin D levels and the prevalence of MASLD. In a meta-analysis of 15 studies involving 20,096 patients, Liu *et al.* [26] reported that patients with nonalcoholic fatty liver disease (NAFLD according to the old classification) had lower 25(OH)D levels compared with the non-NAFLD subjects. Pacifico *et al.* [27] assessed 45 studies conducted between 2007 and 2017 that investigated the links between vitamin D levels and NAFLD. An inverse correlation was confirmed in 29 of these studies. In a cross-sectional study of 9782 patients, Liu *et al.* [26] revealed that lower vitamin D levels are an independent predictor of NAFLD. In a study of 12,835 Korean patients, Park *et al.* reported that vitamin D deficiency can be an independent risk factor for NAFLD [22]. Moreover, an association between vitamin D levels and the severity of steatosis

was reported. Guan *et al.* [23] showed a nonlinear relationship between serum vitamin D levels and MAFLD. When the serum vitamin D level was 44.6 nmol/l (17.84 ng/ml), a negative correlation with MAFLD was detected. Below this level, serum vitamin D levels might promote the progression of MAFLD. Zhang *et al.* [28] showed a nonlinear inverse association between serum 25(OH)D levels and all-cause mortality among patients with MAFLD/NAFLD, with a threshold effect at ~50.0 nmol/l (20 ng/ml) of serum 25(OH)D.

Observational studies investigating the correlation between 25(OH)D levels and NAFLD provided positive results, indicating that vitamin D supplementation might become a beneficial therapeutic intervention. However, data from randomised clinical trials are conflicting. Bjelakovic *et al.* [29] conducted a systematic review of randomised clinical trials investigating the effect of vitamin D supplementation in patients with chronic liver disease, including 11 studies on NAFLD. The investigators looked into the potential

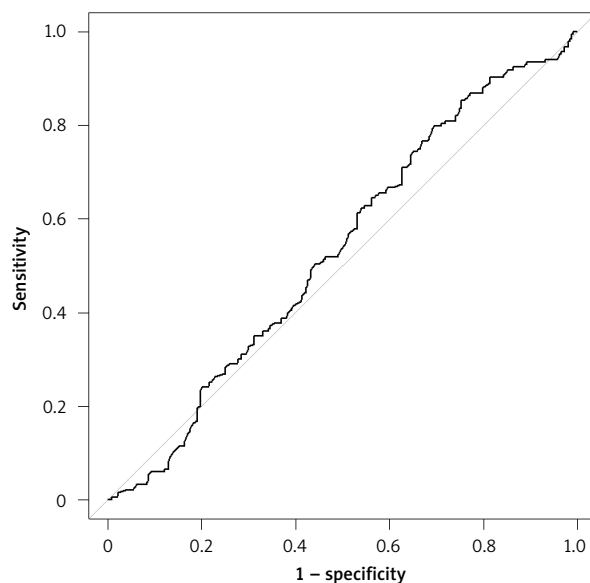
Table 2. Characteristics of patients according to vitamin D levels

Parameter	Vitamin D levels [ng/ml]					P-value
	> 50 N = 24	31–50 N = 81	10–30 N = 239	< 10 N = 102	Total N = 446	
Age						0.0165
Mean (SD)	76.0 (13.3)	68.0 (16.0)	67.0 (16.6)	71.2 (14.8)	68.6 (16.1)	
Age groups [years], n (%)						0.3068
> 79	11 (45.8)	21 (25.9)	57 (23.8)	30 (29.4)	119 (26.7)	
65–79	9 (37.5)	31 (38.3)	95 (39.7)	40 (39.2)	175 (39.2)	
50–64	3 (12.5)	18 (22.2)	46 (19.2)	23 (22.5)	90 (20.2)	
< 50	1 (4.2)	11 (13.6)	41 (17.2)	9 (8.8)	62 (13.9)	
Age ≥ 80 years, n (%)	11 (45.8)	21 (25.9)	57 (23.8)	30 (29.4)	119 (26.7)	0.1170
Sex, n (%)						0.0055
Female	12 (50.0)	60 (74.1)	131 (54.8)	51 (50.0)	254 (57.0)	
Male	12 (50.0)	21 (25.9)	108 (45.2)	51 (50.0)	192 (43.0)	
Diabetes (%)	12 (50.0)	36 (44.4)	N = 236 102 (43.2)	N = 101 40 (39.6)	N = 442 190 (43.0)	0.7943
Hypertension, n (%)	16 (66.7)	46 (56.8)	N = 238 153 (64.3)	54 (52.9)	N = 445 54 (52.9)	0.1942
Overweight or obesity, n (%)	5 (20.8)	17 (21.0)	64 (26.8)	17 (16.7)	103 (23.1)	0.2149
Vitamin D [ng/ml]						
Mean (SD)	78.5 (48.2)	37.3 (5.5)	18.6 (5.8)	6.5 (2.0)	22.4 (20.5)	
MASLD, n (%)	11 (45.8)	24 (29.6)	103 (43.1)	103 (43.1)	183 (41.0)	0.1445
Total cholesterol [mg/dl]	N = 23	N = 81	N = 238	N = 102	N = 444	0.0017
Mean (SD)	149.0 (51.6)	164.1 (44.0)	164.1 (44.0)	140.8 (54.2)	151.0 (50.0)	
LDL-C [mg/dl]	N = 23	N = 80	N = 237	N = 102	N = 444	0.0020
Mean (SD)	87.0 (47.9)	94.0 (34.4)	83.8 (39.2)	75.8 (40.9)	84.0 (39.5)	
HDL-C [mg/dl]	N = 23	N = 80	N = 237	N = 102	N = 444	0.0010
Mean (SD)	37.1 (14.7)	47.2 (17.9)	43.2 (17.2)	38.6 (19.9)	42.6 (18.1)	
Triglycerides [mg/dl]	N = 23	N = 80	N = 236	N = 102	N = 443	0.7114
Mean (SD)	124.9 (48.3)	121.0 (69.5)	121.7 (76.5)	127.1 (81.0)	123.0 (75.0)	
Uric acid [mg/dl]	N = 24	N = 40	N = 235	N = 99	N = 438	0.0107
Mean (SD)	7.1 (3.4)	5.3 (2.2)	5.9 (2.4)	6.2 (2.8)	5.9 (2.5)	
HbA _{1c} (%)	N = 12	N = 39	N = 112	N = 45	N = 208	0.4837
Mean (SD)	7.1 (1.7)	7.2 (1.8)	7.8 (2.7)	8.0 (3.1)	7.7 (2.6)	
AST [U/l]	N = 23	N = 81	N = 239	N = 102	N = 445	0.0513
Mean (SD)	91.8 (112.6)	49.2 (87.6)	51.8 (76.1)	50.9 (74.7)	53.2 (80.4)	
ALT [U/l]	N = 23	N = 81	N = 239	N = 102	N = 445	0.0818
Mean (SD)	74.9 (101.3)	42.8 (62.0)	37.5 (44.5)	35.0 (61.8)	39.9 (56.6)	

LDL-C – low-density lipoprotein cholesterol, HDL-C – high-density lipoprotein cholesterol, HbA_{1c} – glycated haemoglobin A_{1c}, AST – aspartate aminotransferase, ALT – alanine aminotransferase.

Table 3. Predictors of metabolic dysfunction-associated steatotic liver disease in a binary multivariable regression analysis

Variable	Multivariable OR	95% CI	P-value
Age ≥ 80	0.38	0.22–0.65	0.0004
Sex (male)	1.63	1.06–2.52	0.0264
Diabetes	2.72	1.75–4.21	< 0.0001
Obesity or overweight	2.1	1.27–3.5	0.0041
Triglycerides	1.07	1.03–1.1	0.0003
Vitamin D ≤ 27.6 ng/ml	1.65	1–2.73	0.0497

**Figure 1.** Receiver operating characteristic (ROC) curve analysis of the association between vitamin D levels and metabolic dysfunction-associated steatotic liver disease (optimal cutoff value for the development of MASLD 27.6, AUC = 0.5322, 95% CI for AUC = 0.4784–0.586)

benefits of vitamin D supplementation. The therapeutic effect of the supplementation in patients with liver disease was not confirmed, but the authors noted that the results should be interpreted with caution due to the high risk of bias. Guo *et al.* [30] conducted a meta-analysis of randomised controlled trials investigating the effect of vitamin D supplementation on aminotransferase levels and cardiometabolic risk factors in patients with NAFLD. The analysis provided evidence for the beneficial effects of the supplementation on glucose levels and insulin resistance in patients with NAFLD. However, no beneficial effect on aminotransferase levels or lipid profile was confirmed.

Our study has several limitations. Because this was a retrospective study, there may have been some unidentified confounders. Moreover, we did not collect data on vitamin D supplementation in our patients.

Conclusions

The study confirmed that vitamin D deficiency is common among patients with MASLD. Vitamin D deficiency defined as vitamin D levels of 27.6 ng/ml or lower predicts MASLD.

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Ethical approval

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Jan Kochanowski University in Kielce, Poland (no. of consent: KE-29/2023).

Conflict of interest

The authors declare no conflict of interest.

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