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Prevalence and risk factors of metabolic-associated fatty liver disease during 2014–2018 from three cities of Liaoning Province: an epidemiological survey

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ABSTRACT

Objective To investigate the incidence and characteristics of metabolic-associated fatty liver disease (MAFLD) in individuals undergoing physical examination in Liaoning Province (China).

Design Retrospective study.

Setting Single centre.

Participants Adults who underwent routine health examination at Xikang Medical Center in Liaoning Province (Shenyang, Dandong and Dalian cities) between January 2014 and December 2018.

Results Among the 204 394 included subjects, 71 756 were diagnosed with MAFLD, accounting for 35.28%. The total prevalence of MAFLD in Shenyang, Dandong and Dalian cities over the past 5 years was 35.8%, 40.41% and 31.7%, respectively. Men had a prevalence of 46.12%, which was higher than in women (21.80%). The percentage of MAFLD in body mass index (BMI) <23 kg/m^2 and ≥23 kg/m^2 was 6.49% and 53.23%, respectively. In all subjects, BMI, systolic blood pressure, diastolic blood pressure (DBP), fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), alanine transaminase, aspartate transaminase (AST), alkaline phosphatase (ALP), γ-glutamyl transferase (GGT), blood urea nitrogen, serum creatinine (SCr), serum uric acid (SUA), haematocrit (HCT), mean corpuscular volume (MCV) and urine protein were independently associated with MAFLD (all p<0.001). In lean subjects, DBP, FBG, TG, TC, LDL-C, HDL-C, AST, ALP, GGT, SCr, SUA, HCT and MCV were independently associated with MAFLD (all p<0.001).

Conclusion The prevalence of MAFLD in Liaoning Province was found to be associated with sex, cities with different economic statuses, BMI and multiple metabolic indicators.

Strengths and limitations of this study

- The study is a large-scale epidemiological survey.
- This is one of the first epidemiological studies after non-alcoholic fatty liver disease was renamed to metabolic-associated fatty liver disease (MAFLD).
- The study provides time trends from three cities in China with varying economic development.
- There is lack of data on MAFLD patients with type 2 diabetes mellitus in the study.
- Although majority of the metabolic risk factors have been discussed in the study, further comprehensive assessment is required.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease and is defined as the presence of ≥5% hepatic steatosis (HS).[1 2] Recently, it was recommended to rename NAFLD to metabolic-associated fatty liver disease (MAFLD), which might increase awareness of the disease and reduce stigma.[3 4] NAFLD is associated with chronic diseases, such as insulin resistance and/or type 2 diabetes mellitus (T2DM), dyslipidaemia, hypertriglyceridaemia and hypertension.[5–8] The prevalence of NAFLD was reported to be 24%–45%, with an estimated prevalence of 76% in patients with T2DM.[9] In non-obese patients, NAFLD is associated with elevated triglyceride (TG) level, enlarged waist circumference and insulin resistance.[10]

Chinese individuals are at substantially higher risk of NAFLD, even those with noticeably lower body mass index (BMI, kg/m^2) values, compared with the US population.[11] Factors such as waist circumference, T2DM, increased TG level, low high-density lipoprotein cholesterol (HDL-C) level and metabolic syndrome are known as predictive factors for NAFLD in adults, of which metabolic syndrome is considered a strong predictive factor.[12 13] NAFLD is also associated with dyslipidaemia characterised by high TG, high low-density lipoprotein cholesterol (LDL-C) and low HDL-C levels.[14] Determining the risk factors associated with a worse prognosis is essential to develop further effective therapeutic strategies.

Since the 21st century, the prevalence of NAFLD in China has significantly increased to reach about one in three mainland Chinese residents.[12] A recent meta-analysis showed that the incidence of NAFLD is higher in northern China (35.78%) and lower in northwestern China (21.52%).[15] Among provinces in northern China, Heilongjiang has the highest incidence, with up to 50.48%.[15] Nevertheless, the results might be biased due to the small number of studies, and the incidence of NAFLD in northern China remains significantly higher than in the southern provinces. In addition, the risk of NAFLD-related mortality has also increased significantly, mainly due to liver fibrosis-associated diseases.[16] NAFLD has become an important public health concern, negatively influencing the Chinese population as well as increasing the socioeconomic burden.[11 12 15] Therefore, Chinese medical professionals and stakeholders urgently need to develop further accurate early diagnostic methods for NAFLD. Multiple studies have reported that NAFLD is a heterogeneous entity, and its development is related to sex, age, race, mild to moderate alcohol consumption, dietary intake, lifestyle, obesity, metabolism, genetic variations and educational level.[11 12 15 16] With uneven economic development and diverse lifestyles among the different provinces in China, the epidemiology of NAFLD has shown remarkable regional differences. With understanding the epidemiology of NAFLD in Liaoning Province (China), we can conduct targeted education and clinical research for precise prevention and control of NAFLD. Moreover, after NAFLD was renamed to MAFLD, few studies have investigated the prevalence of MAFLD.

There have been no data from large-scale epidemiological investigations of MAFLD in Liaoning Province over the past 10 years. Therefore, the present retrospective study aimed to investigate the incidence and disease characteristics of MAFLD in Liaoning Province. Physical examination data of residents of three cities (Shenyang, Dandong and Dalian) in Liaoning Province with different economic levels were collected from 2014 to 2018.

METHODS

Study subjects

This is a retrospective study of adults who underwent routine health examination at Xikang Medical Center in Liaoning Province (including clinics in Shenyang, Dandong and Dalian) between January 2014 and December 2018.

The three cities are from different parts of Liaoning Province (north, south and east; figure 1) and have different economic levels. Shenyang, located in the north of Liaoning Province, is a highly developed inland city, while Dalian in the south of Liaoning Province is a developed coastal city. Dandong, in the east of Liaoning Province, is a poorly developed city bordering North Korea.

The inclusion criteria were as follows: (1) patients aged >18 years old; (2) patients who have lived in Shenyang, Dalian or Dandong for at least 5 years; (3) participation in annual physical examination; and (4) no missing data (as listed in table 1). The exclusion criteria were as follows: (1) liver cirrhosis; (2) liver cancer; (3) any liver lesions; or (4) no ultrasound examination. For participants undergoing more than one examination during the study period, only the first examination was included in this study. According to the guidelines, the diagnosis of MAFLD is no longer an exclusive diagnosis. Therefore, in diagnosed patients, conditions such as alcohol consumption and other liver diseases were not ruled out

Figure 1 Location of the three study cities in Liaoning Province.

The selected patients were divided into the MAFLD group and the non-MAFLD group based on ultrasound evidence of HS, in addition to one of the following two criteria, namely overweight/obesity (BMI ≥23 kg/m^2, according to the standards recommended by the WHO for Asians,[17] or BMI <23 kg/m^2, with at least two evidence of metabolic dysregulation, such as blood pressure ≥130/85 mm Hg, TG ≥1.70 mmol/L, and HDL-C <1.0 mmol/L for men and <1.3 mmol/L for women).[18] Regrettably, 3156 patients with T2DM who received medical intervention were not included in this study due to serious incomplete medical records.

Patient and public involvement

No patients were involved.

Physical examination

All physical examinations in this study are part of routine examination. Blood pressure measurements, including systolic blood pressure (SBP) and diastolic blood pressure (DBP), were performed twice after participants have seated, in a calm state for at least 5 min, using an electronic sphygmomanometer (HEM-7200; Omron Healthcare, Kyoto, Japan). Height and weight were measured in the morning on an empty stomach.

Laboratory examination

All physical blood tests in this study are part of routine examination. Anterior cubital vein blood was drawn in

Table 1 Characteristics of patients with and without MAFLD

Subgroups	Mean±SD	All N=204 394	Non-MAFLD n=132 638	MAFLD n=71 756	Prevalence (%)	P value
Age (years)						<0.001
20–29		22 822	18 728	4094	17.94	
30–39		80 227	54 671	25 556	31.85	
40–49		44 464	27 913	16 551	37.22	
50–59		30 861	17 173	13 688	44.35	
≥60		26 020	14 153	11 867		
Sex						<0.001
Male	38.8±13.7	111 782	60 222	51 560	46.13	
Female	40.5±13.3	92 612	72 416	20 196	21.81	
BMI (kg/m^2)						<0.001
<23		79 271	74 124	5147	6.49	
≥23		125 123	58 514	66 609	53.23	
City						<0.001
Shenyang	39.3±12.7	78 329	50 265	28 064	36.83	
Dandong	47.8±14.1	42 039	25 048	16 991	40.42	
Dalian	36.3±12.7	84 026	57 325	26 701	31.78	
Overall	39.6±13.6	204 394	132 638	71 756	35.11	

BMI, body mass index; MAFLD, metabolic-associated fatty liver disease.

fasting state (at least 8 hours). A mid-course morning urine specimen was taken as well. Routine blood panel, liver function, kidney function, serum uric acid (SUA) level, fasting blood glucose (FBG) level, blood lipids and routine urine analysis were assessed using a 7600 Autoanalyzer (Hitachi, Tokyo, Japan).

Colour Doppler ultrasound of the liver and gall bladder

A liver ultrasound is part of routine examination and was performed by two experienced ultrasound radiologists with at least 5 years of experience using an IU22 system (Philips Healthcare, Best, The Netherlands). A participant was diagnosed with HS when the ultrasound examination showed that the liver had fatty liver changes (hyperechogenicity due to increased acoustic interface caused by the intracellular accumulation of lipid vesicles, blurring of vascular margins, enlarged liver size and increased acoustic attenuation[10 19]).

Statistical analysis

R V.3.5.3 and R Commander V.2.5-3 were used for statistical analysis. Categorical data were expressed as n (%) and were analysed using χ^2 test. Continuous variables conforming to normal distribution (according to the Kolmogorov-Smirnov test) were expressed as mean±SD and were analysed using Student's t-test. Abnormally distributed continuous variables were presented as median (IQR) and were analysed using Mann-Whitney U test. Factors associated with MAFLD were identified using univariate analysis. Variables with p<0.05 were included in a multivariate logistic regression model. P<0.05 was considered statistically significant.

RESULTS

Characteristics of the subjects

A total of 284 129 subjects were examined during the study period and 204 394 met the eligibility criteria. Table 1 presents the characteristics of the subjects. The subjects' mean age was 39.6±13.6 years old. The number of male and female subjects was 111 782 and 92 612, respectively. The male subjects' mean age was 38.8±13.7 years old and that of female subjects was 40.5±13.3 years old. Shenyang included 78 329 subjects, aged 39.3±12.7 years old. No routine health examination was performed in Dandong in 2014. Dandong included 42 039 subjects, aged 47.8±14.1 years old. Finally, 84 026 subjects were from Dalian, aged 36.3±12.7 years old.

Prevalence of MAFLD among the healthy population

Among the 204 394 included subjects, 71 756 were diagnosed with MAFLD, accounting for 35.28% (table 1). The prevalence of MAFLD increased with age (p<0.001), which was higher in men than in women (p<0.001), higher in overweight/obese subjects than in lean ones (p<0.001), and higher in Dandong, followed by Shenyang and Dalian (p<0.001) (table 1). The prevalence of MAFLD in Shenyang, Dandong and Dalian over the past 5 years was 36.83%, 40.42% and 31.78%, respectively.

Table 2 Changes in the prevalence of MAFLD over time (2014–2018)

Subgroups	Year, % 2014	2015	2016	2017	2018	P value
Age (years)						
20–29	16.43	17.20	17.30	18.82	18.18	0.081
30–39	29.24	28.60	31.05	33.37	34.33	0.006
40–49	35.65	34.50	35.40	39.04	38.69	0.200
50–59	46.32	39.40	41.67	46.96	45.44	0.636
≥60	44.83	40.65	45.34	48.39	46.50	0.234
Sex						
Male	42.60	42.63	44.36	48.12	48.45	0.029
Female	14.85	19.33	21.49	24.63	22.67	0.035
BMI (kg/m^2)						
<23	5.08	5.35	6.68	7.36	6.80	0.058
≥23	54.93	50.37	52.15	55.08	53.76	0.510
City						
Shenyang	34.89	34.80	34.27	37.36	36.92	0.182
Dandong	–	30.06	34.29	42.66	44.17	0.039
Dalian	26.36	29.00	33.20	32.36	32.98	0.048
Overall	30.01	30.11	33.22	34.58	32.19	<0.001

BMI, body mass index; MAFLD, metabolic-associated fatty liver disease.

Prevalence of MAFLD over time

The total prevalence of MAFLD from 2014 to 2018 was 30.01%, 30.11%, 33.22%, 34.58% and 32.19%, respectively. The prevalence of MAFLD over the 5 years mainly increased in the age-based group of 30–39 years old (p=0.006), in men (p=0.029) and in women (p=0.035) (table 2). The prevalence of MAFLD in Shenyang over the past 5 years was basically consistent with the general trend in Liaoning. The prevalence of MAFLD in Dandong significantly increased annually over the past 4 years. The prevalence of MAFLD in Dalian substantially increased in 2016, while it declined in 2017 and 2018 (figure 2). The prevalence rate in men and women over the past 5 years was basically consistent with the general trend of MAFLD in Liaoning (figure 3). The prevalence of MAFLD increases with increase in age in Liaoning.

Biomarkers of MAFLD

Table 3 presents the biomarkers in all subjects and according to lean/overweight-obese. The number of subjects with overweight/obese MAFLD was 66 609, of whom 3550 (5.33%) were patients with T2DM. The number of cases with lean MAFLD was 5147, of whom 143 (2.78%) were patients with T2DM. The number of cases who were diagnosed (for the first time) with FBG level over 7 was 289. Compared with the non-MAFLD group, subjects in the MAFLD group had higher SBP, DBP, FBG,

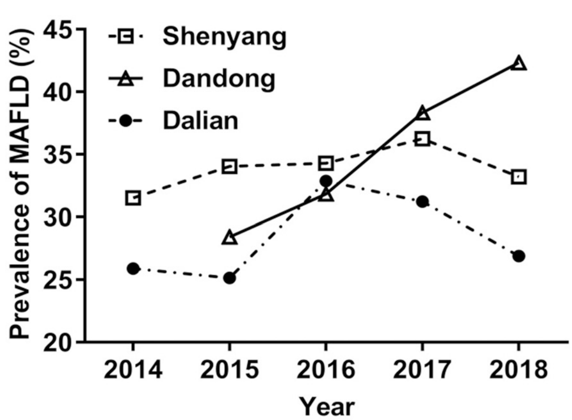

Figure 2 Prevalence of metabolic-associated fatty liver disease (MAFLD) in different cities from 2014 to 2018. Data for Dandong City in 2014 are missing

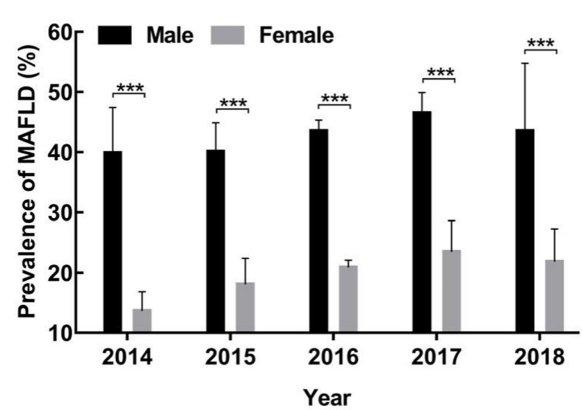

Figure 3 Prevalence of metabolic-associated fatty liver disease (MAFLD) in men is significantly higher than in women (2014–2018). ***P<0.001.

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Table 3 Comparison of metabolic tests between non-MAFLD and MAFLD

Variables	Overall			Lean (BMI <23)			Overweight (BMI ≥23)		
	Non-MAFLD	MAFLD	P value	Non-MAFLD	MAFLD	P value	Non-MAFLD	MAFLD	P value
SBP, mm Hg	118±18	129±19	<0.001	114±16	122±19	<0.001	123±18	129±19	<0.001
DBP, mm Hg	70±11	77±13	<0.001	67±10	73±12	<0.001	72±12	77±13	<0.001
FBG, mmol/L	5.15±1.30	5.82±1.63	<0.001	5.04±1.22	5.63±1.65	<0.001	5.3±1.38	5.83±1.63	<0.001
TG, mmol/L	1.07±0.85	2.12±1.73	<0.001	0.91±0.64	1.79±1.46	<0.001	1.28±1.01	2.14±1.75	<0.001
TC, mmol/L	4.41±1.43	4.96±1.34	<0.001	4.29±1.41	4.94±1.36	<0.001	4.55±1.43	4.97±1.34	<0.001
LDL-C, mmol/L	1.99±1.34	2.42±1.43	<0.001	1.9±1.28	2.46±1.38	<0.001	2.09±1.40	2.42±1.43	<0.001
HDL-C, mmol/L	1.01±0.71	0.9±0.60	<0.001	1.06±0.73	0.99±0.64	<0.001	0.93±0.67	0.9±0.60	<0.001
ALT, U/L	19.37±17.28	36.58±27.98	<0.001	17.09±14.34	27.89±21.40	<0.001	22.19±19.98	37.2±28.29	<0.001
AST, U/L	19.59±11.18	25.85±13.56	<0.001	18.76±10.03	23.55±13.08	<0.001	20.62±12.38	26.02±13.57	<0.001
ALP, U/L	7.01±22.44	9.62±25.91	<0.001	5.51±20.85	8.48±24.35	<0.001	8.98±24.13	9.7±26.02	<0.001
GGT, U/L	18.42±24.10	39.36±42.82	<0.001	15.54±20.76	31.41±48.78	<0.001	21.99±27.27	37.71±42.34	<0.001
BUN, mmol/L	4.32±1.97	4.8±1.80	<0.001	4.17±1.90	4.65±1.77	<0.001	4.51±2.04	4.81±1.80	<0.001
SCr, µmol/L	58.57±26.43	66.63±24.76	<0.001	56.12±25.14	62.05±22.61	<0.001	61.62±27.66	66.96±24.88	<0.001
SUA, µmol/L	283.17±125.06	369.05±135.06	<0.001	263.87±116.14	330.07±123.40	<0.001	307.09±131.43	371.84±135.42	<0.001
HCT, %	21.57±21.35	20.32±22.42	<0.001	21.95±20.97	20.36±21.90	<0.001	21.1±21.80	20.32±22.46	<0.001
MCV, fL	47.2±44.74	41.66±44.42	<0.001	48.78±44.68	42.74±44.70	<0.001	45.23±44.74	41.58±44.40	<0.001
UPRO, n(%)	6.70	9.20	<0.001	6.30	6.20	0.86	7.30	9.40	<0.001
UOB, n (%)	11.10	8.80	<0.001	11.20	9.40	0.00	10.80	8.80	<0.001
GBp, n (%)	7.40	8.90	<0.001	6.20	8.60	<0.001	8.90	9.70	<0.001

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; DBP, diastolic blood pressure; FBG, fasting plasma glucose; GBp, gallbladder polyps; GGT, γ-glutamyl transpeptidase; HCT, haematocrit; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAFLD, metabolic-associated fatty liver disease; MCV, mean corpuscular volume; SBP, systolic blood pressure; SCr, serum creatinine; SUA, serum uric acid; TC, total cholesterol; TG, triglycerides; UOB, urine occult blood; UPRO, urine protein.

TG, total cholesterol (TC), LDL-C, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), γ-glutamyl transferase (GGT), blood urea nitrogen (BUN), serum creatinine (SCr) and SUA, higher frequencies of urine protein (UPRO) and gallbladder polyps (GBp), lower HDL-C, haematocrit (HCT) and mean corpuscular volume (MCV), and lower frequency of urine occult blood (UOB) (all p<0.001). The same tendencies were observed in lean subjects, while there was no significant difference in UPRO (p=0.86).

MAFLD-associated factors

Table 4 presents the results of the univariate and multivariate logistic regression analyses of the factors associated with MAFLD. In all subjects, BMI, SBP, DBP, FBG, TG, TC, LDL-C, HDL-C, ALT, AST, ALP, GGT, BUN, SCr, SUA, HCT, MCV and UPRO were independently associated with MAFLD (all p<0.001), while UOB (p=0.47) and GBp (p=0.21) were not. In lean subjects, DBP, FBG, TG, TC, LDL-C, HDL-C, AST, ALP, GGT, SCr, SUA, HCT and MCV were independently associated with MAFLD (all p<0.001), while SBP (p=0.51), ALT (p=0.27), BUN (p=0.16), UPRO (p=0.57), UOB (p=0.06) and GBp (p=0.06) were not.

DISCUSSION

The present study showed that the prevalence of MAFLD in Shenyang, Dandong and Dalian cities varied, and higher BMI value and age played significant roles in the development of the disease. In addition, biomarkers such as DBP, FBG, TG, LDL-C, ALT, GGT, BUN, SUA, HCT, UPRO, and GBp were independently and positively correlated with the prevalence of MAFLD, whereas HDL-C and MCV were negatively correlated. Therefore, the prevalence of MAFLD in Liaoning was related to sex, cities with different economic statuses, BMI and multiple metabolic indicators.

The increasing trend in the prevalence of NAFLD follows the level of industrialisation and urbanisation. At present, China is the fastest-growing major economy in the world, and there are problems associated with a Westernised diet, sedentary lifestyle and metabolism, which are correlated with MAFLD. Thus, there is a closer relationship between MAFLD and economy than NAFLD. Studies have shown that the increase in the total annual NAFLD prevalence in China is consistent with the improvement in the gross domestic product (GDP) per capita.[20] An increase in morbidity in various regions of mainland China could be related to the increase in GDP per capita, while areas with the highest GDP per capita (≥$13 000) did not exhibit an increased incidence of NAFLD.[21] According to the National Bureau of Statistics of China, the GDP per capita of Liaoning Province has ranked first in northeast China over the past 5 years, whereas it is still in the lower-middle level nationally. The present study revealed that the prevalence of MAFLD in Liaoning (35.1%) was slightly higher than the overall prevalence in China (29.2%).[12] The current study selected two economically developed cities (Dalian and Shenyang) and one city with a moderate development (Dandong). The prevalence of MAFLD in these three cities was inversely proportional to the level of urban economic development. The prevalence of MAFLD in Dalian was lower than that in Shenyang. This could be related to the fact that Dalian is a coastal city, with dietary habits different from those of inland cities.

Differences in age were also confirmed. The prevalence of MAFLD in the age-based group of 20–29 years old was 17.9%, while it was 45.6% in the age-based group of >60 years old, which is in agreement with previous studies which demonstrated that age could play a crucial factor in the prevalence of NAFLD.[11 12 15]

The present study indicated that the overall prevalence of MAFLD in men was higher than in women, which is basically consistent with the previously reported findings in other regions of China.[22] The prevalence of MAFLD in middle-aged men was the highest and reached the peak at 40–49 years old (50.27%). This high prevalence might be related to high stress, irregular work and rest, and decreased metabolism among middle-aged men. The prevalence of MAFLD in women aged over 50 years old was significantly higher, which could be related to the age range for menopause.

Obesity is closely associated with metabolic diseases, such as MAFLD. The current study confirmed that BMI $\geq 23\,kg/m^2$ is an independent risk factor for MAFLD in Liaoning. Therefore, for overweight and obese individuals, it is necessary to improve diet and exercise management, even using drugs or surgery, if required. It has been reported that the global NAFLD prevalence in lean population was 5%–26%.[23] In the present study, the prevalence of NAFLD in lean population was 10.75%, which is similar to previously reported results.[24]

In this study, both lean MAFLD and non-lean MAFLD were closely related to metabolic indicators. Those metabolic indicators were also associated with T2DM, metabolic syndrome, obesity and liver diseases, as supported by previous studies.[11 12 15 22–24] In addition to obesity, variations in the prevalence of MAFLD follow the epidemic trends of T2DM and metabolic syndrome (MetS). The prevalence of MAFLD in patients with hyperlipidaemia and T2DM is higher, reaching 27%–92% and 28%–70%, respectively. Patients with MAFLD mainly have hyperlipidaemia, hypertension, T2DM and metabolic syndrome.[25] In the current study, multivariate logistic regression analysis found that DBP, TG, LDL-C, FBG and SUA were independent risk factors for MAFLD, while HDL-C was independently associated with MAFLD. Therefore, additional attention should be paid to hyperlipidaemia, hypertension and T2DM to assess their influence on the prevention and treatment of MAFLD. Regarding the correlation between SUA and MAFLD, SUA elevation was reported as one of the risk factors for MAFLD.[26]

Although genetic susceptibility was not examined in the current study, it is involved in NAFLD. Polymorphisms in PNPLA3,[27] SREBF-2,[28] CETP[28 29] and APOC3[30] have

Table 4 Multivariable analyses of the factors associated with MAFLD

Variables	Univariable logistical regression			Multivariable logistical regression		
	OR	95% CI	P value	OR	95% CI	P value
MAFLD						
BMI (kg/m^2)						
<23	0.057	0.056 to 0.06	<0.001	0.125	0.119 to 0.13	<0.001
≥23						
SBP, mm Hg	1.033	1.033 to 1.034	<0.001	1.003	1.003 to 1.005	<0.001
DBP, mm Hg	1.053	1.052 to 1.054	<0.001	1.014	1.012 to 1.016	<0.001
FBG, mmol/L	1.541	1.52 to 1.559	<0.001	1.122	1.104 to 1.131	<0.001
TG, mmol/L	2.899	2.854 to 2.953	<0.001	1.651	1.627 to 1.691	<0.001
TC, mmol/L	1.378	1.365 to 1.392	<0.001	0.879	0.866 to 0.893	<0.001
LDL-C, mmol/L	1.267	1.255 to 1.277	<0.001	1.231	1.216 to 1.259	<0.001
HDL-C, mmol/L	0.799	0.785 to 0.813	<0.001	0.717	0.69 to 0.74	<0.001
ALT, U/L	1.04	1.038 to 1.04	<0.001	1.036	1.035 to 1.038	<0.001
AST, U/L	1.055	1.054 to 1.057	<0.001	0.979	0.977 to 0.981	<0.001
ALP, U/L	1.004	1.004 to 1.005	<0.001	0.998	0.998 to 1	<0.001
GGT, U/L	1.025	1.025 to 1.026	<0.001	1.002	1.002 to 1.002	<0.001
BUN, mmol/L	1.145	1.139 to 1.154	<0.001	1.019	1.007 to 1.032	<0.001
SCr, µmol/L	1.014	1.013 to 1.014	<0.001	0.995	0.994 to 0.996	<0.001
SUA, µmol/L	1.005	1.005 to 1.006	<0.001	1.003	1.002 to 1.003	<0.001
HCT, %	0.998	0.997 to 0.998	<0.001	1.006	1.003 to 1.008	<0.001
MCV, fL	0.997	0.997 to 0.997	<0.001	0.994	0.993 to 0.995	<0.001
UPRO, n (%)	1.407	1.342 to 1.462	<0.001	1.112	1.069 to 1.198	<0.001
UOB, n (%)	0.762	0.749 to 0.811	<0.001	1	0.933 to 1.033	0.47
GBp, n (%)	1.233	1.176 to 1.28	<0.001	1.026	0.981 to 1.09	0.21
Lean (BMI <23), MAFLD						
SBP, mm Hg	1.027	1.025 to 1.029	<0.001	1.999	0.995 to 1.002	0.51
DBP, mm Hg	1.046	1.042 to 1.048	<0.001	1.018	1.012 to 1.024	<0.001
FBG, mmol/L	1.393	1.346 to 1.424	<0.001	1.098	1.064 to 1.133	<0.001
TG, mmol/L	2.771	2.642 to 2.891	<0.001	1.878	1.781 to 1.968	<0.001
TC, mmol/L	1.498	1.465 to 1.565	<0.001	0.891	0.86 to 0.941	<0.001
LDL-C, mmol/L	1.455	1.393 to 1.485	<0.001	1.372	1.301 to 1.43	<0.001
HDL-C, mmol/L	1.89	0.831 to 0.92	<0.001	0.695	0.631 to 0.741	<0.001
ALT, U/L	1.028	1.026 to 1.03	<0.001	1.025	1.024 to 1.03	0.27
AST, U/L	1.028	1.026 to 1.03	<0.001	0.971	0.969 to 0.98	<0.001
ALP, U/L	1.006	1.004 to 1.007	<0.001	1	0.998 to 1.001	<0.001
GGT, U/L	1.016	1.016 to 1.018	<0.001	1.001	1.001 to 1.004	<0.001
BUN, mmol/L	1.15	1.133 to 1.182	<0.001	1.022	0.99 to 1.059	0.16
SCr, µmol/L	1.01	1.008 to 1.012	<0.001	0.898	0.987 to 0.993	<0.001
SUA, µmol/L	1.005	1.005 to 1.006	<0.001	1.004	1.004 to 1.004	<0.001
HCT, %	0.996	0.995 to 0.998	<0.001	1.016	1.005 to 1.023	<0.001
MCV, fL	0.997	0.996 to 0.998	<0.001	0.993	0.986 to 0.995	<0.001
UPRO, n (%)	1	0.841 to 1.149	<0.001	0.995	0.795 to 1.13	0.57
UOB, n (%)	0.802	0.716 to 0.926	<0.001	0.947	0.757 to 1.004	0.06
GBp, n (%)	1.444	1.242 to 1.629	<0.001	1.221	0.992 to 1.337	0.06

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; DBP, diastolic blood pressure; FBG, fasting plasma glucose; GBp, gallbladder polyps; GGT, γ-glutamyl transpeptidase; HCT, haematocrit; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAFLD, metabolic-associated fatty liver disease; MCV, mean corpuscular volume; SBP, systolic blood pressure; SCr, serum creatinine; SUA, serum uric acid; TC, total cholesterol; TG, triglyceride; UOB, urine occult blood; UPRO, urine protein.

been found to be associated with lean NAFLD. In addition to genetic polymorphisms, lean NAFLD cases have increased bile acid and Farnesoid X-Activated Receptor (FXR) activity due to metabolic abnormalities and changes in intestinal microbial composition.[31 32] These factors should be assessed in future studies.

Regarding diabetes, because 3156 patients had previously received systemic treatment for diabetes, the current blood glucose levels and metabolic indicators were in the normal range; thus, in order to reduce error in the analysis of risk factors, we excluded these patients. In addition, patients with diabetes analysed in the present study were previously diagnosed, of whom 289 patients were found to have elevated FBG levels for the first time. As physical examinations did not involve Oral Glucose Tolerance Test (OGTT) and repeated tests, we did not classify such patients as diabetic.

This study has some limitations. Although the examinations were performed at the same clinic, they were conducted at three different physical locations over the past 5 years. Bias due to the different locations and changes in practice over time could not be excluded. Due to the large number of physical examinations and no measurement of waist circumference and high-sensitivity C reactive protein, the diagnosis of MAFLD in some patients with normal BMI might be ignored. In addition, ultrasound is operator-dependent and bias in the diagnosis of MAFLD could not be excluded. Finally, this was a cross-sectional study that could not provide any causal relationship between MAFLD and the associated factors.

In conclusion, the prevalence of MAFLD in Liaoning was found to be associated with sex, cities with different economic statuses, BMI and multiple metabolic indicators. Longitudinal studies are necessary to further determine factors associated with the development of MAFLD.

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Ethics approval This study involves human participants and was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the First Hospital of China Medical University ((2020)2020-257-2). The ethics committee waived the requirement for informed consent due to the retrospective nature of the study. Participants gave informed consent to participate in the study before taking part.

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