

BMJ Open Gender-specific prevalence of metabolic-associated fatty liver disease among government employees in Tianjin, China: a cross-sectional study

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ABSTRACT

Objectives To explore the prevalence and risk factors of metabolic-associated fatty liver disease (MAFLD) in Tianjin government employees of different genders.

Design Cross-sectional study.

Setting Health Management Center of Tianjin Union Medical Center.

Participants 16 924 government employees (59.6% male).

Measures Ultrasound liver examination was performed to determine whether there is fat accumulation in the organ. Participants' weight and height were measured, and body mass index (BMI) was calculated.

Results The overall prevalence of MAFLD in this population was 40.76%. The rates were significantly higher in men (49.42%) than in women (27.97%). The prevalence of MAFLD was highest in men aged 40–49 years (54.04%) and women aged 60–69 years (43.44%). In all BMI groups, the prevalence was higher in men than that in women. In both genders, higher BMI was associated with the risk of MAFLD, especially for BMI ≥ 31.9 kg/m².

Conclusions The prevalence of MAFLD in government employees in Tianjin was significantly higher than the average level in China. The prevalence varied by sex and age group, and those with high BMI were at the highest risk of developing MAFLD.

INTRODUCTION

Metabolic-associated fatty liver disease (MAFLD), formerly named non-alcoholic fatty liver disease (NAFLD), is a series of progressive liver diseases ranging from steatosis, fatty liver disease, fibrosis, cirrhosis to hepatocellular carcinoma.^{1 2} Although many preliminary studies have found evidence that associates MAFLD with sedentary lifestyles, overnutrition and metabolic dysfunction, including type 2 diabetes mellitus (T2DM), dyslipidaemia, hypertension and obesity,^{2–4} its genesis is far from being completely clarified.⁵ Other experiments have already verified that gender differences also affect the prevalence of MAFLD.² An International Consensus

Strengths and limitations of this study

- This was a large-scale study on the prevalence of metabolic-associated fatty liver disease (MAFLD) and its risk factors among Tianjin government employees.
- A limitation is that insulin resistance was assessed by the triglyceride-glucose index.
- Another limitation is that waist circumference, haemoglobin A1c and γ -glutamyl peptidase were not measured; only body mass index, fasting plasma glucose and alanine aminotransferase were measured.
- A further limitation is that participants' medication backgrounds were not collected and the severity of coronary heart disease was not considered.

Panel suggested that the nomenclature MAFLD more accurately reflects the current knowledge of fatty liver diseases associated with metabolic dysfunction,² so the change from NAFLD to MAFLD helps identify individuals with a higher risk of liver or cardiovascular outcomes.^{6 7} More recent evidence reveals that Tianjin's abdominal obesity rate ranked first in China in both genders.⁸ This representative cross-sectional study of 174 840 Chinese adults suggested that the higher rates may be related to the breakfast options that are more popular in Tianjin: crispy rice, bean curd and pancake dumplings. A recent study by Pan *et al*⁹ showed that obesity is associated with the level of education in China. Among the male population, education level of male and obesity rates are directly proportional, but the opposite phenomenon is observed among the female population.⁹

The global prevalence of MAFLD is estimated to be 25.24%.¹⁰ Considering the male population, the ranges vary between 4.3% and 42%. The numbers change for the female population: the ranges go from 1.6% to 24%

in different cohorts.¹¹ The incidence of MAFLD extent from 19 to 44.5/1000 person-years in Asia,¹¹ and the prevalence of this condition in China only reaches 29.2%.¹² Moreover, because of the variant obesity rates and the different regional and economic development levels, the prevalence rates are constantly oscillating.^{11–13} In the past 20 years, due to China's rapid economic ascendance, the prevalence of MAFLD in coastal areas has significantly increased with the growth of per capita Gross National Product (GDP).¹⁴

Patients with simple steatosis are prone to develop more severe liver fibrosis and cirrhosis. Studies have found that some patients with this condition are also at risk of developing hepatocellular carcinoma.^{15 16} It has been demonstrated that cardiovascular diseases have become the major cause of death for patients with advanced MAFLD.¹⁷ Among patients with MAFLD, the risk of liver-related morbidity and mortality is very high, and most of them are accompanied by metabolic complications. Those include obesity, dyslipidaemia, T2DM and metabolic syndrome,^{16 18} which may put more pressure on the public health system and increase the economic burden to keep it functional.

Although the prevalence of MAFLD is high all over China, which directly affects its economic system, the high rates of MAFLD and obesity among Tianjin government employees have not yet been explained by any other phenomena. We have designed this cross-sectional study to clarify this issue in Tianjin and to explore the risk factors of MAFLD to provide a novel basis for relevant departments to plan effective preventive measures.

METHODS

Participants

A total of 18 190 government employees from the Tianjin Union Medical Center-Health Management Center undergoing an annual health examination took part in this study from January 2020 to December 2020. Participants with incomplete physical examination data, such as height, weight, biochemical analysis and abdominal ultrasound, were excluded (n=706). To avoid duplication of information, we only use the first physical examination data of participants who underwent multiple physical examinations throughout the year (n=560). Finally, a total of 16 924 participants with complete health examination data were included in the study, which accounted for 93.04% of the total (online supplemental figure 1).

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the design and implementation of the study. There are no plans to involve patients in dissemination.

Covariables

Following the standard measurement method, all participants enrolled in this study were examined by a

professional doctor for physical examination, with steps that included measuring height (m), weight (kg), blood pressure (mm Hg) and heart rate (subdegree/degree). It is noteworthy that height and weight were measured to an accuracy of 0.1. Body mass index (BMI) was calculated by dividing body weight (kg) by the square of body height (m²). Following the Chinese Obesity Standard,¹⁹ those with BMI <18.5 kg/m² were considered lean, 18.5–23.9 kg/m² or 23.9–27.9 kg/m² were considered overweight, and individuals with BMI ≥27.9 kg/m² were considered obese. The group of participants with obesity was further divided into three categories: 27.9–31.9 kg/m², 31.9–35.9 kg/m² and ≥35.9 kg/m². After a 10-minute rest in the seat, we used the electronic sphygmomanometer to measure the right upper arm blood pressure twice in a row. The interval between the two measurements was 1 min to reduce the measurement error. Systolic blood pressure greater than 140 mm Hg, and diastolic blood pressure greater than 90 mm Hg or previously diagnosed as hypertension were considered higher than normal. After 8 hours of fasting overnight, venous blood was extracted for the examination of alanine aminotransferase (ALT), fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and serum uric acid. Blood glucose greater than 6.1 mmol/L or previously diagnosed as diabetes was considered higher than normal. MAFLD was diagnosed according to the imaging evidence of fat accumulation in the liver, in addition to one of the three following criteria: the presence of T2DM, overweight/obesity, or evidence of metabolic dysregulation.²⁰

DATA ANALYSIS

As the continuous variables were normally distributed by K-S normal test except for TG, the independent two-sample t-test or the Mann-Whitney U test was used to compare the continuous variables. The X² test was performed using the categorical variables. A binary logistic regression analysis was performed to determine which factors were strongly related to MAFLD. All statistical analyses were conducted using SPSS V.25.0. The p value less than 0.05 was considered significantly different. The p value was double tailed.

RESULTS

A total of 18 190 government employees routinely undergoing an annual health examination took part in this study. Excluding those with incomplete physical examination data (n=706) and multiple physical examinations within 1 year (n=560), 16 924 participants were finally recruited in the study (online supplemental figure 1). The clinical characteristics stratified by gender and MAFLD are displayed in table 1. The overall prevalence of MAFLD was 40.76% (49.42% in men and 27.97% in women), and six participants were diagnosed with cirrhosis (men, n=5).

Table 1 Clinical characteristics of the study participants by gender and MAFLD*

Variables	Female 40.4% (n=6828)				Male 59.6% (n=10 096)				P value	t/χ ²	P value
	Non-MAFLD		MAFLD		Non-MAFLD		MAFLD				
	72% (n=4918)	28% (n=1910)	50.6% (n=5107)	49.4% (n=4989)							
Age, years	44.31±13.21	52.46±12.30	47.04±12.96	46.49±11.54	2.24	0.025					
BMI, kg/m ²	22.82±2.83	27.06±3.56	24.60±2.90	28.24±3.46	-57.26	<0.001					
ALT, U/L	14.56±11.95	24.85±21.15	21.27±15.96	35.84±28.02	-32.01	<0.001					
Cr, μmol/L	56.85±8.25	56.66±9.38	76.55±11.95	75.60±11.45	4.10	<0.001					
SUA, μmol/L	260.22±55.38	309.53±69.75	352.91±75.08	393.03±83.77	-25.32	<0.001					
FPG, mg/dL	90.84±15.05	104.67±31.57	97.83±23.22	106.41±31.61	-15.52	<0.001					
TC, mmol/L	4.89±0.98	5.33±1.08	4.79±0.90	5.03±0.94	-13.18	<0.001					
TG, mg/dL	82.40 (62.02~110.75)	138.22 (103.66~190.49)	106.32 (77.97~147.076)	163.91 (117.84~230.36)	-40.96	<0.001					
HDL, mmol/L	1.55±0.30	1.38±0.27	1.32±0.27	1.23±0.29	15.97	<0.001					
LDL, mmol/L	3.22±0.78	3.55±0.85	3.14±0.73	3.26±0.75	-8.58	<0.001					
TyG index	8.25±0.50	8.88±0.59	8.57±0.55	9.08±0.62	-43.61	<0.001					
Metabolic syndrome, n (%)	259 (5.27)	701 (36.7)	1009 (19.76)	2745 (55.02)	1343.59	<0.001					
Hyperglycaemia, n (%)	217 (4.41)	428 (22.41)	606 (11.87)	1242 (24.89)	286.47	<0.001					
CHD, n (%)	64 (1.3)	57 (2.98)	116 (2.27)	129 (2.59)	1.05	0.305					
Hypertension, n (%)	812 (16.51)	794 (41.57)	1632 (31.96)	2459 (49.29)	314.56	<0.001					

*Continuous variables are expressed as mean±SD or median (upper quartile to lower quartile), while classified variables are expressed as percentages.

ALT, alanine aminotransferase; BMI, body mass index; CHD, coronary heart disease; Cr, creatinine; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MAFLD, metabolic-associated fatty liver disease; SUA, serum uric acid; TC, total cholesterol; TG, triglycerides; TyG, triglyceride-glucose.

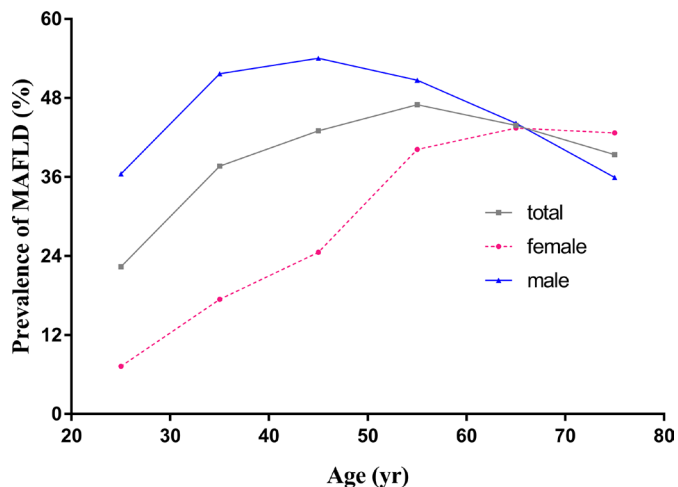


Figure 1 Prevalence of MAFLD in different age groups stratified by gender. MAFLD, metabolic-associated fatty liver disease.

The average age of men with MAFLD was 46.49 years old and the average age of women was 52.46 years old. The triglyceride-glucose (TyG) index of the MAFLD group was significantly higher than that of the non-MAFLD group, regardless of gender. In patients with MAFLD, 55.02% of men and 36.7% of women had more complicated conditions due to metabolic syndrome. A precise analysis of the differences between the MAFLD group and the non-MAFLD group showed that there were significant differences in all indicators of both genders, except for the prevalence of coronary heart disease (CHD).

To better understand the influence of different age groups on the prevalence of MAFLD, we further divided the participants by age, as shown in figure 1. After stratification by age, the prevalence of MAFLD among men was significantly higher than that among women before the age group of 50–59 years ($p < 0.001$). However, there was no significant difference in the prevalence of MAFLD in both gender groups aged 60–69 years ($p = 0.715$) and aged 70 years or older ($p = 0.072$). In the male group, the highest prevalence rate was found in the group of people from 40 to 49 years old (54.04%). We have noticed that this rate gradually decreased with age, especially after 50 years old. The lowest prevalence rate of 35.95% was found in the group of participants over 70 years old (refer to figure 1). Interestingly, in the female group, the lowest prevalence was 7.27% in the group formed by those who were younger than 29 years old, and the highest rate—43.44%—was observed in the group aged 60–69 years old, but it slightly decreased after 70 years old. However, in the general population, the prevalence gradually increased with age, more specifically before 50–59 years old. This group reached a peak of 47%, and then the rates started to gradually decrease with age.

The overweight and obesity rate of male Tianjin government employees was higher than that of female—44.5% and 30.4%, respectively (figure 2). Additionally, differences in the prevalence of MAFLD across gender groups

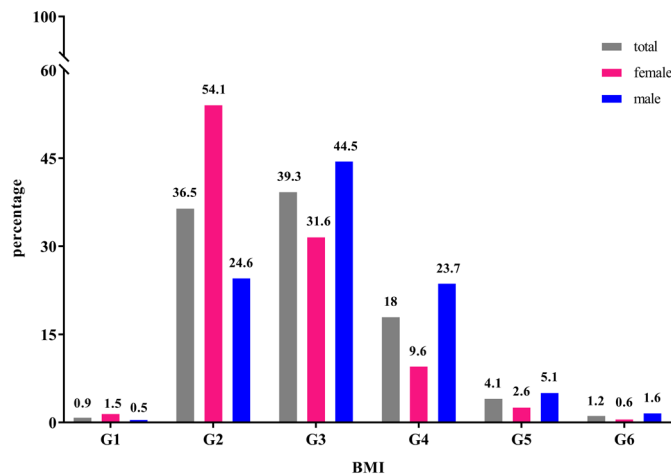


Fig 2. percentage of different BMI groups in females and males

Figure 2 Percentage of different BMI groups in women and men/BMI groups, G1: <18.5, G2: 18.5~23.9, G3: 23.9~27.9, G4: 27.9~31.9, G5: 31.9~35.9, G6: ≥35.9. BMI, body mass index.

increased proportionally with BMI (figure 3). Men had a significantly higher prevalence of MAFLD than women at any given BMI. So, we have concluded that MAFLD was positively associated with the levels of BMI in all the participants, regardless of gender.

The association between BMI, age and MAFLD is exhibited in figure 4. After adjusting for ALT, TC, HDL-C, LDL-C, uric acid, TyG index and history of diseases, the risk of MAFLD kept rising as BMI increased. Especially when BMI ≥31.9 kg/m², the risk increased significantly for both men and women. With BMI <31.9 kg/m², the risk of MAFLD in women was slightly higher than that in men, but it is worth noting that when BMI ≥31.9 kg/m², the risk of MAFLD in men (31.9 kg/m² ≤ BMI < 35.9 kg/m², OR 17.47; 95% CI 12.64 to 24.14; $p < 0.001$; BMI ≥35.9 kg/m², OR 23.4; 95% CI 11.85 to 46.21; $p < 0.001$) was significantly higher than that in women (31.9 kg/m² ≤ BMI < 35.9 kg/m²,

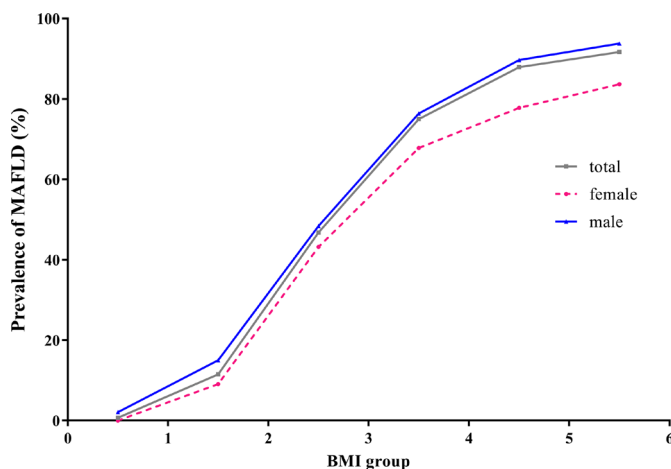


Figure 3 Prevalence of MAFLD in BMI groups stratified by gender/BMI groups, G1: <18.5, G2: 18.5~23.9, G3: 23.9~27.9, G4: 27.9~31.9, G5: 31.9~35.9, G6: ≥35.9. BMI, body mass index; MAFLD, metabolic-associated fatty liver disease.

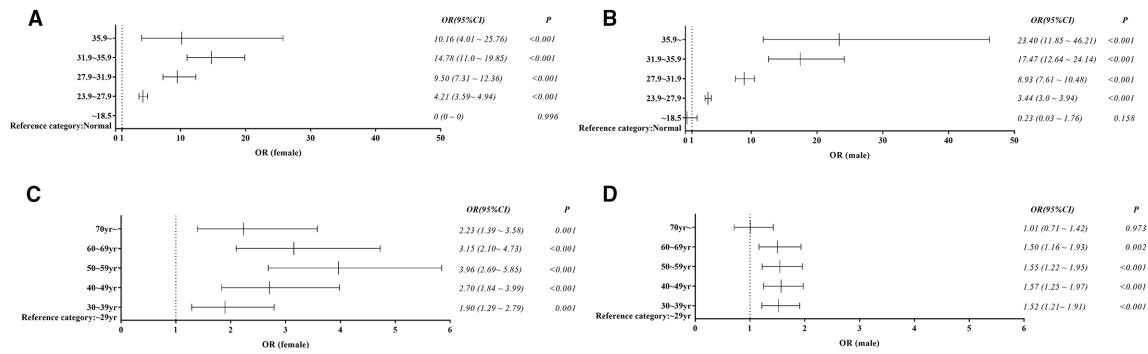


Figure 4 Forest map for binary logistic regression analysis of women and men. (A) OR for the association between body mass index (BMI) and MAFLD of women. (B) OR for the association between BMI and MAFLD of men. (C) OR for the association between age and MAFLD of women. (D) OR for the association between age and MAFLD of men. MAFLD, metabolic-associated fatty liver disease.

m^2 , OR 14.78; 95% CI 11.0 to 19.85; $p < 0.001$; BMI $\geq 35.9 \text{ kg/m}^2$, OR 10.16; 95% CI 4.01 to 25.76; $p < 0.001$). The highest risk of MAFLD among women was among the group of individuals from 50 to 59 years old (OR 3.96; 95% CI 2.69 to 5.85), while the risk among men tends to be the same in all age groups except for those over 70 years old.

DISCUSSION

In the current study, we found that the prevalence of MAFLD among government employees who underwent annual health examination in the Health Management and Examination Center of Tianjin People's Hospital in 2020 was 40.76%. Considering two different gender groups, we have confirmed that the prevalence for men was 49.42% and that for women was 27.97%. The difference is considerable and should make people highly vigilant about this issue. Furthermore, we analysed its risk factors and found that BMI $\geq 31.9 \text{ kg/m}^2$ and women aged between 50 and 59 years old had the highest risk of developing MAFLD compared with those younger than 29 years old.

This is the first large-scale cross-sectional study that explores the prevalence of MAFLD and its related risk factors among government employees in Tianjin. MAFLD is closely related to metabolic disorders, especially obesity. More recent evidence highlights that the prevalence of abdominal obesity in Tianjin ranks first in China regardless of gender,⁸ which may partly explain the high prevalence of MAFLD among government employees in Tianjin. The typical breakfast option in that region includes rice crust, bean curd and pancake fruit, all high-fat options that might lead to obesity. Currently, the prevalence of MAFLD in China is 29.2% and it keeps rising at an alarming rate with changes in people's lifestyles and the rapid development of the national economy, especially in economically developed regions.¹² A systematic review by Zhu *et al.*¹⁴ on the relationship between China's economy and the prevalence of MAFLD found that the number of MAFLD cases had rapidly increased with economic development in the past few decades, especially

in coastal areas. Scholars have researched other areas of the country and found that prevalence of MAFLD among employees in Taipei, Taiwan is 48.4%,²¹ that in Shanghai is 38.17%²² and that in Hong Kong is 42%,²³ all higher than that in Chengdu, an inland city, where the prevalence rate is only 12.5%.²⁴ Tianjin is an independently administered municipal district and is also a coastal region with a well-developed economy, which may be one reason for the high prevalence of MAFLD in that area. In addition, another reason for this phenomenon may be that our research subjects are government employees, who usually have a sedentary lifestyle and lack a healthy routine of exercises, which are factors associated with MAFLD. Williams *et al.*²⁵ conducted a prospective study on the prevalence of MAFLD among 400 middle-aged people, showing that people who develop this condition are those who often eat fast food and exercise less. Therefore, the high prevalence of MAFLD among government employees in Tianjin is worth paying attention to.

We analysed the distribution of the prevalence of MAFLD in men and women at different ages. Among men, the rate reached its peak among those from 40 to 49 years old. Among women, the highest rate was found in the group of individuals from 60 to 69 years old. The prevalence of this condition among men was significantly higher than that among women before the age of 50–59 years. Interestingly, women aged 50–59 years have the highest risk of MAFLD, while men have no significant difference in risk among different age groups, except those aged over 70 years. The outcomes of our research indicate that young and middle-aged men and postmenopausal women are high-risk groups for MAFLD. Many studies in China and abroad have previously emphasised that age is closely related to the occurrence and development of MAFLD.^{26 27} A study conducted in China Health Big Data (China Biobank) Project has shown that waist circumference and visceral fat area increase with age²⁸ so, from a long-term perspective, it is necessary to pay attention to young and middle-aged men to prevent or reverse the progress of MAFLD. Similar to part of our research results, a study conducted by Fung *et al.*²³ pointed out that



significant gender differences affected the MAFLD rates among the young and middle-aged population. However, the study did not analyse whether gender also impacts the rates among the elderly population (over 70 years old), which is essential for women of this age group to attach importance to the prevention of MAFLD. Previous studies have shown that oestrogen is a protective factor for MAFLD in premenopausal women,^{23 29} which explains our results. We have found that the prevalence of MAFLD in postmenopausal women has soared, since the level of oestrogen decreases at this stage. Women from 50 to 59 years old are part of the risk group and the highest occurrence rate was found among them. In this case, changing the lifestyle—which may include moderate physical activity and a balanced diet—is important for young and middle-aged men and postmenopausal women and can help to reduce the high prevalence of MAFLD, prevent and eventually reverse the progress of the disease.

In our study, we found that the prevalence of MAFLD was positively associated with BMI, and the prevalence in men was higher than in women. The overweight rate and obesity rate of men were 44.5% and 30.4%, respectively, and were higher than that of women. Through binary logistic regression analysis, we have concluded that overweight and obesity were the primary risk factors for MAFLD in both genders. When BMI ≥ 31.9 kg/m², the risk of male MAFLD was significantly higher than in women, indicating that obese men should pay more attention to weight management and prevention of MAFLD. Similar to our findings, a study from Pan *et al*⁹ showed that the obesity rate of men was positively correlated with education level, while the obesity rate of women showed an opposite trend. A recent study conducted by Sarkar *et al*³⁰ showed that reduced testosterone levels in obese men independently associated with fatty liver may partially explain this phenomenon, but further analysis is necessary to accurately understand these mechanisms. Although our recent review of the literature on this topic suggests that the obesity index is not at all associated with the prevalence rate of MAFLD, some preliminary studies consistent with our research results have pointed out that overweight and obesity are independent risk factors for MAFLD.^{31 32} Other scholars have also associated the rising obesity rate with the simultaneous rise in the prevalence of MAFLD.^{18 33 34} However, a growing body of literature has pointed out that weight loss can prevent MAFLD from progressing to more serious fatty hepatitis and liver cirrhosis, or even completely reverse the condition,^{35–37} which has attracted our attention. Combining our outcomes with the results of the aforementioned studies, we have concluded that new strategies are necessary to effectively curb the further spread of MAFLD. A healthy routine of exercises and a balanced diet are methods that can help to control the increasing incidence rate of this condition and may help reduce the existing prevalence rate, especially in Tianjin, where a significant part of the population is obese.

This is the first large-scale study on the prevalence of MAFLD and its risk factors among Tianjin government

employees. All measurements and statistical analyses were performed in strict accordance with the standard procedures to ensure data accuracy. However, the limitations of our study should also be addressed. First, we did not use the homeostatic model assessment of insulin resistance (HOMA-IR), surrogated with the TyG index easily applied in routine physical check-up. Recent studies have shown that TyG index can replace HOMA-IR to evaluate insulin resistance,³⁸ and its evaluation effect is even stronger than HOMA-IR.³⁹ Second, we did not include all the risk factors, such as waist circumference, haemoglobin A1c and γ -glutamyl peptidase which were not measured during the routine physical check-up, but we measured BMI, FPG and ALT. Finally, we did not collect the participants' medication information and the severity classification of CHD, which may cause slight bias to the basic understanding of the conditions of patients with MAFLD.

CONCLUSIONS

MAFLD is a very common condition among the group of Tianjin government employees, especially in postmenopausal women and obese men and men aged 40–49 years. Overweight or postmenopausal women and obese men or men aged 40–49 years should consider changing their lifestyles which include moderate physical activities and a balanced diet to their daily routine in order to improve their conditions. These changes may help to formulate personalised prevention and treatment strategies for the occurrence and progress of MAFLD in high-risk groups.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study involves human participants and was approved by the Institutional Review Board of Tianjin Union Medical Center (No. 2021C06). Participants gave informed consent to participate in the study before taking part.

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