Gender-Specific Prevalence and Influencing Factors of Non-alcoholic Fatty Liver Disease: A Post-print

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Abstract

Background Fatty liver disease (FLD) is a common and frequently occurring condition in daily life, and the number of patients with non-alcoholic fatty liver disease (NAFLD) is increasing annually, significantly impacting public health. Different gender populations exhibit variations in lifestyle and basal metabolism, which may lead to different prevalence patterns of NAFLD; however, current research on NAFLD prevalence across different genders remains limited. Objective To investigate the prevalence status and influencing factors of NAFLD in different gender populations, thereby providing references for clinical prevention and management of NAFLD. Methods We retrospectively selected 29,271 individuals who underwent health examinations at the Health Examination Center of Jinshan Hospital affiliated with Fudan University from August 2020 to August 2021 as study subjects. General information, physical examination data, laboratory indicators, comorbidities, and imaging findings were collected. Based on NAFLD diagnostic criteria, examinees were divided into an NAFLD group (n=10,524) and a control group (n=18,747) to analyze the prevalence characteristics of NAFLD across different genders. Multivariate Logistic regression analysis was employed to explore gender-specific influencing factors for NAFLD, while receiver operating characteristic (ROC) curves were used to evaluate the predictive value of relevant indicators for NAFLD risk in different gender populations, with calculation of the area under the ROC curve (AUC), sensitivity, and specificity. Results Among 29,271 examinees, 10,524 were diagnosed with NAFLD, yielding an overall prevalence of 35.95%. The cohort included 18,322 males (62.59%), with 7,854 male NAFLD patients (prevalence 42.87%), and 10,949 females (37.41%), with 2,670 female NAFLD patients (prevalence 24.39%). The difference in NAFLD prevalence between genders was statistically significant (2=1,016.505, P<0.001). Multivariate Logistic

regression analysis revealed that waist circumference, BMI, age, alanine aminotransferase, uric acid, triglyceride, fasting blood glucose, and electrocardiogram results were influencing factors for NAFLD in both gender populations (P<0.05). Additionally, cholesterol and systolic blood pressure were independent influencing factors for male examinees (P<0.05), while creatinine was an independent influencing factor for female examinees (P<0.05). Waist circumference, BMI, and their combination demonstrated high predictive value for NAFLD across genders. For male examinees, waist circumference predicted NAFLD risk with sensitivity of 0.778, specificity of 0.613, and optimal cutoff of 85.5 cm; BMI predicted NAFLD risk with sensitivity of 0.720, specificity of 0.711, and optimal cutoff of 24.6 kg/m2; the combination of waist circumference and BMI yielded an AUC of 0.789, sensitivity of 0.744, and specificity of 0.692. For female examinees, waist circumference predicted NAFLD risk with sensitivity of 0.815, specificity of 0.754, and optimal cutoff of 78.5 cm; BMI predicted NAFLD risk with sensitivity of 0.797, specificity of 0.759, and optimal cutoff of 23.6 kg/m2; the combination yielded an AUC of 0.872, sensitivity of 0.853, and specificity of 0.734. Conclusion The influencing factors for NAFLD differ slightly between males and females; however, age, gender, alanine aminotransferase, uric acid, triglyceride, cholesterol, fasting blood glucose, electrocardiogram results, waist circumference, and BMI are all influencing factors for NAFLD across gender populations. Regardless of gender, waist circumference, BMI, and their combination exhibit high predictive value for NAFLD risk and can be applied for NAFLD screening.

Full Text

Analysis of the Prevalence and Influencing Factors of Non-alcoholic Fatty Liver Disease in Different Gender Groups

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Abstract

Background: Fatty liver disease (FLD) is a common and frequently-occurring condition in daily life, and the number of patients with non-alcoholic fatty liver disease (NAFLD) has been increasing annually, significantly impacting public health. Differences in lifestyle and basal metabolism between gender groups may lead to variations in NAFLD prevalence, yet few studies have investigated the epidemiological patterns of NAFLD across different gender populations.

Objective: To examine the prevalence and influencing factors of NAFLD in different gender groups, providing evidence for clinical prevention and treatment strategies.

Methods: This retrospective case-control study included 29,271 individuals who underwent physical examination at the Health Examination Center of Jinshan Hospital, Fudan University between August 2020 and August 2021. General information, physical examination data, laboratory indices, comorbidities, and imaging findings were collected. Based on NAFLD diagnostic criteria, participants were divided into an NAFLD group (n = 10,524) and a control group (n = 18,747). The prevalence and characteristics of NAFLD were analyzed across gender groups. Multivariate logistic regression was used to identify gender-specific influencing factors, while receiver operating characteristic (ROC) curves were constructed to evaluate the predictive value of relevant indicators, with area under the curve (AUC), sensitivity, and specificity calculated.

Results: Among 29,271 participants, 10,524 NAFLD cases were identified, yielding an overall prevalence of 35.95%. The cohort comprised 18,322 males (62.59%) with 7,854 NAFLD cases (42.87% prevalence) and 10,949 females (37.41%) with 2,670 NAFLD cases (24.39% prevalence). The difference in NAFLD prevalence between genders was statistically significant (^{2} = 1,016.505, $P < 0.001$). Multivariate logistic regression revealed that waist circumference, BMI, age, alanine aminotransferase, uric acid, triglycerides, fasting blood glucose, and electrocardiogram results were influencing factors for NAFLD across gender groups ($P < 0.05$). Notably, cholesterol and systolic blood pressure were independent influencing factors for male participants ($P < 0.05$), while creatinine was an independent risk factor for female participants ($P < 0.05$). Waist circumference, BMI, and their combination demonstrated high predictive value for NAFLD in both genders. For males, waist circumference predicted NAFLD risk with sensitivity of 0.778 and specificity of 0.613 (optimal cutoff: 85.5 cm); BMI showed sensitivity of 0.720 and specificity of 0.711 (optimal cutoff: 24.6 kg/m^2); and the combined model achieved an AUC of 0.789 with sensitivity of 0.744 and specificity of 0.692. For females, waist circumference yielded sensitivity of 0.815 and specificity of 0.754 (optimal cutoff: 78.5 cm); BMI showed sensitivity of 0.797 and specificity of 0.759 (optimal cutoff: 23.6 kg/m^2); and the combined model achieved an AUC of 0.872 with sensitivity of 0.853 and specificity of 0.734.

Conclusion: While influencing factors for NAFLD show slight gender differ-

ences, age, gender, alanine aminotransferase, uric acid, triglycerides, cholesterol, fasting blood glucose, electrocardiogram results, waist circumference, and BMI are all significant factors across gender groups. Waist circumference, BMI, and their combination demonstrate high predictive value for NAFLD risk in both males and females, offering practical tools for NAFLD screening in health examinations.

Keywords: Non-alcoholic fatty liver disease; Prevalence; Sex factors; Root cause analysis

Introduction

With economic development and shifts in dietary patterns and lifestyle, the prevalence of fatty liver disease (FLD) has increased annually. Non-alcoholic fatty liver disease (NAFLD), defined as excessive hepatic fat accumulation unrelated to alcohol consumption, represents a metabolic stress-related liver injury closely associated with insulin resistance and genetic susceptibility. As hepatitis B vaccination has become widespread, NAFLD has emerged as the leading chronic liver disease globally. Chinese data indicate a national NAFLD prevalence of 29.2% between 2008-2018, while international studies report a global prevalence of 25.24%. NAFLD can progress to cirrhosis, hepatitis, and hepatocellular carcinoma, and is associated with cardiovascular disease, peripheral vascular disease, diabetes, cholelithiasis, colorectal neoplasms, and increased risks of breast and pancreatic cancers.

Gender differences in lifestyle, physiology, and metabolism may create distinct risk profiles and prevalence patterns for NAFLD. Early identification of gender-specific risk factors is crucial for individualized prevention and chronic disease management. Most patients experience minimal symptoms, leading to under-recognition of NAFLD. Research indicates higher NAFLD prevalence in males, potentially due to protective effects of estrogen in females. This study, conducted at Jinshan Hospital—a tertiary comprehensive hospital in Shanghai with a large, diverse examination population—aims to analyze the epidemiological characteristics, prevalence, and influencing factors of NAFLD across gender groups to inform prevention and treatment strategies.

Methods

Study Population This retrospective study included individuals undergoing physical examination at the Health Examination Center of Jinshan Hospital, Fudan University from August 2020 to August 2021. Inclusion criteria for NAFLD patients followed the *Guidelines for the Prevention and Treatment of Non-alcoholic Fatty Liver Disease (2018 Update)*: (1) presence of hepatic pathological or imaging changes; (2) alcohol consumption < 210 g/week for males and

< 140 g/week for females within the past year; (3) no use of medications such as amiodarone, methotrexate, tamoxifen, or glucocorticoids; and (4) exclusion of specific conditions causing FLD, including genotype 3 hepatitis C infection, Wilson' s disease, autoimmune hepatitis, and total parenteral nutrition. Exclusion criteria comprised pregnancy and incomplete data. The study was approved by the Jinshan Hospital Ethics Committee (JIEC2022-S05) with waiver of informed consent.

Data Collection **General Information:** Name, gender, age, contact information, examination number, and examination date.

Physical Examination: Conducted by qualified physicians, including height, weight, BMI, waist circumference, blood pressure, heart rate, and electrocardiogram. Waist circumference was measured at the narrowest point between the iliac crest and lower rib margin with participants standing, arms at sides, and breathing normally. According to Chinese obesity guidelines, waist circumference $\geq$ 90 cm in males and $\geq$ 80 cm in females indicates obesity; BMI $\geq$ 28.0 kg/m^2 defines obesity. Blood pressure and heart rate were measured using calibrated electronic devices after resting.

Laboratory Tests: After overnight fasting $\geq$ 8 hours, morning venous blood samples were analyzed using automated biochemical analyzers for: (1) liver function (alanine aminotransferase, aspartate aminotransferase); (2) kidney function (urea, creatinine, uric acid); (3) lipids (cholesterol, triglycerides); and (4) fasting blood glucose.

Imaging: Abdominal ultrasound was performed using a PHILIPS Affiniti 30 system by experienced sonographers following the *Guidelines for Ultrasound Diagnosis of Liver Disease*. NAFLD was diagnosed based on enhanced near-field hepatic echo, far-field echo attenuation, and unclear intrahepatic vascular structures.

Grouping and Statistical Analysis Participants were stratified into age groups (14-<20, 20-<30, 30-<40, 40-<50, 50-<60, 60-<70, 70-<80, 80-<90, and 90-99 years) to analyze age-specific prevalence by gender. Based on NAFLD diagnosis, participants were assigned to the NAFLD group (n = 10,524) or control group (n = 18,747).

Statistical analysis was performed using SPSS 21.0. Non-normally distributed continuous data were expressed as median (P25, P75) and compared using Mann-Whitney U tests. Categorical data were presented as frequencies and compared using ^{2} tests or Fisher' s exact test. Multivariate logistic regression analyzed gender-specific influencing factors. ROC curves assessed predictive value of indicators, with AUC, sensitivity, specificity, and optimal cutoff values calculated. Statistical significance was defined as $P < 0.05$.

Results

NAFLD Prevalence Among 54,285 registered examinees, 29,271 were included after excluding 14 cases with hepatitis B, 10 with alcohol consumption > 210 g/week, and 1 breast cancer patient on tamoxifen. The final cohort included 10,524 NAFLD patients (overall prevalence: 35.95%). Males accounted for 18,322 participants (62.59%) with 7,854 NAFLD cases (42.87% prevalence), while females comprised 10,949 participants (37.41%) with 2,670 NAFLD cases (24.39% prevalence). The gender difference in prevalence was statistically significant (^{2} = 1,016.505, P < 0.001). Using waist circumference criteria, obesity rates were 63.42% (6,674/10,524) in the NAFLD group versus 21.41% (4,013/18,747) in controls. Using BMI criteria, obesity rates were 23.94% (2,519/10,524) in the NAFLD group versus 3.43% (643/18,747) in controls.

Age-Specific Prevalence by Gender Male NAFLD prevalence was higher than females in age groups 20-<30, 30-<40, 40-<50, 50-<60, and 80-<90 years, but lower in the 70-<80 age group (P < 0.05). No significant gender differences were observed in the 14-<20, 60-<70, and 90-99 age groups (P > 0.05) .

Univariate Analysis of Influencing Factors The NAFLD group showed significantly higher proportions of males, older age, increased waist circumference, BMI, blood pressure, alanine aminotransferase, aspartate aminotransferase, urea, creatinine, uric acid, triglycerides, cholesterol, fasting blood glucose, abnormal electrocardiogram results, hypertension, diabetes, and coronary artery disease compared to controls (P < 0.05). No significant differences were found in heart rate or proportions of stroke and cholecystitis .

Multivariate Logistic Regression Analysis Multivariate analysis identified age, gender, alanine aminotransferase, uric acid, triglycerides, cholesterol, fasting blood glucose, waist circumference, BMI, systolic blood pressure, and electrocardiogram results as influencing factors for NAFLD (P < 0.05) .

Gender-Specific Influencing Factors Male Participants: Univariate analysis showed the male NAFLD group had significantly higher age, waist circumference, BMI, heart rate, blood pressure, alanine aminotransferase, aspartate aminotransferase, creatinine, uric acid, triglycerides, cholesterol, fasting blood glucose, abnormal electrocardiogram results, and proportions of hypertension and diabetes compared to male controls (P < 0.05). No significant differences were observed in urea levels or coronary artery disease proportion . Multivariate regression revealed age, alanine aminotransferase, uric acid, triglycerides, cholesterol, fasting blood glucose, waist circumference, BMI, systolic blood pressure, and electrocardiogram results as independent influencing factors for NAFLD in males (P < 0.05) .

Female Participants: Univariate analysis showed the female NAFLD group

had significantly higher age, waist circumference, BMI, blood pressure, alanine aminotransferase, aspartate aminotransferase, urea, uric acid, triglycerides, cholesterol, fasting blood glucose, abnormal electrocardiogram results, and proportions of hypertension and diabetes compared to female controls ($P < 0.05$). No significant differences were found in creatinine levels or coronary artery disease proportion . Multivariate regression identified age, alanine aminotransferase, creatinine, uric acid, triglycerides, cholesterol, fasting blood glucose, waist circumference, BMI, and electrocardiogram results as influencing factors for NAFLD in females ($P < 0.05$) .

Predictive Value of Indicators ROC analysis demonstrated that waist circumference, BMI, age, alanine aminotransferase, uric acid, triglycerides, fasting blood glucose, and electrocardiogram results had predictive value for NAFLD risk . Overall, waist circumference predicted NAFLD with sensitivity 0.730, specificity 0.736 (optimal cutoff: 83.5 cm); BMI showed sensitivity 0.805, specificity 0.682 (optimal cutoff: 23.9 kg/m^2); and their combination achieved an AUC of 0.829 with sensitivity 0.887 and specificity 0.600 [Figure 1: see original paper].

Gender-Specific Predictive Performance: - **Males:** Waist circumference AUC showed sensitivity 0.778, specificity 0.613 (cutoff: 85.5 cm); BMI showed sensitivity 0.720, specificity 0.711 (cutoff: 24.6 kg/m^2); combined model AUC was 0.789 with sensitivity 0.744 and specificity 0.692 [Figure 2: see original paper] . - **Females:** Waist circumference AUC showed sensitivity 0.815, specificity 0.754 (cutoff: 78.5 cm); BMI showed sensitivity 0.797, specificity 0.759 (cutoff: 23.6 kg/m^2); combined model AUC was 0.872 with sensitivity 0.853 and specificity 0.734 [Figure 3: see original paper] .

Discussion

NAFLD prevalence is notably high, yet most patients have mild disease, making early detection and intervention critical to prevent progression. This study found an overall NAFLD prevalence of 35.95%, with male prevalence (42.87%) significantly higher than female (24.39%), consistent with previous research attributing lower female rates to estrogen' s protective effects. However, females aged 70-<80 years showed higher prevalence than males, highlighting the importance of age-specific prevention strategies, particularly for older women.

NAFLD is influenced by multiple factors including age, gender, hormones, ethnicity, lifestyle, genetics, gut microbiota, and metabolic status, prompting proposals to rename it metabolic-associated fatty liver disease (MAFLD). Our results demonstrate that age, alanine aminotransferase, uric acid, triglycerides, cholesterol, fasting blood glucose, electrocardiogram results, waist circumference, and BMI are significant influencing factors across genders. Each 1 mg/dL increase in serum uric acid raises NAFLD risk by approximately 1.03-fold. While

creatinine levels differed significantly between NAFLD and control groups, multivariate analysis showed an OR of 0.989 (OR < 1), suggesting it may not be a risk factor but potentially a protective factor requiring further validation.

Gender-specific analysis revealed that elevated systolic blood pressure was a risk factor for males (P = 0.047, OR = 1.002) but not females, possibly due to estrogen' s vascular protective effects. Although creatinine differed between groups in univariate analysis, it was not an independent influencing factor in multivariate models. Okamura et al. reported that serum creatinine alone does not significantly affect NAFLD, but a low creatinine-to-body-weight ratio predicts lower NAFLD risk, a finding supported by Chinese studies. Notably, elevated total cholesterol lost its significance as a risk factor in females after multivariate adjustment, likely reflecting gender-specific physiological differences requiring further investigation.

Comorbidity analysis showed hypertension was a significant influencing factor, while diabetes, coronary artery disease, stroke, and cholecystitis were not, possibly due to underreporting during history-taking in busy examination settings.

ROC analysis confirmed waist circumference and BMI as valuable screening tools with good predictive performance in both genders. The combination of both measures improved predictive accuracy, with AUCs of 0.789 for males and 0.872 for females. These simple, practical metrics can be readily applied in physical examination settings for NAFLD screening.

This study has several limitations. First, as a single-center retrospective study, missing data led to numerous exclusions, and incomplete information on medical history (e.g., hypertension, diabetes, coronary artery disease, hepatitis B) and personal history (e.g., alcohol consumption) may have introduced bias. Second, NAFLD diagnosis relied on abdominal ultrasound rather than more precise imaging modalities. Future large-scale, multicenter prospective studies using advanced imaging techniques are needed to further explore gender-specific NAFLD influencing factors.

Despite these limitations, this study provides valuable insights into gender-specific NAFLD epidemiology and risk factors using health examination data from a tertiary hospital. The findings underscore the need for gender- and age-tailored health education to improve NAFLD awareness, promote lifestyle modifications, and reduce disease incidence and severity.

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Author Contributions

WANG Lina conceptualized the study, designed the research, implemented the investigation, and drafted the manuscript. WANG Lina, GE Ying, YAN Wei, and CAO Fan collected and organized data. WANG Lina and HE Daikun performed statistical analysis and created figures and tables. HE Daikun and GAO Pengfei revised the manuscript. HE Daikun supervised quality control and was responsible for overall manuscript oversight.

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Tables and Figures:

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Multivariate logistic regression analysis of NAFLD in male subjects
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AUC of each indicator to predict the risk of NAFLD in all subjects
AUC of each indicator to predict the risk of NAFLD in male subjects
AUC of each indicator to predict the risk of NAFLD in female subjects
[Figure 1: see original paper] ROC curves for each indicator to predict the risk of NAFLD in all subjects
[Figure 2: see original paper] ROC curves for each indicator to predict the risk of NAFLD in male subjects
[Figure 3: see original paper] ROC curves for each indicator to predict the risk of NAFLD in female subjects

Note: Figure translations are in progress. See original paper for figures.