Original Article

Prevalence trends of non-alcoholic fatty liver disease among young men in Korea: A Korean military population-based cross-sectional study

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Running title: Prevalence trends of NAFLD among young Korean men

Abbreviations
AAPP, average annual percent change; ALT, alanine aminotransferase; APC, annual percent change; APRI, AST-to-platelet ratio index; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; FIB-4, fibrosis-4; γGTP, gamma-glutamyl transpeptidase; HDL, high-density lipoprotein; HSI, hepatic steatosis index; LDL, low-density lipoprotein; MAFLD, metabolic-associated fatty liver disease; NAFLD, non-alcoholic fatty liver disease; SBP, systolic blood pressure; SD, standard deviation; SMD, standardized mean difference; TC, total cholesterol; TG, triglycerides; WBC, white blood cell.
Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) has become a major concern in Korea since its emergence as a dominant cause of chronic liver disease. However, no study has explored its prevalence in adults under 30 years of age. Therefore, we performed a cross-sectional study to investigate the prevalence of NAFLD in Korean men in their early twenties.

Methods: We collected data on 596,359 Korean soldiers who participated in a health examination between January 2015 and July 2021. A total of 571,872 individuals were analyzed after excluding those with missing data and hepatitis B antigen positivity. Hepatic steatosis was determined using the hepatic steatosis index (HSI). Participants with an HSI >36 were considered to have NAFLD.

Results: All participants were men, and the mean age was 20.9 ± 1.3 years. Of the 571,872 participants screened, 77,020 (13.47%) were classified as having NAFLD. The prevalence of NAFLD consistently increased from 2015 to 2021 (10.66% vs. 16.44%, P<0.001). Increases from 2015 to 2021 were also noted in the prevalence of hypercholesterolemia, hyperglycemia, and hypertension (P<0.001 for all). The mean body mass index also increased from 23.3 ± 3.0 kg/m² to 23.9 ± 3.1 kg/m² between 2015 and 2021 (P<0.001).

Conclusions: The prevalence of NAFLD and of other metabolic dysfunctions in Korean men in their early twenties increased from 2015 to 2021.

Keywords: Non-alcoholic fatty liver disease; Metabolic syndrome; Prevalence; Young adult; Korea

Graphical abstract

Highlight

Overall prevalence of NAFLD in young men during the study period (from year 2015 to year 2021) was 13.47%.

Prevalence of NAFLD kept rising in last 7 years with prevalence rate of 10.66% in year 2015 and 16.44% in year 2021. The Korean society should be alert for an increase in the disease prevalence and continue making efforts to reduce the associated complications.
INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has become a major global concern since its emergence as a dominant cause of chronic liver disease.\(^1\) In the Republic of Korea, various studies have reported that its prevalence ranges from 15% to 50%.\(^2-4\) A recent study noted that the prevalence of NAFLD in the Korean adult population is rising and is predicted to reach 44% by 2035.\(^5\) This has increased the awareness of the NAFLD risk in the Korean society. NAFLD is defined as the accumulation of fat in the liver in the absence of alcohol consumption. The prevalence of NAFLD is higher in patients with diabetes mellitus or obesity than in the general population.\(^6\) Moreover, the awareness of its association with metabolic disorders also increased, and the term “metabolic-associated fatty liver disease (MAFLD)” was described recently in an International consensus.\(^7,8\) MAFLD is diagnosed by “positive criteria,” which do not preclude an alcohol consumption history. The proposed positive criteria are based on the evidence of hepatic steatosis with any of the following: type 2 diabetes mellitus, obesity, or other metabolic dysregulations.

Regarding the NAFLD prognosis, a meta-analysis of 11 studies which performed paired liver biopsies revealed that the annual fibrosis progression rates were 0.07 and 0.14 stages in NAFLD and NASH patients, respectively.\(^9\) In our institute, a study involving a national population-based cohort demonstrated that NAFLD had a significantly higher hazard ratio for the incidence of gastrointestinal tract malignancies.\(^10\) A recent Swedish study demonstrated that the mortality rate in young patients with NAFLD was five times higher than that in the general population, thereby emphasizing the importance of NAFLD development at a young age.\(^11\)

There have been several studies on the prevalence and comorbidities of NAFLD in the Korean population.\(^12-15\) However, the cohort sizes in some of these were insufficient to represent the entire population. Moreover, most of the enrolled participants were limited to the elderly, and no study has explored the prevalence of NAFLD in young adults aged<30 years.

In Korea, men in their early twenties are obligated to serve in the armed forces and are forbidden from consuming alcohol in the military facilities. We accessed the Korean military database to evaluate the prevalence of NAFLD in conscripted young male individuals. To evaluate liver steatosis, we used the hepatic steatosis index (HSI). Developed by a Korean study group, the HSI represents a noninvasive modality for assessing hepatic steatosis.\(^16\) It has a high predictive value for NAFLD, which has been validated in the original and in subsequent studies.\(^17,18\)

We performed the present cross-sectional study in a Korean military population comprising 596,359 men in their early 20s. Our study can be considered as a nearly complete enumeration survey of men in their...
early 20s, because almost all men in Korea serve in the military. We aimed to determine the trends in the prevalence of NAFLD over the last 7 years in this population and the association of NAFLD with other metabolic disorders, such as dyslipidemia, hypertension, and hyperglycemia.

METHODS

Study population

In Korea, young men aged between 18 and 31 years are obligated to serve in the military for 19–23 months; when promoted to the rank of a Corporal, soldiers are required to undergo medical examinations. Data collected at these examinations are recorded in the Korean armed forces database (New Defense Medical Information System, NDEMIS). In this study, we extracted the medical data of 596,359 men, which were recorded in the NDEMIS between January 2015 and July 2021. After excluding those positive for the hepatitis B surface antigen and those with missing data, 571,872 men were included in this cross-sectional study (Fig. 1). This study was approved by the institutional review board of the Korean Armed Forces Medical Command (AFMC-202106-HR-041-01). Informed consent was not required, because of the retrospective nature of the study.

Measurements

With the participant’s barefoot and wearing light clothing, the height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively. The body mass index (BMI; kg/m²) was calculated from the measured height and weight. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured to the nearest 2 mmHg using a sphygmomanometer (BPBIO330N; InBody Co. Ltd. Seoul, Republic of Korea) after 5 min of rest. Blood samples were collected from the antecubital vein after overnight fasting. The levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (γGTP), triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), glucose, and creatinine were measured using a TBA-2000 FR Chemistry Analyzer (Toshiba, Tokyo, Japan). The complete blood count, hemoglobin level, hematocrit, and platelet count were measured using an XN-1000™ Hematology Analyzer (Sysmex, Kobe, Japan). Hepatitis B surface antigen and antibody levels were analyzed using electrochemiluminescence immunoassays with a Cobas 6000 analyzer (Roche Diagnostics, Basel, Switzerland).
Definitions

Hepatic steatosis was determined using the HSI, which was calculated by the following formula: HSI = 8×(ALT/AST) + BMI (kg/m²) (+2, if female; +2, if having diabetes mellitus). Participants with HSIs greater than 36 were considered to have liver steatosis. Because the population participating in this study served in the armed forces, they were prohibited from drinking alcohol in the military facilities, where they spent most of their time during the period of service. Therefore, considering the circumstances wherein access to alcohol was extremely limited, NAFLD was defined as the presence of hepatic steatosis without any evidence of viral hepatitis in this study. Hypercholesterolemia and hypertriglyceridemia were defined in accordance with the Korean guidelines for management of dyslipidemia (fourth edition). Accordingly, hypercholesterolemia was defined by TC ≥240 mg/dL, while hypertriglyceridemia was defined by TG ≥ 200 mg/dL. Dyslipidemia was diagnosed if any of the following criteria were met: TC ≥240 mg/dL, TG ≥200 mg/dL, HDL<40 mg/dL, and LDL ≥160 mg/dL. Hypertension was defined by an SBP ≥140 mmHg or by a DBP ≥90 mmHg in accordance with the 2018 guidelines from the Korean Society of Hypertension. Participants who had impaired fasting glucose levels or diabetes mellitus were considered as having hyperglycemia; an 8-hour fasting glucose level >100 mg/dL was considered for the diagnosis.

The Fibrosis-4 (FIB-4) index and the AST-to-platelet ratio index (APRI) were used to evaluate fibrosis among those classified as having NAFLD. The FIB-4 index is a widely used non-invasive predictive score for hepatic fibrosis. It is based on serologic tests, and is calculated using the following formula: (age × AST level in IU/L)/(platelet counts in 10⁹/L×ALT level in IU/L). An FIB-4 index of 1.3 was considered as the cut-off for excluding hepatic fibrosis. The APRI was calculated using the variables AST level, the upper normal limit of AST, and platelet count. The upper normal limit of AST was set at 32 U/L by a previous study on a Korean population. The APRI is calculated as follows:

APRI = (AST level in IU/L)/(the upper normal limit of AST in IU/L)/(platelet counts in 10⁹/L).

An APRI score of >1.0 was considered to indicate severe fibrosis.

Statistical analyses

All statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA) and R version 4.0.3 (R Foundation Inc.; http://cran.r-project.org [Accessed on November 1st, 2021]). Continuous variables were expressed as means with standard deviations (SD). The standardized mean difference (SMD) is
the difference between two means divided by a pooled SD and was calculated when comparing two different groups with continuous variables. Student’s t-test was performed to compare the continuous variables between two different groups, while an analysis of variance was performed to compare continuous variables between three or more different groups. Categorical variables were compared using the chi-square test. The Cochran–Armitage trend test was performed to confirm the trends in the NAFLD prevalence over time. Moreover, to measure the annual percent change (APC) and the average annual percent changes (AAPC) of prevalence during the 7-year examination period, the joinpoint model was applied using Joinpoint Regression Program Version 4.9.0.0 (Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute, Rockville, MD, USA). Statistical significance was set at P <0.05.

RESULTS

Characteristics of the study participants

A total of 571,872 participants whose medical data were registered in the NDEMIS from January 2015 to July 2021 were included in the analysis. Table 1 shows the participants’ characteristics. Of these, 77,020 participants were classified as having NAFLD and were included in the NAFLD cohort. All participants were men. The mean ages were 20.9±1.3 and 21.0±1.4 years in the non-NAFLD and NAFLD cohorts, respectively (P<0.001). The mean BMI was higher in the NAFLD (28.4 kg/m²) than in the non-NAFLD cohort (22.9 kg/m²). The mean SBP and DBP were also higher in the NAFLD than in the non-NAFLD cohort (mean SBP: 125.7 mmHg vs. 118.2 mmHg, mean DBP: 75.0 mmHg vs. 69.7 mmHg; P<0.001). Regarding the lipid profile, the mean TC, LDL-C, and TG levels were higher in the NAFLD than in the non-NAFLD cohort (TC: 184.8 mg/dL vs. 168.9 mg/dL, LDL-C: 117.9 mg/dL vs. 101.5 mg/dL, and TG: 125.9 mg/dL vs. 79.1 mg/dL; P<0.001 for all). Conversely, the mean HDL-C level was higher in the non-NAFLD than in the NAFLD cohort (HDL-C: 55.0 mg/dL vs. 48.9 mg/dL, P<0.001). A comparison of the blood test results revealed higher white blood cell counts, hemoglobin levels, hematocrit, and platelet count in the NAFLD than in the non-NAFLD cohort. The AST, ALT, and γGTP levels were also significantly higher in the NAFLD than in the non-NAFLD cohort (P<0.001 for all).

Year-wise comparison of the prevalence of NAFLD

The prevalence of NAFLD from 2015 to 2021 is presented in Fig. 2. The overall prevalence of NAFLD during the entire study period was 13.47% (77,020/571,872 participants evaluated as having NAFLD). In 2015, the prevalence was estimated to be 10.66% (9,798/91,911 participants). It continued to rise over the
years with 11.81% in 2016 (11,040/93,469 participants), 12.09% in 2017 (11,698/96,378 participants), 14.42% in 2018 (12,345/85,599 participants), and 15.75% in 2019 (13,022/83,483 participants). At 15.30%, the prevalence seemed to slightly decline in 2020 (11,439/74,776 participants); however, with 16.44%, the upward trend was recovered in 2021 (7,678/46,707). The prevalence of NAFLD showed a tendency to increase over the years, with \( P \) for trend<0.001. The absolute change in the prevalence over the 7-year period was 5.78%, indicating an annual increase of approximately 0.83%.

**Year-wise comparison of the baseline characteristics in the entire cohort**

The baseline characteristics of the cohorts in each year are presented in Table 2. The mean BMI, ALT, TC, and platelet count kept rising until 2021; their values were the lowest in 2015 and the highest in 2021 (BMI \([\text{kg/m}^2]\): 23.29 vs. 23.91, ALT (mg/dL): 21.35 vs. 24.85, TC (mg/dL): 169.72 vs. 174.32, platelet count (\(\times 10^3/L\): 239.1 vs. 251.9; \(P<0.001\) for all). The fasting glucose levels were also the highest in 2021. However, the mean TG levels and white blood cell counts were the lowest in 2021 (TG [mg/dL]: 85.66 in 2015 vs. 82.43 in 2021, WBC [\(\times 10^3/L\): 6.86 in 2015 vs. 6.47 in 2021; \(P<0.001\) for both).

**Comparison of the prevalence of metabolic dysfunctions between 2015–2017 and 2018–2021**

We categorized the participants into Group A (n=282,118; medical data collected during 2015–2017) and Group B (n=289,754; medical data collected during 2018–2021) to ensure that the group sizes were matched. The prevalence of metabolic dysfunction was compared between these two groups (Fig. 3). The prevalence of hypertriglyceridemia did not differ significantly between Group A (3.69%) and Group B (3.64%) (\(P=0.282\)). Conversely, the prevalence of hypertension was significantly higher in Group B (3.00%) than in Group A (2.42%) (\(P<0.001\)). Hyperglycemia was significantly more prevalent in Group B (9.99%) than in Group A (8.69%) (\(P<0.001\)). The prevalence of hypercholesterolemia was significantly higher in Group B (2.08%) than in Group A (1.89%) (\(P<0.001\)). Overall, the prevalence of hypertension, hyperglycemia, and hypercholesterolemia increased over time.

**NAFLD prevalence by subgroups**

We compared the NAFLD prevalence between the presence and absence of comorbidities. Figure 4 is a bar plot graph that shows the subgroup-wise prevalence of NAFLD. The number of participants with and without hypertension was 15,501 (hypertension group, 2.71%) and 556,371 (non-hypertension group, 97.29%),
respectively. The prevalence of NAFLD was higher in the hypertension group (38.9%) than in the non-hypertension group (12.8%) (P<0.001). The number of participants with and without hyperglycemia was 53,456 (hyperglycemia group; 9.35%) and 518,416 (non-hyperglycemia group; 90.65%) respectively. The prevalence of NAFLD was higher in the hyperglycemia group (18.8%) than in the non-hyperglycemia group (12.9%) (P<0.001). The numbers of participants with and without dyslipidemia were 71,117 (dyslipidemia group) and 500,755 (non-dyslipidemia group), respectively. The prevalence of NAFLD was higher in the dyslipidemia group (33.6%) than in the non-dyslipidemia group (10.6%) (P<0.001).

**Evaluation of fibrosis using serologic tools**

First, using the FIB-4 index, the prevalence of fibrosis among patients with NAFLD was found to be only 0.08% (61/77,020) with cut-off values of 1.3. Then, using the APRI, the prevalence of severe fibrosis among patients with NAFLD was found to be 1.64% (1,261/77,020); these patients had an APRI >1.0. Furthermore, we used the same serologic indices to estimate the prevalence of fibrosis among patients without NAFLD. The prevalence was estimated to be 0.69% (3,443/494,852) and 0.98% (4,833/494,852) using the FIB-4 index and the APRI, respectively.

**Future prediction of NAFLD prevalence using the joinpoint model**

We used the joinpoint regression analysis to calculate the APC and the AAPC of prevalence. The APC was 10.1% from 2015 to 2019 and 1.9% from 2019 to 2021. Overall, the AAPC in the NAFLD prevalence during the study period was 7.9% (4.9%–10.9%, 95 confidence interval) per year. We predicted the future prevalence of NAFLD among young men using a formula driven from the joinpoint regression analysis as follows:

\[
\ln(\text{prevalence}) = -150.129 + \text{Year} \times 0.07569.
\]

Using the aforementioned formula, the estimated prevalence in year 2030 was calculated to be 33.91% (Fig. 5).

**DISCUSSION**

Our study analyzed the data of young men in Korea (mean age: 20.9 years) and found that the prevalence of NAFLD increased over time from 10.66% in 2015 to 16.44% in 2021 (annual increase: approximately 0.83%). This trend was statistically significant (P<0.001). Using the joinpoint model, the AAPC
of NAFLD prevalence was 7.9% and the prevalence is expected to reach 33.91% by the year 2030 using the aforementioned model. The prevalence of metabolic dysfunctions (hypercholesterolemia, hyperglycemia, and hypertension) also increased from 2015 to 2021. The BMI also showed a clear tendency to increase.

These results and the observed tendency were in line with the findings of previous studies conducted in Korea and other parts of the world. Kang et al. showed that the prevalence of NAFLD has increased over time (with an annual increase rate of 2.3%), and is predicted to reach 43.8% by 2035. Many studies in Korea have also reported an increase in NAFLD prevalence over time. Outside Korea, Arshad et al. investigated 4,654 young adults (aged 12–29 years) from the United States; they also reached a similar conclusion that the prevalence of NAFLD among individuals aged 18–24 years increased during 2007–2016.

Our study also showed that the prevalence of NAFLD tended to be higher among patients with metabolic dysfunctions, such as hyperglycemia, dyslipidemia, and hypertension. The NAFLD prevalence was 38.5% in the hypertension group and 12.8% in the non-hypertension group. Although lower than in the hypertension group, the prevalence of NAFLD was higher in the hyperglycemia and dyslipidemia groups than in the non-hyperglycemia and non-dyslipidemia groups, respectively. In line with our findings, the association between the metabolic syndrome and NAFLD has been widely reported. Furthermore, the recently proposed term “MAFLD” encompasses metabolic dysfunctions as criteria for diagnosis, implying that it is crucial to consider metabolic dysfunctions while treating NAFLD.

As the majority of individuals aged > 30 years are willing to undergo health examinations, sufficient data have been reported on the prevalence of NAFLD in this age group. However, little is known concerning the prevalence of NAFLD in younger adults not only in Korea, but also worldwide, due to a lack of need for medical surveys. To the best of our knowledge, this study is the first to present the prevalence of NAFLD and metabolic dysfunction in Korean young adults with a sufficient sample size. As most men in their early twenties are obligated to serve in the military, it can be assumed that our study has a credibility close to that of a full-scale survey.

Considering the findings of previous studies, an increase in populations with NAFLD might pose a severe threat to the society. The all-cause mortality was up to five times higher in young adults with NAFLD, and there are reports that NAFLD might be associated with compromised reproductive health in both men and women. Furthermore, NAFLD is also known to be associated with many other extra-hepatic comorbidities such as cardiovascular disease and chronic kidney disease. Based on these reports, our findings can be crucial to society, as they indicate that the national health can be threatened by NAFLD complications in the
Recently, Korean society underwent rapid change in lifestyle and social habit. According to the Korea National Health and Nutrition Examination Survey, South Koreans showed a clear tendency of consuming more high-fat foods and were less likely to perform high-intensity exercise in the last decade\(^4\). The increasing prevalence of NAFLD may be partly elucidated by foregoing facts. Nevertheless, the participants in this study serve in military where strict lifestyle is required which raises question about the nutritional balance of Korean army. Convenience stores in military bases provide many kinds of food, including instant food and high-fat food, which might provoke nutritional imbalance and metabolic disorders\(^5\). Therefore, we propose a routine Korean military nutritional survey, as KNHANES have done over decades with Korean populations, to stratify possible risk factors regarding nutrition and to intervene in dietary patterns following the outcomes of the survey. By improving the nutritional balance of young men serving military, Republic of Korea Armed Forces may contribute to Korean society by lowering the estimated prevalence of NAFLD which is predicted to reach 33.91% at year 2030.

This study had some limitations. First, it used a non-invasive method, the HSI, to determine liver steatosis. Although the HSI is primarily designed for Korean populations and is well-validated in other studies, ultrasonography and biopsy are preferable for defining fatty liver with a higher reliability. Second, we only used serologic tools for evaluating fibrosis. The FIB-4 index and the APRI are among the most commonly used serologic tools for detecting hepatic fibrosis. However, several previous studies have noted that the FIB-4 index had a low predictive value for hepatic fibrosis in patients aged < 35 years and advised using it with caution.\(^6\) In addition, in the case of APRI, it reportedly has a low predictive efficiency for fibrosis in those aged <30 years.\(^7\) Considering the low predictive value and the discrepancy between the results from these tools, further studies using biopsy or magnetic resonance elastography are required to better predict the prevalence of significant fibrosis among patients with NAFLD. Third, selection bias cannot be ruled out. Although most Korean men serve in the military, some with physical disabilities are advised not to. In order to receive military exemption for fatty liver, advanced fibrosis must be proven through biopsy, which is very difficult in real-life practice. Finally, insufficient data were provided to discriminate other chronic liver disease such as alcoholic fatty liver and chronic hepatitis C. There was no questionnaire asking regarding alcohol consumption, although we can presume that extremely low percentage of participants would have alcoholic fatty liver disease given the fact that their mean age was only 21 and that time of examination was 1 year after the enlistment. Regarding HCV infection, only selected participants who showed elevated ALT or AST levels were tested for HCV serology,
although no one among them showed positive for HCV antibody. In contrast, according to the data from the Korean National Health and Nutritional Examination Survey, only 0.2% of Koreans in their 20s had hepatitis C which implies that there would be only little portion of participants with positive HCV antibody. Although these possibilities for having chronic liver diseases are low, complete exclusion of the aforementioned disease would be preferable in evaluating the prevalence of NAFLD.

In conclusion, we used the HSI and showed that the prevalence of NAFLD among young Korean men increased in the last 7 years. The prevalence of metabolic dysfunctions has also increased. This is a critically important result as it implies an increase in socio-economic disease burden for young men with NAFLD. Therefore, the Korean society should remain alert for an increase in NAFLD prevalence and continuously undertake efforts to reduce its complications. In this context, although efficient treatment options are important, active screening of patients with metabolic disorders should be considered. Further longitudinal studies are required to demonstrate the possible risk and socio-economic costs of NAFLD in young adults.

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Authors’ contribution
Study concept and design: Si Hyun Bae, Jaejun Lee, Data collection: Jaejun Lee, Taeyun Kim; Data analysis and interpretation: Jaejun Lee, Hyun Yang and Si Hyun Bae; manuscript writing: Jaejun Lee and Si Hyun Bae; Final approval of the version to be published: All authors

Conflicts of interest
The authors declare no conflicts of interest. The funders had no role in the study design; in the collection, analyses, or interpretation of the data; in the writing of the manuscript; or in the decision to publish the results.

Institutional Review Board Statement
The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional review board of the Korean Armed Forces Medical Command (AFMC-202106-HR-041-01).

**Informed Consent Statement**

Informed consent was not required, because this research was retrospective study.
1 References


Figure legends

**Figure 1.** Flow-gram of patient selection. HBsAg, hepatitis B surface antigen; HSI, hepatic steatosis index.
Figure 2. Comparison in estimated prevalence of NAFLD over years

Figure 3. Linear plot on prevalence of metabolic disorder (2015-2017 vs. 2018-2021)
(A) NAFLD prevalence in participants with or without HTN

<table>
<thead>
<tr>
<th>Condition</th>
<th>NAFLD Prevalence (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN (n=15,501)</td>
<td>38.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Without HTN (n=556,371)</td>
<td>12.8%</td>
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</tbody>
</table>

(B) NAFLD prevalence in participants with or without hyperglycemia

<table>
<thead>
<tr>
<th>Condition</th>
<th>NAFLD Prevalence (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperglycemia (n=53,456)</td>
<td>18.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Without hyperglycemia (n=518,416)</td>
<td>12.9%</td>
<td></td>
</tr>
</tbody>
</table>
Figure 4. NAFLD prevalence by subgroups (A) NAFLD prevalence in participants with or without hypertension. (B) NAFLD prevalence in participants with or without hyperglycemia. (C) NAFLD prevalence in participants with or without dyslipidemia.

Figure 5. Future prediction on prevalence of NAFLD using the joinpoint model; APC, annual percent change, AAPP, average annual percent changes.
Table 1. Baseline characteristics of entire participants

<table>
<thead>
<tr>
<th></th>
<th>Non-NAFLD cohort (n=494,852)</th>
<th>NAFLD (n=77,020)</th>
<th>SMD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M/F</td>
<td>494852(100) / 0(0)</td>
<td>77020(100) / 0(0)</td>
<td>0.120</td>
</tr>
<tr>
<td>Age</td>
<td>20.9 ± 1.3</td>
<td>21.0 ± 1.4</td>
<td>0.120</td>
<td>&lt;0.001</td>
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<tr>
<td>Height (cm)</td>
<td>174.3 ± 5.6</td>
<td>174.4 ± 5.8</td>
<td>0.017</td>
<td>&lt;0.001</td>
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<td>Weight (kg)</td>
<td>69.7 ± 8.3</td>
<td>86.7 ± 11.2</td>
<td>1.725</td>
<td>&lt;0.001</td>
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<td>BMI (kg/cm²)</td>
<td>22.9 ± 2.3</td>
<td>28.4 ± 3.1</td>
<td>2.066</td>
<td>&lt;0.001</td>
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<td>SBP (mm/Hg)</td>
<td>118.2 ± 12.0</td>
<td>125.7 ± 12.5</td>
<td>0.613</td>
<td>&lt;0.001</td>
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<td>DBP (mm/Hg)</td>
<td>69.7 ± 9.0</td>
<td>75.0 ± 9.8</td>
<td>0.563</td>
<td>&lt;0.001</td>
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<tr>
<td>Lipid profile</td>
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<td></td>
<td></td>
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<tr>
<td>Total cholesterol</td>
<td>168.9 ± 28.0</td>
<td>184.8 ± 33.0</td>
<td>0.520</td>
<td>&lt;0.001</td>
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<tr>
<td>HDL-choleserol</td>
<td>55.0 ± 10.5</td>
<td>48.9 ± 9.5</td>
<td>0.602</td>
<td>&lt;0.001</td>
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<td>LDL-choleserol</td>
<td>101.5 ± 24.0</td>
<td>117.9 ± 28.0</td>
<td>0.629</td>
<td>&lt;0.001</td>
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<td>Triglyceride</td>
<td>79.1 ± 45.7</td>
<td>125.9 ± 84.9</td>
<td>0.687</td>
<td>&lt;0.001</td>
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<td>Fasting Glucose</td>
<td>90.4 ± 8.1</td>
<td>92.3 ± 8.9</td>
<td>0.228</td>
<td>&lt;0.001</td>
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<td>WBC</td>
<td>6.6 ± 1.6</td>
<td>7.2 ± 1.7</td>
<td>0.384</td>
<td>&lt;0.001</td>
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<td>Hemaglobin</td>
<td>15.5 ± 0.9</td>
<td>15.9 ± 0.9</td>
<td>0.393</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>45.6 ± 2.5</td>
<td>46.5 ± 2.5</td>
<td>0.356</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Platelet (10⁹/L)</td>
<td>241.9 ± 45.4</td>
<td>258.2 ± 49.4</td>
<td>0.344</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.96 ± 0.13</td>
<td>0.94 ± 0.13</td>
<td>0.142</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AST</td>
<td>23.8 ± 18.7</td>
<td>28.9 ± 16.6</td>
<td>0.292</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT</td>
<td>18.8 ± 10.8</td>
<td>46.1 ± 38.9</td>
<td>0.958</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>γGTP</td>
<td>17.9 ± 8.2</td>
<td>33.4 ± 23.4</td>
<td>0.885</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as n (%) or mean ± SD. SMD: standardized mean difference, NAFLD: non-alcoholic fatty liver disease, SBP: systolic blood pressure, DBP: diastolic blood pressure, HDL: high-density lipoprotein, LDL: low-density lipoprotein, WBC: white blood cell, AST: aspartate aminotransferase, ALT: alanine aminotransferase, γGTP: gamma-glutamyl transpeptidase.
Table 2. Comparison of baseline characteristics by year

<table>
<thead>
<tr>
<th></th>
<th>2015 (n=91,911)</th>
<th>2016 (n=93,469)</th>
<th>2017 (n=85,999)</th>
<th>2018 (n=82,672)</th>
<th>2019 (n=74,776)</th>
<th>2020 (n=46,707)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>23.29±2.9</td>
<td>23.47±3.0</td>
<td>23.58±2.9</td>
<td>23.79±3.1</td>
<td>23.81±3.2</td>
<td>23.84±3.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT</td>
<td>21.35±17.4</td>
<td>21.25±18.1</td>
<td>21.60±18.1</td>
<td>22.42±19.7</td>
<td>23.36±23.4</td>
<td>23.99±20.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FBS</td>
<td>90.81±8.6</td>
<td>89.94±8.1</td>
<td>90.10±8.2</td>
<td>90.53±8.4</td>
<td>91.16±8.5</td>
<td>90.75±7.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TC</td>
<td>169.72±28.8</td>
<td>171.69±29.2</td>
<td>171.03±28.8</td>
<td>170.56±29.0</td>
<td>169.94±29.2</td>
<td>171.73±29.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TG</td>
<td>85.66±55.2</td>
<td>85.29±54.9</td>
<td>85.12±55.3</td>
<td>86.74±56.2</td>
<td>87.84±57.6</td>
<td>83.29±52.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WBC</td>
<td>6.86±1.7</td>
<td>6.80±1.7</td>
<td>6.82±1.6</td>
<td>6.65±1.6</td>
<td>6.47±1.6</td>
<td>6.52±1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PLT</td>
<td>239.1±45.1</td>
<td>240.4±45.6</td>
<td>241.9±46.0</td>
<td>242.9±46.2</td>
<td>247.4±46.7</td>
<td>250.7±46.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. BMI: body mass index, ALT: alanine aminotransferase, FBS: fasting blood sugar, TC: total cholesterol, TG: triglycerides, WBC: white blood cell, PLT: platelet.