



Fatty Liver & Diabetes Statistics in Korea: Nationwide Data 2009 to 2017

Eugene Han¹, Kyung-Do Han², Yong-ho Lee³, Kyung-Soo Kim⁴, Sangmo Hong⁵, Jung Hwan Park⁶, Cheol-Young Park⁷,
on Behalf of Fatty Liver Research Group of the Korean Diabetes Association

¹Department of Internal Medicine, Keimyung University School of Medicine, Daegu,

²Department of Statistics and Actuarial Science, Soongsil University, Seoul,

³Department of Internal Medicine, Yonsei University College of Medicine, Seoul,

⁴Division of Endocrinology and Metabolism, Department of Internal Medicine, CHA Bundang Medical Center, CHA University School of Medicine, Seongnam,

⁵Division of Endocrinology and Metabolism, Department of Internal Medicine, Hanyang University Guri Hospital, Hanyang University College of Medicine, Guri,

⁶Division of Endocrinology and Metabolism, Department of Internal Medicine, Hanyang University College of Medicine, Seoul,

⁷Division of Endocrinology and Metabolism, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

Background: This study investigated the changes of fatty liver disease prevalence in general Korean population.

Methods: This study analyzed data from the Korean National Health Insurance Service from 2009 to 2017 that included individuals aged 20 years or older who had undergone a medical health examination. Fatty liver disease was assessed using the fatty liver index (FLI). The disease severity was defined by FLI cutoff, ≥ 30 as moderate, and ≥ 60 as severe fatty liver disease.

Results: The prevalence of Korean adults aged 20 years or over with fatty liver disease (FLI ≥ 60) increased from 13.3% in 2009 to 15.5% in 2017 (P for trend < 0.001). The increase in fatty liver disease prevalence was prominent in men (from 20.5% to 24.2%) and the young age (20 to 39 years) group (from 12.8% to 16.4%) (P for interaction < 0.001). The prevalence of fatty liver disease was the highest in type 2 diabetes mellitus (T2DM, 29.6%) population compared to that of prediabetes or normoglycemia (10.0% and 21.8%) in 2017. The prevalence of fatty liver disease had statistically increased in individuals with T2DM and prediabetes (P for trend < 0.001). Its prevalence increased more steeply in the young-aged population with T2DM, from 42.2% in 2009 to 60.1% in 2017. When applying a lower FLI cutoff (≥ 30) similar results were observed.

Conclusion: The prevalence of fatty liver disease in the Korean population has increased. Individuals who are young, male, and have T2DM are vulnerable to fatty liver disease.

Keywords: Comorbidity; Diabetes mellitus, type 2; Epidemiology; Fatty liver; Non-alcoholic fatty liver disease

INTRODUCTION

As obesity has become epidemic, obesity-related comorbidities, including diabetes, and metabolic syndrome have also increased [1]. In Korea, the prevalence of obesity has increased steadily over a decade reaching 36.6% in the general population, 46.2% in men, and 27.3% in women [2]. Along with this era of obesity, the consequences of ectopic fat have emerged.

Fatty liver disease is a hepatic manifestation of ectopic fat distribution and is one of the most prevalent chronic liver diseases worldwide [3]. Fatty liver disease was recognized as a benign condition because simple steatosis without metabolic components exhibited favorable outcomes [4]. However, recent studies have demonstrated that fatty liver disease is a progressive form of liver injury, leading to liver fibrosis and hepatocellular carcinoma, and causing other metabolic disorders such as hy-

Corresponding author: Cheol-Young Park <https://orcid.org/0000-0002-9415-9965>
Division of Endocrinology and Metabolism, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 29 Saemunan-ro, Jongno-gu, Seoul 03181, Korea
E-mail: cydoctor@chol.com

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

hypertension and diabetes [5].

The etiologies of fatty liver disease are diverse. Metabolic dysfunction associated fatty liver disease (MAFLD) has been proposed to compensate for the conventional concept of non-alcoholic fatty liver disease (NAFLD), which is an exclusion diagnosis of fatty liver disease derived from alcoholism or hepatitis virus [6]. Unlike NAFLD criteria, the diagnosis of MAFLD emphasizes metabolic derangements in fatty liver disease and distinguishes those with metabolically uncomplicated fatty liver [7]. The presence of obesity or diabetes is the essential diagnostic factor of MAFLD. Although further validation of MAFLD in long-term prognosis is needed, the transition from NAFLD to MAFLD may ensure the identification of metabolically complicated fatty liver and distinguish metabolic features that overwhelm other causes of chronic liver diseases such as viral hepatitis or drinking alcohol.

Of the metabolic components in the MAFLD definition, type 2 diabetes mellitus (T2DM) is one of the main contributors in parallel with obesity. The close association between fatty liver disease and T2DM probably originates from the central role of the liver in glucose and lipid metabolism, independent of other risk factors such as hypertension, dyslipidemia, and chronic systematic inflammation [8]. The co-presence of fatty liver disease and T2DM increases overall and liver-related mortality [9]. Additionally, T2DM is the strongest predictor for hepatic fibrosis in fatty liver disease even in lean patients [10]. In this respect, verifying the current status of fatty liver disease and its association with T2DM has important clinical relevance and public health implications.

Thus, the current study aimed to investigate the prevalence of fatty liver disease in both the general Korean population and individuals with T2DM using data from the Korean National Health Insurance Service (NHIS).

METHODS

Study populations

This nationwide cohort study used data collected from participants in the National Health Insurance database maintained by the Korean NHIS, the single insurer in the Korean public health insurance sector that provides national health examinations for all the Korean population [11]. The NHIS database includes almost the entire Korean population; therefore, it can be used as a population-based, national source to study various diseases [12]. A public health checkup is performed biannually

and contains anthropometric measurements, blood pressure, medical history, lifestyle patterns, and laboratory tests after overnight fasting. Past medical history, alcohol consumption, smoking history, and physical activity patterns are collected by standardized self-reporting questionnaires. Among the individuals of the general health checkup program, NHIS provided a sample research cohort database that includes approximately 2% of the total population, representing the entire population with standardization [13]. We selected participants aged 20 years or older who had undergone a health examination between 2009 and 2017 and fulfilled the fatty liver index (FLI) assessment.

All participants provided written informed consent to participate in the original NHIS. The study was approved by the Institutional Review Board of Soongsil University (SSU-202007-HR-236-01). All study procedures involving human participants were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Assessment of fatty liver disease and definition of T2DM

The hepatic steatosis was assessed by using the FLI, which is well-validated and widely accepted among noninvasive diagnostic modalities [14]. FLI was calculated by the following formula: $(e^{0.953 \times \log(\text{triglycerides}) + 0.139 \times \text{body mass index [BMI]} + 0.718 \times \log(\text{gamma-glutamyl transpeptidase [GGT]} + 0.053 \times \text{waist circumference} - 15.745)}) / (1 + e^{0.953 \times \log(\text{triglycerides}) + 0.139 \times \text{BMI} + 0.718 \times \log(\text{GGT}) + 0.053 \times \text{waist circumference} - 15.745}) \times 100$. We applied two cutoff values, 30 (moderate) and 60 (severe) to investigate the dose-dependent effect of hepatic steatosis [14]. Additionally, other noninvasive and validated markers, including hepatic steatosis index (HSI) and simple NAFLD score are used to assessing fatty liver disease; a HSI > 36 [15] and a simple NAFLD score ≥ 8 [16] were considered of having fatty liver disease. T2DM was defined as at least one service claim with a diagnosis of T2DM, either in outpatient or inpatient care. The diagnosis of T2DM was based on the International Statistical Classification of Disease and Related Health Problems, 10th Revision (ICD-10; codes E11–E14). Additionally, glycemic status was defined by the Korean Diabetes Association guideline [17], which is identical to the American Diabetes Association guideline [18]; (1) T2DM was defined in subjects with at least one service claim for a diagnosis of diabetes, either in outpatient or inpatient care, and at least one prescription of hypoglycemic agents or whose fasting glucose concentration was ≥ 126 mg/dL; (2) impaired fasting glucose (IFG) was defined as fasting

glucose concentration ≥ 100 and < 126 mg/dL and without any service claim or prescription of hypoglycemic medication; and (3) others were identified as normoglycemia.

Statistical analysis

The estimated prevalence of fatty liver disease was presented as a percentage. Subgroup analysis was performed according to sex, age, and glycemic status. We divided the study population according to their ages at the NHIS checkup as 20–39 years (young aged), 40–64 years (middle-aged), and over 65 years (old aged) [19]. Repeated measures of analysis of variance (ANOVA) were used for the evaluation of statistical significance by time period within subgroups. A two-sided *P* value < 0.05 was considered statistically significant. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Increasing prevalence of fatty liver disease in the general population

The prevalence of fatty liver disease has steadily increased from 2009 to 2017 (Fig. 1A) (*P* for trend < 0.001). This trend was observed in both men and women (Fig. 1B and C) (all *P* for trend < 0.001). In 2009, the prevalence of severe fatty liver disease for total, men, and women was 13.3%, 20.5%, and 4.7% respectively. In 2017, the prevalence of severe fatty liver disease was 15.5% overall, 24.2% in men, and 5.8% in women among Korean adults aged over 20 years. During the study period, men had a higher prevalence of both severe and moderate fatty liver disease than women, and there was more increase in fatty liver prevalence in men (*P* for interaction < 0.001). Similar findings were observed when fatty liver disease was defined using HSI and simple NAFLD score (Supplementary Table 1). When applying a moderate cutoff FLI score of 30, the prevalence of overall moderate fatty liver disease and that of men and women increased (*P* for trend < 0.001) while the proportion of individuals with FLI ranges 30 to 60 remained during the study period (*P* for trend = 0.529).

High prevalence of fatty liver disease in young aged population

In age subgroups, the prevalence of fatty liver disease was higher in young and middle age groups in 2017 (16.4% in age 20–39 years and 16.3% in age 40–64 years) than in the older popula-

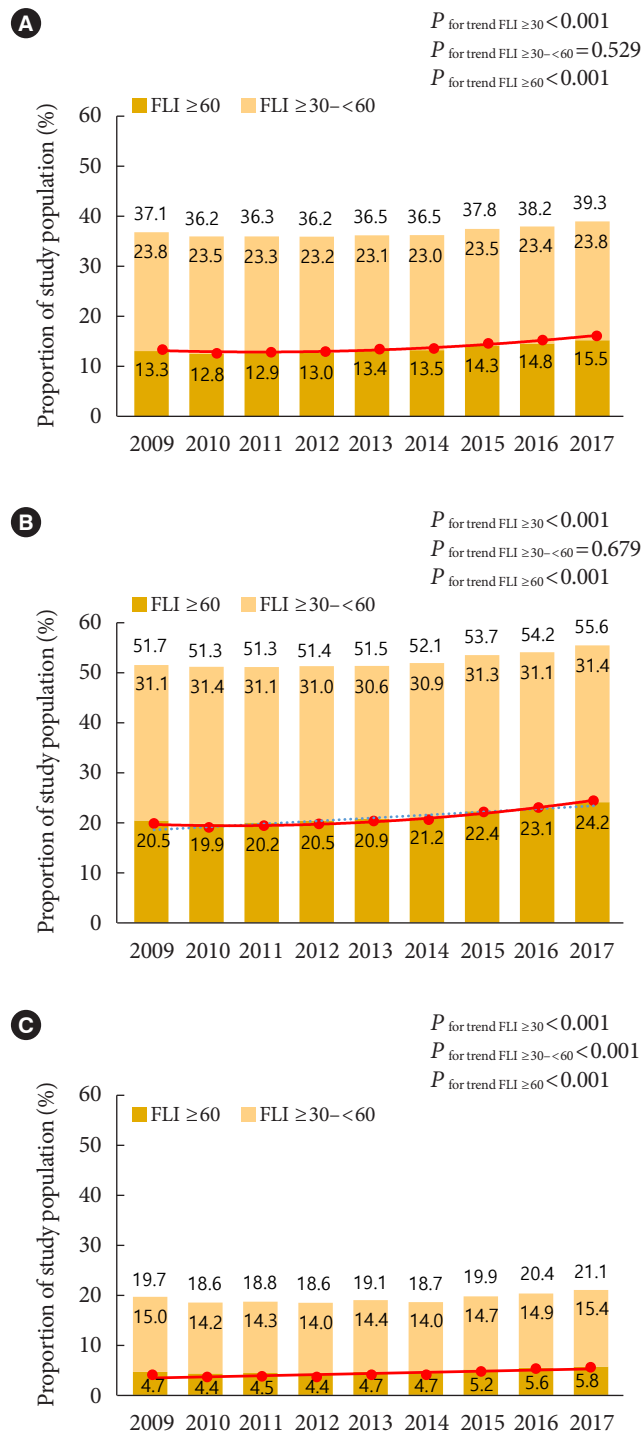


Fig. 1. Proportion of fatty liver disease in the general Korean population. (A) Overall, (B) men, and (C) women. *P* for interaction between sex and fatty liver disease (fatty liver index [FLI] ≥ 30) < 0.001 ; *P* for interaction between sex and fatty liver disease (FLI ≥ 30 to < 60) < 0.001 ; *P* for interaction between sex and fatty liver disease (FLI ≥ 60) < 0.001 .

tion (aged ≥ 65 years, 11.1%) ($P < 0.05$) (Table 1). In 2017, the proportion of individuals with moderate fatty liver disease (FLI ranges ≥ 30 to < 60) was 17.9%, 24.7%, and 29.3% for those aged 20–39, 40–64, and over 65 years, respectively. The prevalence of severe fatty liver disease in all age subgroups had increased during the study period (12.8%–14.2% for age 20–39 years, P for

Table 1. The proportion of fatty liver disease in Korean general population between 2009 and 2017 by age groups

| Year | Age 20–39 years | | | Age 40–64 years | | | Age ≥ 65 years | | | | | |
|--------------------|-----------------|---|--------------------|-----------------|---------|---|---------------------|-----------|--------|---|--------------------|-----------|
| | Number | Proportion of fatty liver disease by FLI, % | | | Number | Proportion of fatty liver disease by FLI, % | | | Number | Proportion of fatty liver disease by FLI, % | | |
| | | ≥ 30 | ≥ 30 – < 60 | ≥ 60 | | ≥ 30 | ≥ 30 – < 60 | ≥ 60 | | ≥ 30 | ≥ 30 – < 60 | ≥ 60 |
| 2009 | 61,925 | 31.1 | 18.3 | 12.8 | 115,515 | 39.5 | 25.3 | 14.2 | 27,366 | 40.6 | 29.6 | 10.9 |
| 2010 | 66,803 | 29.5 | 17.6 | 11.9 | 130,654 | 38.7 | 25.1 | 13.7 | 29,700 | 40.4 | 29.7 | 10.8 |
| 2011 | 66,317 | 30.7 | 18.0 | 12.8 | 136,197 | 38.4 | 24.7 | 13.7 | 30,685 | 38.9 | 29.0 | 9.9 |
| 2012 | 65,405 | 30.3 | 17.3 | 13.0 | 142,791 | 38.4 | 24.7 | 13.7 | 32,939 | 38.4 | 28.4 | 10.0 |
| 2013 | 65,115 | 31.5 | 17.5 | 14.0 | 141,682 | 38.3 | 24.3 | 14.0 | 34,771 | 38.6 | 28.5 | 10.1 |
| 2014 | 68,042 | 31.3 | 17.4 | 13.8 | 153,868 | 38.5 | 24.3 | 14.2 | 37,892 | 38.1 | 28.1 | 10.0 |
| 2015 | 66,767 | 32.3 | 17.6 | 14.7 | 158,253 | 39.8 | 24.7 | 15.1 | 39,583 | 39.0 | 28.5 | 10.5 |
| 2016 | 70,153 | 33.0 | 17.4 | 15.6 | 174,200 | 40.1 | 24.6 | 15.5 | 43,767 | 39.3 | 28.3 | 11.0 |
| 2017 | 69,865 | 34.3 | 17.9 | 16.4 | 177,226 | 41.0 | 24.7 | 16.3 | 45,681 | 40.4 | 29.3 | 11.1 |
| <i>P</i> for trend | | < 0.001 | 0.021 | < 0.001 | | < 0.001 | 0.002 | < 0.001 | | 0.636 | 0.019 | 0.006 |

P for interaction between age and fatty liver disease (FLI ≥ 30) < 0.001 ; *P* for interaction between age and fatty liver disease (FLI ≥ 30 to < 60) = 0.072; *P* for interaction between age and fatty liver disease (FLI ≥ 60) < 0.001 .
FLI, fatty liver index.

Table 2. The changes in proportion of fatty liver disease in Korean general population by glycemic status between 2009 and 2017

| Year | Normoglycemia | | | Impaired fasting glucose | | | Type 2 diabetes mellitus | | | | | |
|--------------------|---------------|---|--------------------|--------------------------|--------|---|--------------------------|-----------|--------|---|--------------------|-----------|
| | Number | Proportion of fatty liver disease by FLI, % | | | Number | Proportion of fatty liver disease by FLI, % | | | Number | Proportion of fatty liver disease by FLI, % | | |
| | | ≥ 30 | ≥ 30 – < 60 | ≥ 60 | | ≥ 30 | ≥ 30 – < 60 | ≥ 60 | | ≥ 30 | ≥ 30 – < 60 | ≥ 60 |
| 2009 | 139,678 | 30.0 | 20.6 | 9.5 | 46,659 | 48.5 | 29.4 | 19.1 | 18,469 | 61.9 | 33.9 | 28.0 |
| 2010 | 155,911 | 29.0 | 20.1 | 8.9 | 50,998 | 48.3 | 29.6 | 18.7 | 20,248 | 61.3 | 34.3 | 27.1 |
| 2011 | 159,144 | 28.9 | 19.8 | 9.0 | 52,512 | 49.0 | 29.9 | 19.1 | 21,543 | 59.9 | 33.4 | 26.4 |
| 2012 | 163,026 | 28.7 | 19.7 | 9.0 | 54,998 | 48.8 | 29.4 | 19.3 | 23,111 | 59.5 | 33.1 | 26.4 |
| 2013 | 160,042 | 28.7 | 19.5 | 9.2 | 57,510 | 48.3 | 28.7 | 19.6 | 24,016 | 60.0 | 33.2 | 26.7 |
| 2014 | 168,596 | 28.3 | 19.3 | 9.0 | 64,618 | 48.6 | 28.9 | 19.7 | 26,588 | 59.4 | 32.5 | 26.9 |
| 2015 | 168,307 | 28.9 | 19.5 | 9.4 | 68,282 | 50.1 | 29.4 | 20.7 | 28,014 | 61.0 | 33.0 | 28.0 |
| 2016 | 179,857 | 29.2 | 19.4 | 9.7 | 76,276 | 50.1 | 29.0 | 21.1 | 31,987 | 61.1 | 32.6 | 28.4 |
| 2017 | 179,009 | 29.7 | 19.7 | 10.0 | 79,829 | 51.2 | 29.4 | 21.8 | 33,934 | 61.7 | 32.2 | 29.6 |
| <i>P</i> for trend | | 0.867 | < 0.001 | < 0.001 | | < 0.001 | 0.054 | < 0.001 | | 0.218 | < 0.001 | < 0.001 |

(1) Type 2 diabetes mellitus was defined as at least one service claim with a diagnosis of diabetes, either in outpatient or inpatient care and at least one prescription of hypoglycemic agents or whose fasting glucose concentration was ≥ 126 mg/dL; (2) Impaired fasting glucose was defined as fasting glucose concentration ≥ 100 and < 126 mg/dL and without any service claim or prescription of hypoglycemic medication; and (3) others were identified as normoglycemia.

P for interaction between glycemic status and fatty liver disease (FLI ≥ 30) < 0.001 ; *P* for interaction between glycemic status and fatty liver disease (FLI ≥ 30 to < 60) = 0.259; *P* for interaction between glycemic status and fatty liver disease (FLI ≥ 60) = 0.758.
FLI, fatty liver index.

trend <0.001; 14.2%–16.3% for age 40–64 years, *P* for trend <0.001; 10.9%–11.1% for age over 65, *P* for trend=0.006). The results of moderate fatty liver disease prevalence change were similar (*P* for trend <0.001). The increase in severe fatty liver disease prevalence in the young age group (20 to 39 years) was steeper than that of other groups (*P* for interaction <0.001). When applying a lower FLI cutoff, similar results were found. The proportion of individuals with FLI 30 to 60 decreased during the study period though all age groups (all *P* for trend <0.05) and there was no statistical significance between age and moderate fatty liver disease prevalence (*P*=0.072).

High prevalence of severe fatty liver disease in individuals with T2DM

When dividing individuals by glycemic status, the prevalence of severe fatty liver disease was the highest in the T2DM group, followed by the IFG group (*P*<0.001). The prevalence of severe fatty liver disease though all glycemic groups had increased with statistical significance (*P* for trend <0.001). In 2009, the prevalence of severe fatty liver disease was 28.0%, 19.1%, and 9.5%, which was 29.6%, 21.8%, and 10.0% in 2017 for T2DM, IFG, and normoglycemia, respectively (Table 2). The test for interaction between glycemic status and severe fatty liver disease was not significant (*P* for interaction=0.758). When applied moderate FLI cutoff, the prevalence of moderate fatty liver disease was remained in individuals with normoglycemia

and T2DM, whereas increase of moderate fatty liver disease was observed in IFG group (*P* for trend=0.867, <0.001, and =0.218 for normoglycemia, IFG, and T2DM, respectively).

Increasing prevalence of severe fatty liver disease in young T2DM population

As fatty liver disease was prevalent in T2DM population, we further analyzed in individuals with T2DM. Among individuals with T2DM, the prevalence of severe fatty liver disease was 36.6% for men and 18.0% for women in 2017, which was 35.0% and 16.6% in 2009 (Table 3). The prevalence of severe fatty liver disease in both men and women with T2DM had increased with statistical significance (both *P* for trend <0.001). Men with T2DM tended to have fatty liver disease than women with T2DM during the study period (*P*<0.05). The test for interaction between sex and severe fatty liver disease was not significant (*P* for interaction=0.383). When applied moderate severe fatty liver disease cutoff, there was only increase in prevalence of moderate fatty liver disease in men (*P* for trend=0.036, *P* for interaction=0.046).

Subgroup analysis according to age in T2DM, the prevalence of severe fatty liver disease was the highest in young aged T2DM compared to middle or old aged T2DM groups (60.1% vs. 33.6% vs. 17.8%, *P*<0.05). There was an increase in severe fatty liver prevalence in young and middle age groups (42.2%–60.1% for those aged 20–39 years, *P* for trend <0.001; 30.7%–

Table 3. The changes in proportion of fatty liver disease in population with type 2 diabetes mellitus by sex

| Year | Men with T2DM | | | | Women with T2DM | | | |
|--------------------|---------------|---|---------|--------|-----------------|---|---------|-------|
| | Number | Proportion of fatty liver disease by FLI, % | | | Number | Proportion of fatty liver disease by FLI, % | | |
| | | ≥30 | ≥30–<60 | ≥60 | | ≥30 | ≥30–<60 | ≥60 |
| 2009 | 11,399 | 69.7 | 34.7 | 35.0 | 7,070 | 49.3 | 32.8 | 16.6 |
| 2010 | 12,542 | 69.0 | 35.7 | 33.3 | 7,706 | 48.9 | 32.0 | 17.0 |
| 2011 | 13,130 | 68.5 | 34.9 | 33.6 | 8,413 | 46.4 | 31.0 | 15.4 |
| 2012 | 14,240 | 67.7 | 34.2 | 33.6 | 8,871 | 46.4 | 31.5 | 14.9 |
| 2013 | 14,707 | 68.1 | 34.6 | 33.5 | 9,309 | 47.1 | 31.0 | 16.1 |
| 2014 | 16,301 | 68.0 | 34.2 | 33.8 | 10,287 | 45.7 | 29.8 | 15.8 |
| 2015 | 17,376 | 68.8 | 33.9 | 34.9 | 10,638 | 48.1 | 31.4 | 16.7 |
| 2016 | 19,677 | 69.7 | 34.2 | 35.5 | 12,310 | 47.2 | 30.1 | 17.1 |
| 2017 | 21,144 | 70.0 | 33.4 | 36.6 | 12,790 | 48.0 | 30.1 | 18.0 |
| <i>P</i> for trend | | 0.036 | 0.001 | <0.001 | | 0.478 | 0.002 | 0.001 |

P for interaction between sex and fatty liver disease (FLI ≥30)=0.046; *P* for interaction between sex and fatty liver disease (FLI ≥30 to <60)=0.298; *P* for interaction between sex and fatty liver disease (FLI ≥60)=0.383.

T2DM, type 2 diabetes mellitus; FLI, fatty liver index.

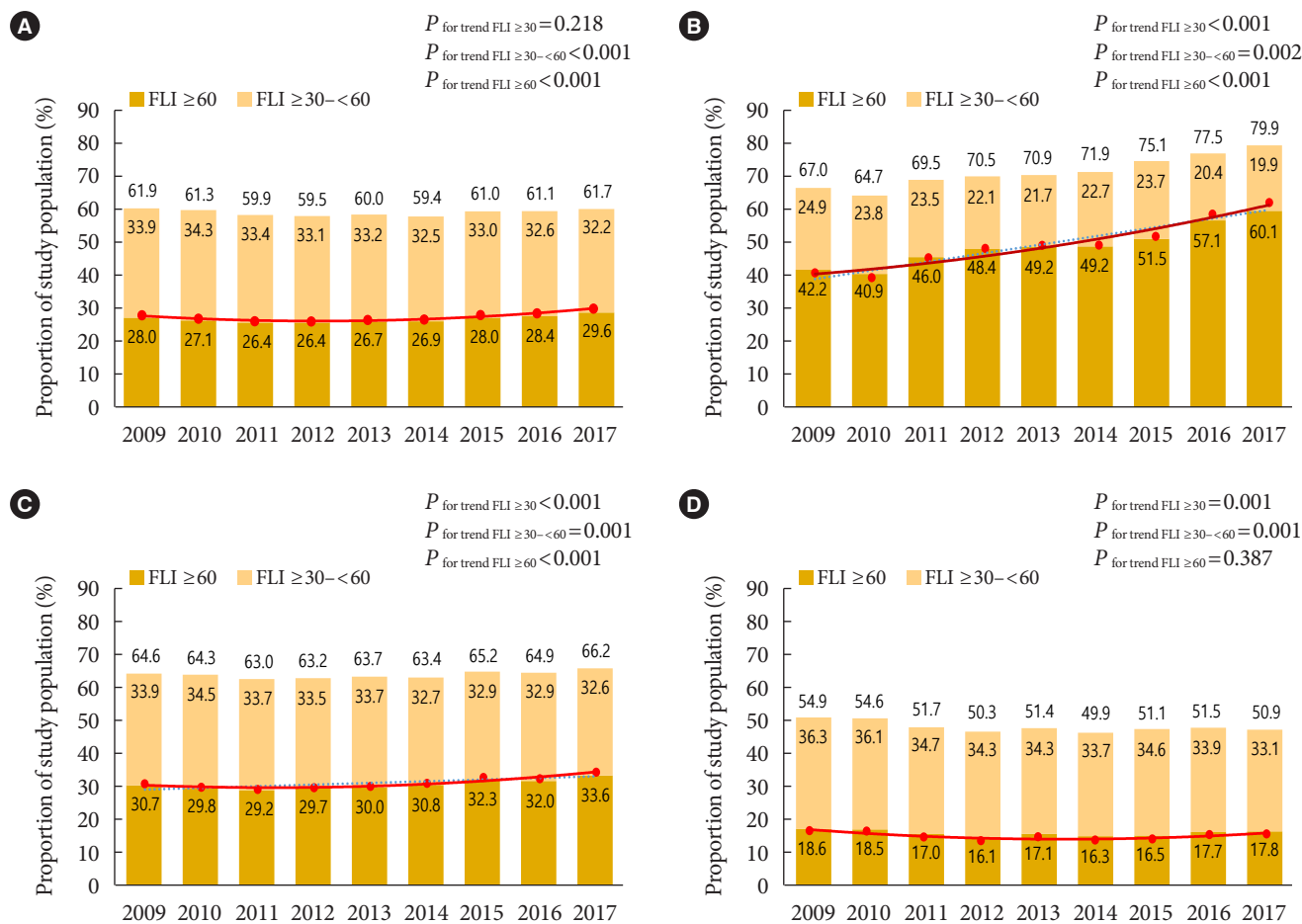


Fig. 2. The changes in the proportion of fatty liver disease in a population with type 2 diabetes mellitus. (A) Overall, (B) age 20 to 39, (C) age 40 to 64, and (D) age ≥ 65 years. P for interaction between age and fatty liver disease (fatty liver index [FLI] ≥ 30) < 0.001 ; P for interaction between age and fatty liver disease (FLI ≥ 30 to < 60) = 0.321; P for interaction between age and fatty liver disease (FLI ≥ 60) < 0.001 .

33.6% in those aged 40–64 years, P for trend < 0.001) while the prevalence of fatty liver disease in old-age population was maintained (18.6% to 17.8%, P for trend = 0.387) (Fig. 2). There was more steep increase in severe fatty liver disease in young aged group; the test for interaction between age and severe fatty liver disease was significant (P for interaction < 0.001). After applied moderate fatty liver disease cutoff, similar results were observed.

DISCUSSION

The prevalence of both moderate and severe fatty liver disease steadily increased from 2009 to 2017. The estimated prevalence of Korean adults aged 20 years or older with severe fatty liver disease (by FLI ≥ 60) had increased from 12.8% in 2009 to

16.4% in 2017. The increase in fatty liver disease prevalence was prominent in men and the young-aged population (age 20 to 39 years). The prevalence of severe fatty liver disease was higher in individuals with T2DM, accounting for 29.6% in 2017. In the young-aged population with T2DM, we noted that more than half (60.1%) had severe fatty liver disease. Additionally, the prevalence of severe fatty liver disease in the young-aged population with T2DM has increased sharply compared with the other age groups with T2DM.

This study has several clinical implications. First, our research demonstrates the current status and recent trends in the prevalence of fatty liver disease in the Korean general population using a nationwide cohort database. With epidemics of obesity [2] and diabetes [20], an expansion of fatty liver disease in the Korean population is expected. In 2017, the prevalence

of severe fatty liver disease was 15.5% (FLI ≥ 60), and 23.8% of the total population remained at risk of fatty liver disease (FLI ≥ 30 to < 60). The prevalence of fatty liver disease was higher in men than in women (24.2% vs. 5.8%). This is similar to the global prevalence of fatty liver disease, particularly among Asians [21,22]. Like obesity prevalence in Korea [2], the prevalence of moderate fatty liver disease (FLI ≥ 30 to < 60) in overall and men is seemed to reach a plateau in the current study. These results showed the increases of fatty liver disease (FLI ≥ 30) were mostly contributed to increase in severe fatty liver disease (FLI ≥ 60) in those populations.

There was significant increase of severe fatty liver disease all age groups. However, the most notable change was more increase in the prevalence of severe fatty liver disease among adults aged 20 to 39 years (P for interaction < 0.001). Although Korea remains an intermediate endemic area for hepatitis B infection, the prevalence of hepatitis B infection in the young population has decreased [23]. Meanwhile, the prevalence of NAFLD in young men has consistently increased over recent decades with an increase in hypertension, dyslipidemia, and hyperglycemia [24]. In a United States study analyzing the National Health and Nutrition Examination Survey (NHANES) conducted in 2011 to 2018, the increase in MAFLD prevalence with statistical significance was only observed in the young-aged population (age 19 to 39) while other age groups showed an increase without statistical significance [22]. Additionally, nonalcoholic steatohepatitis (NASH) has increased as an indication for liver transplantation in those below the age of 40 in the United States [25]. An alarming finding from this study was that 30% of individuals died and 11.5% of patients underwent re-transplantation mostly due to NASH recurrence within 45.8 months from the first transplantation [25].

Second, regarding the association between fatty liver disease and glycemic status, our reports demonstrate a high prevalence of fatty liver disease in the T2DM population than in individuals with normoglycemia or IFG. In 2017, less than one-third of T2DM individuals (29.6%) had severe fatty liver disease, and less than another one-third of T2DM patients (32.2%, FLI ≥ 30 to < 60) were at risk of fatty liver disease. Although the prevalence of fatty liver disease in the T2DM population varies according to the diagnosis modalities (e.g., ultrasound, magnetic resonance spectroscopy, and other fatty liver scores), this prevalence rate determined by gamma-glutamyl transpeptidase is similar to those previously reported [26,27]. From 2009 to 2017, the prevalence of fatty liver disease in

T2DM had increased (28.0% to 29.6%) in both men and women; likely, the prevalence of fatty liver disease in people with IFG also increased. We also noticed a steep increase of severe fatty liver disease in T2DM individuals aged 20 to 39 years, and the estimated prevalence in this population reached 60.1% in 2017. The estimated prevalence in the young T2DM population was double and triple that of the middle-aged (40 to 64 years), and older population (over 65 years). Considering the growing burden of fatty liver disease in the young age population as aforementioned, particularly people with T2DM, an early screening strategy should be considered in these populations.

Third, considering the close association between NAFLD and T2DM, identification of NAFLD in established T2DM patients is important to determine individuals at a high risk of T2DM complications. Accumulated evidence strongly indicates that NAFLD is linked with cardiovascular disease [8,28]. Similarly, it has been known that individuals with both NAFLD and T2DM showed a significantly higher prevalence of chronic vascular complications of T2DM including coronary, cerebral, and peripheral vascular disease [27,29]. In this respect, high risk patient identification, and early intervention are important to decrease future disease burden. The current study results showed the characteristics of high risk individuals with T2DM in Korea; high prevalence of fatty liver disease in men and young-age population. Moreover, the prevalence of moderate and severe fatty liver disease had increased, while the proportion of individuals with FLI 30 to 60 remained, suggesting more increase in severity of fatty liver disease in Korea. These findings imply a more active and systematic evaluation for fatty liver disease-related comorbidities in those population and a view to implementing an earlier and more aggressive treatment whenever indicated.

Despite the clinical implications of our study, there were several limitations. First, although a well-validated fatty liver disease prediction model was applied, liver imaging and histological information were not available. Second, we could not assess the influences of T2DM management modalities in fatty liver disease. Third, due to the lack of information, we could not consider the family history or dietary habits of each individual, which can affect T2DM or fatty liver disease development. Lastly, as we did not established the exclusion criteria, the etiologies of fatty liver disease in the current study is diverse.

In conclusion, the prevalence of fatty liver disease in Korea has increased, especially severe fatty liver disease. The increase

in fatty liver disease prevalence was prominent in men and young adults. One-third of T2DM adults had fatty liver disease and two-thirds of young adults with T2DM had fatty liver disease. These findings call for greater awareness of fatty liver disease in Korean adults, particularly in the young population. A systematic search for fatty liver disease development in adult patients with T2DM needs to be established, in addition to a disease risk strategy for fatty liver disease in populations with T2DM.

SUPPLEMENTARY MATERIALS

Supplementary materials related to this article can be found online at <https://doi.org/10.4093/dmj.2022.0444>.

CONFLICTS OF INTEREST

Yong-ho Lee has been associate editor of the *Diabetes & Metabolism Journal* since 2022. He was not involved in the review process of this article. Otherwise, there was no conflict of interest.

AUTHOR CONTRIBUTIONS

Conception or design: E.H., K.D.H., Y.L., K.S.K., S.H., J.H.P., C.Y.P.

Acquisition, analysis, or interpretation of data: E.H., K.D.H., Y.L., K.S.K., S.H., J.H.P., C.Y.P.

Drafting the work or revising: E.H., K.D.H., C.Y.P.

Final approval of the manuscript: C.Y.P.

ORCID

Eugene Han <https://orcid.org/0000-0002-3237-3317>

Cheol-Young Park <https://orcid.org/0000-0002-9415-9965>

FUNDING

None

ACKNOWLEDGMENTS

None

REFERENCES

1. Huh Y, Cho YJ, Nam GE. Recent epidemiology and risk factors of nonalcoholic fatty liver disease. *J Obes Metab Syndr* 2022;31:17-27.
2. Korean Society for the Study of Obesity. Obesity fact sheet 2021. Seoul: Korean Society for the Study of Obesity; 2021.
3. Fan JG, Kim SU, Wong VW. New trends on obesity and NAFLD in Asia. *J Hepatol* 2017;67:862-73.
4. Wong VW, Chan WK, Chitturi S, Chawla Y, Dan YY, Duseja A, et al. Asia-Pacific Working Party on non-alcoholic fatty liver disease guidelines 2017. Part 1: definition, risk factors and assessment. *J Gastroenterol Hepatol* 2018;33:70-85.
5. Ampuero J, Aller R, Gallego-Duran R, Crespo J, Calleja JL, Garcia-Monzon C, et al. Significant fibrosis predicts new-onset diabetes mellitus and arterial hypertension in patients with NASH. *J Hepatol* 2020;73:17-25.
6. Eslam M, Sanyal AJ, George J; International Consensus Panel. MAFLD: a consensus-driven proposed nomenclature for metabolic associated fatty liver disease. *Gastroenterology* 2020;158:1999-2014.
7. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. *J Hepatol* 2020;73:202-9.
8. Han E, Lee YH, Kim YD, Kim BK, Park JY, Kim DY, et al. Non-alcoholic fatty liver disease and sarcopenia are independently associated with cardiovascular risk. *Am J Gastroenterol* 2020;115:584-95.
9. Stepanova M, Rafiq N, Makhlof H, Agrawal R, Kaur I, Younoszai Z, et al. Predictors of all-cause mortality and liver-related mortality in patients with non-alcoholic fatty liver disease (NAFLD). *Dig Dis Sci* 2013;58:3017-23.
10. Park H, Yoon EL, Cho S, Jun DW, Nah EH. Diabetes is the strongest risk factor of hepatic fibrosis in lean patients with non-alcoholic fatty liver disease. *Gut* 2022;71:1035-6.
11. Han E, Han KD, Lee BW, Kang ES, Cha BS, Ko SH, et al. Severe hypoglycemia increases dementia risk and related mortality: a nationwide, population-based cohort study. *J Clin Endocrinol Metab* 2022;107:e1976-86.
12. Han E, Lee JY, Han KD, Cho H, Kim KJ, Lee BW, et al. Gamma glutamyltransferase and risk of dementia in prediabetes and diabetes. *Sci Rep* 2020;10:6800.
13. Kim MK, Han K, Lee SH. Current trends of big data research using the Korean National Health Information Database. *Diabetes Metab J* 2023;47:347-355 <https://e-dmj.org>

- betes *Metab J* 2022;46:552-63.
14. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, et al. The fatty liver index: a simple and accurate predictor of hepatic steatosis in the general population. *BMC Gastroenterol* 2006;6:33.
 15. Lee JH, Kim D, Kim HJ, Lee CH, Yang JI, Kim W, et al. Hepatic steatosis index: a simple screening tool reflecting nonalcoholic fatty liver disease. *Dig Liver Dis* 2010;42:503-8.
 16. Lee YH, Bang H, Park YM, Bae JC, Lee BW, Kang ES, et al. Non-laboratory-based self-assessment screening score for non-alcoholic fatty liver disease: development, validation and comparison with other scores. *PLoS One* 2014;9:e107584.
 17. Hur KY, Moon MK, Park JS, Kim SK, Lee SH, Yun JS, et al. 2021 Clinical practice guidelines for diabetes mellitus of the Korean Diabetes Association. *Diabetes Metab J* 2021;45:461-81.
 18. American Diabetes Association Professional Practice Committee. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2022. *Diabetes Care* 2022;45(Suppl 1):S17-38.
 19. Lee HJ, Kim HK, Han KD, Lee KN, Park JB, Lee H, et al. Age-dependent associations of body mass index with myocardial infarction, heart failure, and mortality in over 9 million Koreans. *Eur J Prev Cardiol* 2022;29:1479-88.
 20. Bae JH, Han KD, Ko SH, Yang YS, Choi JH, Choi KM, et al. Diabetes fact sheet in Korea 2021. *Diabetes Metab J* 2022;46:417-26.
 21. Ye Q, Zou B, Yeo YH, Li J, Huang DQ, Wu Y, et al. Global prevalence, incidence, and outcomes of non-obese or lean non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2020;5:739-52.
 22. Wong RJ, Cheung R. Trends in the prevalence of metabolic dysfunction-associated fatty liver disease in the United States, 2011-2018. *Clin Gastroenterol Hepatol* 2022;20:e610-3.
 23. Yim SY, Kim JH. The epidemiology of hepatitis B virus infection in Korea. *Korean J Intern Med* 2019;34:945-53.
 24. Lee J, Kim T, Yang H, Bae SH. Prevalence trends of non-alcoholic fatty liver disease among young men in Korea: a Korean military population-based cross-sectional study. *Clin Mol Hepatol* 2022;28:196-206.
 25. Alkhouri N, Hanouneh IA, Zein NN, Lopez R, Kelly D, Eghtesad B, et al. Liver transplantation for nonalcoholic steatohepatitis in young patients. *Transpl Int* 2016;29:418-24.
 26. Williamson RM, Price JF, Glancy S, Perry E, Nee LD, Hayes PC, et al. Prevalence of and risk factors for hepatic steatosis and nonalcoholic fatty liver disease in people with type 2 diabetes: the Edinburgh Type 2 Diabetes Study. *Diabetes Care* 2011;34:1139-44.
 27. Lee YH, Cho Y, Lee BW, Park CY, Lee DH, Cha BS, et al. Non-alcoholic fatty liver disease in diabetes. Part I: epidemiology and diagnosis. *Diabetes Metab J* 2019;43:31-45.
 28. Kim Y, Han E, Lee JS, Lee HW, Kim BK, Kim MK, et al. Cardiovascular risk is elevated in lean subjects with nonalcoholic fatty liver disease. *Gut Liver* 2022;16:290-9.
 29. Targher G, Lonardo A, Byrne CD. Nonalcoholic fatty liver disease and chronic vascular complications of diabetes mellitus. *Nat Rev Endocrinol* 2018;14:99-114.