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ORIGINAL ARTICLE

Observational Study

Correlation between non-alcoholic fatty liver disease and metabolic parameters in persons with newly diagnosed type 2 diabetes mellitus

Supriyo Mukherjee, Sushmita Mukherjee, Chun Shing Kwok, Anne Phillips

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Abstract

BACKGROUND

There are limited studies investigating the association between type 2 diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD) in the region of Bihar, India.

AIM

To estimate the prevalence of NAFLD in persons with newly diagnosed T2DM in the population of North Bihar, India.

METHODS

This single centre cross-sectional study was undertaken in the Research Centre for Diabetes Hypertension and Obesity, Samastipur, Bihar, India. Data were collected from persons newly diagnosed with T2DM or those diagnosed within 6 months of when the study was conducted between December 2022 to May 2023.

RESULTS

A total of 148 people with newly diagnosed T2DM were included (median age 47 years, 46.6% female) and 109 patients with liver disease on ultrasound evaluation. The persons with liver disease consumed more fats and oils (88.1% *vs* 74.4%, *P* =

0.042) and they had significantly greater body mass index (27.4 *vs* 23.0, $P < 0.001$), waist circumference (37 *vs* 33, $P < 0.001$), and waist-to-hip ratio (1.00 *vs* 0.70, $P = 0.025$). Females were associated with greater liver disease [odds ratio (OR): 3.09, 95% confidence interval (CI): 1.09-8.80, $P = 0.32$]. Waist circumference (OR: 1.42, 95%CI: 1.22-1.66, $P < 0.001$) and low-density lipoprotein cholesterol (OR: 1.01, 95%CI: 1.01-1.02, $P = 0.048$) were associated with any liver disease. The factors most associated with grade 2/3 liver disease was right upper quadrant pain or heaviness (OR: 5.22, 95%CI: 1.40-19.41, $P = 0.14$), greater income (OR: 3.58, 95%CI: 1.28-10.04, $P = 0.015$) and waist circumference (OR: 1.31, 95%CI: 1.02-1.69, $P = 0.036$).

CONCLUSION

NAFLD is common in new/recently diagnosed T2DM and disease burden is high and common among patients who are either high consumers of fats and oils or have obesity-associated markers.

Key Words: Type 2 diabetes mellitus; Non-alcoholic fatty liver disease; Prevalence; Waist circumference; Obesity

Core Tip: This study evaluated the association between type 2 diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD). Nearly 3 of 4 patients with T2DM had evidence of NAFLD. This study also concluded that NAFLD is common in patients who consume high amounts of fats and oils. A higher percentage of females were diagnosed with NAFLD and exhibited higher body mass index, waist circumference and lipid levels. Serum alanine aminotransferase levels have potential as a screening tool, aligning with recommendations for universal screening in T2DM populations. Early identification of NAFLD in T2DM patients may enable interventions to mitigate disease progression.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a common, chronic, progressive, and heterogenous disorder characterized by insulin resistance and beta cell dysfunction resulting in failure to regulate elevated blood sugar levels. In 2021, the International Diabetes Foundation estimated that there are 537 million adults worldwide living with diabetes, and around 240 million people that are undiagnosed[1]. In India, the burden of diabetes is significant as the Indian Council of Medical Research-India Diabetes study estimates that there are 101 million people with diabetes and 136 million people with prediabetes [2]. The increasing prevalence of diabetes poses a significant burden on health services on top of the existing challenges such as malnutrition, poverty, and socioeconomic problems in India[3]. It has been suggested that there is an association between T2DM and non-alcoholic fatty liver disease (NAFLD)[4]. It is believed that lipid accumulation in the liver can cause T2DM[5]. Both conditions also share risk factors such as genetic predisposition, diet rich in fat, sedentary lifestyle, metabolic syndrome, and obesity[6]. When NAFLD manifests in T2DM patients, the spectrum of disease is broad, from simple steatosis to non-alcoholic steatohepatitis (NASH) cirrhosis and hepatocellular carcinoma. The identification of NAFLD in T2DM patients is important, as patients with both conditions are at risk of developing cirrhosis, cardiovascular disease, chronic kidney disease, and death[7]. Therefore, early detection of NAFLD and its management may be important in preventing the progression to liver fibrosis, cirrhosis, and hepatocellular carcinoma[4].

There are limited studies that have been undertaken in India to evaluate NAFLD prevalence among newly diagnosed T2DM patients and its correlation with body mass index (BMI), haemoglobin A1c (HbA1c) and standard lipid profile. A recent retrospective trial in India found that 44.48% of the population living with diabetes (newly/recently detected) have NAFLD, and that among those diagnosed a large proportion were male (58.6%)[8]. However, there is not much data in the literature from the state of Bihar. The main objective of this study was to estimate the prevalence of NAFLD in newly diagnosed T2DM patients in North Bihar to provide insight into the extent of NAFLD among the region's T2DM patients.

MATERIALS AND METHODS

Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki and Indian Council of Medical Research. Ethical approval was obtained from Gurushree Hi-Tech Multi Specialty Hospital Ethics Committee (8/22/004IEC) and the Faculty Academic Ethics Committee in the Health, Education and Life Sciences at Birmingham City University (Mukherjee/#10953/sub2/R(C)/2022/Nov/HELS FAEC). The study was prospectively registered on Clinical Trial

Registry-India (CTRI/2022/09/045835) on 23rd September 2022. Informed consent was taken from all included patients.

Study design and setting

This study is a single centre cross-sectional study undertaken in the outpatient department at Research Centre for Diabetes Hypertension and Obesity (RCDHO), Samastipur, Bihar, India. The RCDHO is a private welfare clinic which caters to 20000 resource constrained people[9].

Study population

The study inclusion criteria were male or female patients who were aged 18 years or older, who had a new T2DM diagnosis or were recently diagnosed within 6 months, and who consented to take part in the study (Figure 1). Patients were excluded from the study if they had a diagnosis of type 1 diabetes mellitus, consumed alcohol regularly, were pregnant or breastfeeding, had a history of traditional medicine use, or had a history of acute hepatitis, chronic liver disease, or malignancy that might involve the liver.

Data collection

A case report form which contained sections with data for demographic information, comorbidities, risk factors anthropometric measurements (height, weight, waist circumference, hip circumference, waist-to-hip ratio, pulse, and blood pressure), BMI (overweight was defined as BMI between 23-25 kg/m^2 and obese was defined as BMI ≥ 25) according to World Health Organization (WHO) guidelines for the Asian population (based on the WHO Asia Pacific Guidelines, 2000)[10]. Central obesity was considered in males with a waist circumference > 90 cm and females with a waist circumference > 80 cm, and metabolic syndrome was assessed based on the criteria of the National Cholesterol Education Program Adult Treatment Panel III[11]. T2DM was defined based on WHO criteria [fasting plasma glucose values of ≥ 7.0 mmol/L (126 mg/dL), 2-hour post-load plasma glucose ≥ 11.1 mmol/L (200 mg/dL)[12], HbA1c ≥ 6.5% (48 mmol/mol); or a random blood glucose ≥ 11.1 mmol/L (200 mg/dL)] in the presence of signs and symptoms considered related to diabetes[13].

Indian Guideline on Hypertension-IV (2019) criteria were used to define hypertension[14]. Blood tests included fasting blood glucose, HbA1c, alanine aminotransferase (ALT), and fasting lipid profile. To assess the presence and severity of fatty liver disease, an ultrasound examination of the abdomen was performed by a single experienced sonographer who was blinded regarding all details of study participants. A 24-hour dietary recall-based approach by a trained dietitian was used to estimate dietary intake of individuals in this study.

Study outcomes

The primary outcome of the study was the prevalence of NAFLD by ultrasound scan according to presence of bright liver, increased hepatic echotexture over that of renal echotexture, presence of vascular blurring, and narrowing of hepatic veins[15,16]. Grade I (mild steatosis) was defined as presence of fine diffuse hyper-echogenicity of liver. Grade II (moderate steatosis) was defined as moderate but diffuse hepatic hyper-echogenicity and impaired visualization of intrahepatic vessels and diaphragm. Grade III (severe steatosis) was diagnosed if there was marked hepatic hyper-echogenicity, borders of intrahepatic vessels, and impaired visualization of diaphragm and posterior portion of right lobe of liver[15]. The secondary objective was to determine if there was any association between NAFLD and BMI, HbA1c and measures in the standard lipid profile.

Statistical analysis

Data from case report forms were inputted into Microsoft Excel, and statistical analysis was undertaken by Stata (version 13.0; College Station, TX, United States) and SSPS 28 (IBM Corp., Armonk, NY, United States). Descriptive statistics were presented for the collected variables for the overall cohort and stratified according to the presence or absence of NAFLD. For continuous variables that were normally distributed, the mean and standard deviations were reported. For those that were not normally distributed, the median and interquartile range were reported. For categorical variables, the number of patients and the percentages were reported. To test for statistical differences in characteristics between the group with NAFLD and the group without NAFLD, the *t*-test (for normally distributed continuous data), median test (in Stata for data that was not normally distributed and continuous data), and χ^2 test were used (for categorical variables). Stepwise multiple logistic regressions were used to identify independent factors associated with any liver disease and grade 2/3 liver disease with a cutoff of < 0.20 for candidate variables in the final model. For statistical significance, a P value of < 0.05 was considered statistically significant at the 95% confidence interval (CI) for all analyses.

RESULTS

A total of 179 people with newly diagnosed T2DM were screened, out of which 148 persons were found eligible (Figure 1). The patient characteristics are shown in Table 1.

Dietary intake and liver disease

The proportion of patients with liver disease (n = 109) was significantly greater in patients who consumed more fats and oils (88.1% *vs* 74.4%, P = 0.042) but there was no difference in dietary consumption of protein, vegetables, and fruits (P = 0.27), carbohydrates (P = 0.78), dairy and cheese (P = 0.77), and dietary sweets and confectionaries (P = 0.63). In terms of

Table 1 Patient demographics, lifestyle, and comorbidities according to liver disease on ultrasound

Variable	Total (*n* = 148)	No liver disease (*n* = 39)	Liver disease (*n* = 109)	*P* value[1]
Age in year	47 (40-55)	49 (40-61)	47 (40-54)	1
Female	69 (46.6)	11 (28.2)	58 (53.2)	0.007
Social class				0.36
Manual	21 (14.2)	3 (7.7)	18 (16.5)	
Non-skilled	65 (43.9)	16 (41.0)	49 (45.0)	
Semiskilled	11 (7.4)	5 (12.8)	6 (5.5)	
Skilled manual	9 (6.1)	4 (10.3)	5 (4.6)	
Skilled non-manual	6 (4.1)	2 (5.1)	4 (3.7)	
Professional	36 (24.3)	9 (23.1)	27 (24.8)	
Income class				0.3
Poor	6 (4.1)	1 (2.6)	5 (4.6)	
Lower middle	46 (31.1)	17 (43.6)	29 (26.6)	
Middle	83 (56.1)	19 (48.7)	64 (58.7)	
Upper middle	10 (6.8)	1 (2.6)	9 (8.3)	
Upper	3 (2.0)	1 (2.6)	2 (1.8)	
Willingness to pay, yes	148 (100)	39 (100)	109 (100)	-
Education				0.79
Primary school	87 (58.8)	25 (64.1)	62 (56.9)	
Secondary school	21 (14.2)	5 (12.8)	16 (14.7)	
Undergraduate	34 (23.0)	7 (18.0)	27 (24.8)	
Postgraduate	6 (4.1)	2 (5.1)	4 (3.7)	
Sleep in hour				0.96
7	7 (4.7)	2 (5.1)	5 (4.6)	
8	120 (81.1)	31 (79.5)	89 (81.7)	
9	15 (13.8)	6 (15.4)	15 (13.8)	
Dietary fats and oils				0.042
Normal	23 (15.5)	10 (25.6)	13 (11.9)	
High	125 (84.5)	29 (74.4)	96 (88.1)	
Dietary protein				-
Normal	148 (100)	39 (100)	109 (100)	
Dietary vegetables and fruits				0.27
Normal	76 (51.4)	23 (59.0)	53 (48.6)	
High	72 (48.7)	16 (41.0)	56 (51.4)	
Dietary carbohydrates				0.78
Normal	3 (2.0)	1 (2.6)	2 (1.8)	
High	145 (98.0)	38 (97.4)	107 (98.2)	
Dietary dairy and cheese				0.77
Normal	28 (18.9)	8 (20.5)	20 (18.4)	
High	120 (81.1)	31 (79.5)	89 (81.7)	
Dietary sweets and confectionaries				0.63
Normal	54 (36.5)	13 (33.3)	41 (37.6)	

High	94 (63.5)	26 (66.7)	68 (62.4)	
Hypertension	24 (16.2)	8 (20.5)	16 (14.7)	0.4
Hypercholesterolaemia	2 (1.4)	1 (2.6)	1 (0.9)	0.45
Previous myocardial infarction	2 (1.4)	1 (2.6)	1 (0.9)	0.45
Previous stroke	1 (0.7)	1 (2.6)	0 (0)	0.093
Polycystic ovarian syndrome	0 (0)	0 (0)	0 (0)	-
Obstructive sleep apnoea	13 (8.8)	4 (10.3)	9 (8.3)	0.71
Vitamin D deficiency	3 (2.0)	0 (0)	3 (2.8)	0.3
Hypothyroidism	4 (2.7)	0 (0)	4 (3.7)	0.23
Family history of type 2 diabetes	58 (39.2)	17 (43.6)	41 (37.6)	0.51
Family history of liver disease	0 (0)	0 (0)	0 (0)	-

[1]χ^2 test.
Data are median (interquartile range) or *n* (%).

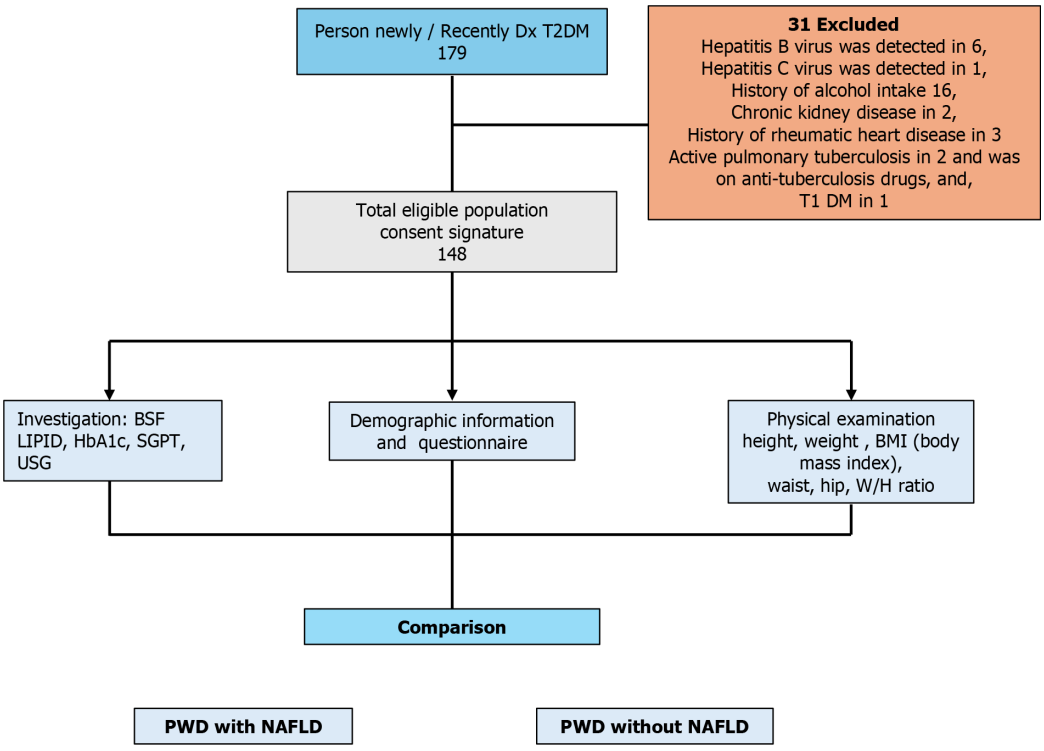

Figure 1 Flow diagram of patient inclusion. T2DM: Type 2 diabetes mellitus; NAFLD: Non-alcoholic fatty liver disease; HbA1c: Haemoglobin A1c; BSF: Blood sugar fasting; SGPT: Serum glutamate pyruvate transaminase; USG: Ultrasonography; PWD: Persons with diabetes.

comorbid illness, there was no difference between the groups with/without liver disease. The graphical representations of clinical measures and blood test results are shown in Figure 2.

Correlation of anthropometric measurements and lipid profile with liver disease

Liver disease was greater in patients with greater median BMI (27.4 *vs* 23.0, $P < 0.001$). Median waist circumference and median hip circumference was also greater in patients with liver disease (37 *vs* 33, $P < 0.001$ and 37 *vs* 34, $P < 0.001$, respectively) (Supplementary Table 1). The waist-to-hip ratio was greater in patients with liver disease (1.00 *vs* 0.70, $P = 0.025$). The patients with liver disease also had greater total cholesterol (205 *vs* 178, $P = 0.12$) and triglycerides (227 *vs* 184, $P = 0.009$) (Supplementary Table 1). Among the patients with liver disease, grade 1, grade 2 and grade 3 Liver disease was detected in 46.8% ($n = 51$), 46.8% ($n = 51$) and 6.4% ($n = 7$) of patients, respectively (Supplementary Table 1). Table 2 shows the stepwise multiple logistic regression to explore predictors of any liver disease on ultrasound.

Waist circumference [odds ratio (OR): 1.42, 95%CI: 1.22-1.66, $P < 0.001$] and low-density lipoprotein (LDL) cholesterol (OR: 1.01, 95%CI: 1.01-1.02, $P = 0.048$) were significantly associated with any liver disease (Supplementary Table 1).

Table 2 Stepwise logistic regression to identify significant factors associated with any liver disease on ultrasound

Variable	Odds ratio (95%CI)	*P* value
Females	3.09 (1.09-8.80)	0.034
Waist circumference	1.42 (1.22-1.66)	< 0.001
LDL cholesterol	1.01 (1.00-1.02)	0.048

Cutoff of $P < 0.20$ for univariable logistic regression for consideration in multivariable model; variables included in the model were age, sex, social class, income, education, sleep, high dietary consumption of different foods, symptoms, body mass index, heart rate, respiratory rate, systolic and diastolic blood pressures, waist-to-hip ratio, hip circumference, random blood glucose, haemoglobin A1c, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and alanine aminotransferase levels. LDL: Low-density lipoprotein.

Female sex was associated with greater liver disease, but the association did not reach statistical significance (OR: 3.09, 95%CI: 1.09-8.80, $P = 0.32$). Table 3 shows the stepwise multiple logistic regression to explore predictors of grade 2/3 liver disease.

Factors associated with liver disease

The factors most associated with grade 2/3 liver disease were right upper quadrant pain or heaviness (OR: 5.22, 95%CI: 1.40-19.41, $P = 0.14$), income (OR: 3.58, 95%CI: 1.28-10.04, $P = 0.015$), and waist circumference (OR: 1.31, 95%CI: 1.02-1.69, $P = 0.036$). Factors associated with a reduction in grade 2/3 liver disease were involuntary weight loss or gain (OR: 0.11, 95%CI: 0.02-0.52, $P = 0.004$), tingling, pain or numbness of the hands and feet (OR: 0.20, 95%CI: 0.05-0.80, $P = 0.023$), excessive hunger (OR: 0.25, 95%CI: 0.06-0.95, $P = 0.042$), and education (OR: 0.33, 95%CI: 0.12-0.85, $P = 0.023$).

DISCUSSION

This study found that nearly 3 out of every 4 patients with newly or recently diagnosed T2DM have evidence of liver disease and 40% have grade 2 or 3 liver disease. Patients with liver disease are more likely to be female, high consumers of fats and oils and have greater BMI, waist circumference, hip circumference, waist-to-hip ratio, total cholesterol, and triglycerides. Patients with grade 2/3 liver disease are more likely to have right upper quadrant pain/heaviness, greater waist circumference, triglyceride levels, ALT levels, and greater income, and are less likely to experience involuntary weight gain or loss, tingling pain, numbness of hands/feet, or excessive hunger, and to have better education levels. These findings suggest that liver disease is a problem among newly diagnosed T2DM patients and it may be important to screen these patients, particularly those with obesity, for NAFLD.

The current study builds on literature from around the world that describes the prevalence of NAFLD in T2DM. In an Indian multicentre study (189 centres), the prevalence of NAFLD varied from 44.1% to 72.4%[17], which was similar to the range found in a larger Italian study ($n = 38880$)[18]. Among 233 patients with T2DM in Sri Lanka, the overall prevalence of NAFLD was 62.6%[19]. In a Nigerian case-control study of 336 subjects, NAFLD was detected in 16.7% of patients with T2DM compared to 1.2% in non-diabetic controls[20]. A meta-analysis of 17 studies with 10897 patients reported the overall prevalence of NAFLD in patients with T2DM as 54%[21]. The current study of 148 patients reported a higher prevalence (72.3%) in the Indian region of Northern Bihar among newly and recently diagnosed T2DM patients compared to many existing studies. While the exact reason for the higher prevalence is not known, it likely relates to prevalence of risk factors within this population, such as genetic predisposition, obesity, diet, exercise, and health-related behaviours.

Our study found a greater proportion of females among the T2DM patients with NAFLD. Similar results were observed in a Indian multicentric study by Kalra *et al*[17]. However, no significant difference was found in Sri Lanka[1]. In contrast, data from Nigeria shows higher occurrence of NAFLD in men[20]. In the general population including patients without T2DM, the prevalence and severity of NAFLD is higher in men compared to women during reproductive age, but NAFLD occurs at a higher rate in postmenopausal women, suggesting that oestrogen is protective against NAFLD[22]. Postmenopausal women have a greater NAFLD risk and higher rates of severe hepatic fibrosis relative to premenopausal women. Furthermore, older women with NAFLD experience greater mortality than their male counterparts[23].

The National Family Health Survey (NFHS-5) India 2019-2021 has revealed that a greater number of females (33.2%) than males (29.8%) in India are overweight/obese and in Bihar more females (25.2%) than males (18.7%) are obese[24]. These findings may complement the higher prevalence of NAFLD in female patients across India, especially in northern states. An interesting finding from the current study was that women were more likely to have liver disease of mild severity. This sex preponderance raises the possibility that females with T2DM also had higher risk of liver disease[25]. However, due to these contrasting findings, it is unclear whether biological sex plays a significant role in NAFLD, particularly among older individuals with T2DM[19].

In this study, individuals with liver disease were more likely to be high consumers of fats and oils, especially butter oil, refined oil, palm, and mustard oil and to have greater BMI, waist circumference, hip circumference, waist-to-hip ratio, total cholesterol, and triglycerides. In a double-blind and randomized trial of overweight individuals, overeating

Table 3 Stepwise logistic regression to identify factors associated with grade 2/3 liver disease on ultrasound

Variable	Odds ratio (95%CI)	*P* value
Triglyceride levels	1.01 (1.00-1.01)	0.004
Income	3.58 (1.28-10.04)	0.015
Education	0.33 (0.12-0.85)	0.023
Excessive hunger	0.25 (0.06-0.95)	0.042
Alanine aminotransferase levels	1.02 (1.00-1.03)	0.032
Right upper quadrant pain or heaviness	5.22 (1.40-19.41)	0.014
Involuntary weight loss or gain	0.11 (0.02-0.52)	0.005
Tingling, pain or numbness of hands and feet	0.20 (0.05-0.80)	0.023
Waist circumference	1.31 (1.02-1.69)	0.036

Cutoff of $P < 0.20$ for univariable logistic regression for consideration in multivariable model; variables included in the model were age, sex, social class, income, education, sleep, high dietary consumption of different foods, symptoms, body mass index, heart rate, respiratory rate, systolic and diastolic blood pressures, waist-to-hip ratio, hip circumference, random blood glucose, haemoglobin A1c, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and alanine aminotransferase levels.

saturated fatty acids from palm oil causes pronounced liver fat accumulation and both circulating liver enzymes and ceramides increased, indicating hepatocellular injury[26]. In contrast, despite similar weight gain, overeating polyunsaturated fatty acids from sunflower oil completely blocked liver fat accumulation and even improved the blood lipid profile. Interestingly, it was suggested that the adverse metabolic effects induced by saturated fatty acids normalized after weight loss. There is a potential link between a high-fat diet and the presence of liver disease that raises the possibility of reducing liver disease by reduced consumption of fats and oils[27].

The likelihood of NASH resolution and fibrosis regression with low-fat hypocaloric diet (750 kcal less than daily requirement) and low intensity exercise (200 min/week) was proportional to the degree of weight loss, specifically 45%-90% in individuals losing ≥ 10% of total body weight[28]. Weight loss is also highly effective in preventing or delaying the onset of T2DM in people at high risk of T2DM as shown in the Diabetes Prevention Program Outcomes Study[29]. Therefore, there may be a definite benefit with early identification of NAFLD in these T2DM individuals, as intervention accepted and followed by patients may reduce disease progression.

Among the clinical measures analysed, BMI, waist circumference, hip circumference, and waist-to-hip ratio demonstrated significant associations with liver disease, and these are also the parameters of obesity. Similarly, other studies have shown a positive association between waist-to-hip ratio liver disease and T2DM[30,31]. The key question is whether T2DM has an additive effect on the impact of obesity on liver disease or if obesity directly causes patients to be predisposed to liver disease.

Blood test results provided insights into the association between lipid profiles and liver disease. In other studies, NAFLD is independently linked with total cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol[32,33]. Despite a lack of association with LDL cholesterol, NAFLD was associated with higher LDL particle concentration and lower LDL particle size, suggesting that NAFLD is associated with the atherogenic dyslipidaemia phenotype in a dose-dependent fashion[33]. These findings suggested that dyslipidaemia, specifically elevated total cholesterol and triglyceride levels, may have contributed to the development of liver disease in this population.

In a study of 101 patients with T2DM, NAFLD was positively associated with higher waist circumference and ALT levels[34]. Similarly, in this study, patients with NAFLD had significantly higher ALT and lower HDL cholesterol levels. ALT may be more related to liver fat accumulation than aspartate aminotransferase[35]. More research is needed, however, to evaluate the temporal evolution of HDL levels and other lipid parameters in newly diagnosed T2DM patients and their association with NAFLD.

In this study, the prevalence of NAFLD in newly and recently detected diabetes is high (72.3%). Reasons for development of liver disease in T2DM patients are higher BMI, waist circumference, hip circumference, and waist-to-hip ratio, as well as dyslipidaemia, specifically elevated total cholesterol and triglyceride levels. In a previous South Korean study, obesity, insulin resistance, and ultrasound-diagnosed NAFLD at baseline (alone or in combination) approximately doubled the risk of T2DM at 5-year follow-up. Furthermore, in patients with all three risk factors, T2DM risk increased approximately 15-fold[36].

Serum ALT levels predicted severe but not mild liver disease in this study. Serum ALT could be used alone or as a part of a screening tool for NAFLD in patients with newly and recently detected T2DM. The goal of screening for NAFLD is to identify patients at risk for adverse health outcomes associated with such as cirrhosis, hepatocellular carcinoma, and death from liver disease[37]. The American Diabetes Association (ADA) recommends universal screening of people with T2DM and prediabetes for fatty liver disease and offers new recommendations for management in those with the condition or who are at risk for it[38-40]. The new ADA guidance aligns with those of other professional societies, including the American Association for the Study of Liver Disease, the American Gastroenterological Society, and the American Association of Clinical Endocrinology[41]. In the current study, we found that NAFLD is common in newly

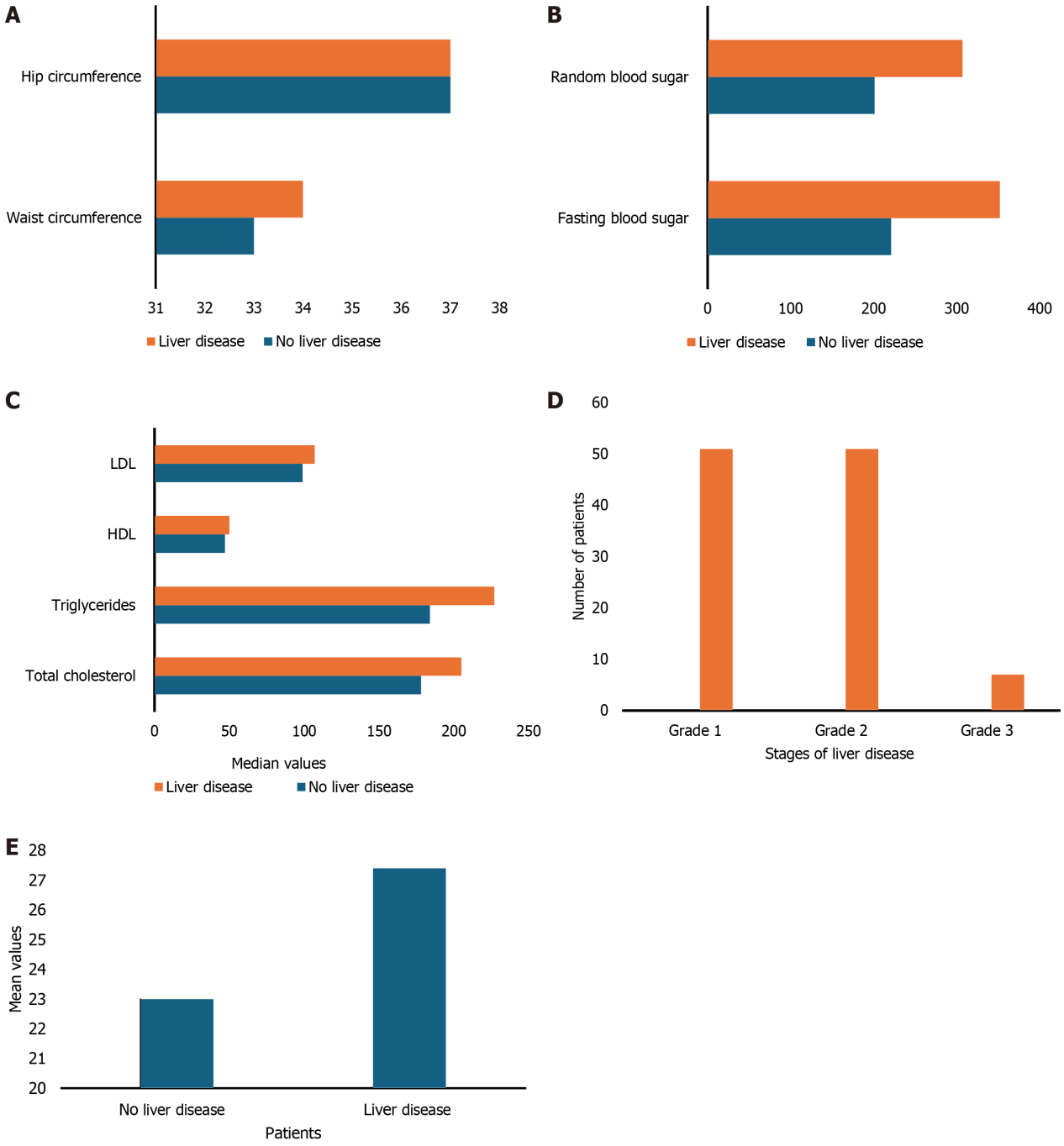

Figure 2 Graphical representation of clinical measurements, blood tests and ultrasound findings in patients with or without liver disease.
A: Anthropometric measurements ($P < 0.001$ for both); B: Glycaemic measurements (fasting blood sugar: $P = 0.81$; random blood sugar: $P = 0.74$); C: Lipid profile measurements (low-density lipoprotein cholesterol: $P = 0.31$, high-density lipoprotein cholesterol: 0.27, triglycerides: $P = 0.009$, total cholesterol: $P = 0.012$); D: Ultrasound scan findings ($P < 0.001$); E: Mean body mass index ($P < 0.001$).

and recently diagnosed individuals with T2DM, hence our findings support screening practices recommended in international guidelines.

This study has a few limitations, namely its cross-sectional design, small sample size, and ultrasound basis of diagnosis for liver disease. There may be some variability in imaging and interpretation depending on the sonographer, though the same experienced sonographer conducted all the scans in this study. Ideally, the diagnosis of liver disease should be based on liver biopsy. Although ultrasound of the liver is often used as a screening test for fatty liver, its sensitivity is low for NAFLD, as NAFLD can only be reliably diagnosed if steatosis is > 33%. Moreover, ultrasound scan of the liver does not provide information about liver fibrosis, which is a prognostic marker.

CONCLUSION

In conclusion, NAFLD is common in new and recently diagnosed T2DM. There are many factors associated with liver disease in the T2DM population, including elevated BMI, waist-to-hip ratio, total cholesterol and triglyceride levels, as well as female sex. More studies are needed to determine the optimal screening strategy and management for patients who are found by ultrasound to have NAFLD, in order to reduce progression of or completely reverse the liver disease.

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FOOTNOTES

Author contributions: Mukherjee S and Mukherjee S conceptualized the study and performed the data curation and analysis; Kwok CS and Phillips A contributed to the study methodology and interim manuscript review. All authors reviewed and approved the final manuscript.

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