



Relationship Between Fasting Plasma Glucose And Nonalcoholic Fatty Liver Disease In Type 2 Diabetes Mellitus Patients

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ABSTRACT

Introduction: Doctors and patients often overlook Nonalcoholic Fatty Liver Disease (NAFLD) because of its non-specific clinical manifestations and is sometimes found incidentally on liver examination. However, NAFLD can undergo poor pathophysiological progression to Hepatocellular Carcinoma (HCC). It is known that the prevalence of NAFLD is approximately twofold higher in Type 2 Diabetes Mellitus (T2DM). Several studies reveal a relationship between them. This study aimed to determine whether or not there was a relationship between Fasting Plasma Glucose (FPG), one of the laboratory parameters of T2DM, and the incidence of NAFLD in the T2DM patient population.

Methods: The study design was cross-sectional with a simple random sampling technique. The secondary data source is the patient's medical record. The study included T2DM patients who met the specified inclusion and exclusion criteria. The subjects were tracked for age, sex, USG, and FPG data. Descriptive analysis of demographic data will be shown with range, mean \pm standard deviation, and proportion. Meanwhile, Chi-Square is used for relationship analysis.

Results: Out of 93 T2DM patients, 48 had positive NAFLD results with an age range of 23-86 years. A total of 33 NAFLD patients had uncontrolled FPG, and 15 samples had controlled FPG. The results of the chi-square correlation test show that there is no significant relationship between FPG and NAFLD.

Conclusions: FPG was not significantly related to the incidence of NAFLD in T2DM patients.

Keywords: Nonalcoholic Fatty Liver Disease; Type 2 Diabetes Mellitus; Fasting Plasma Glucose.

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INTRODUCTION

Nonalcoholic Fatty Liver Disease (NAFLD) is when fat builds up in the liver and makes up at least 5% of the hepatocytes, which can be seen through imaging or histopathology, even if the person isn't drinking too much, taking medications, or having a virus [1]. This condition can progress to inflammation, Nonalcoholic Steatohepatitis (NASH), fibrosis, cirrhosis, liver failure, and even Hepatocellular Carcinoma (HCC) [2]. Ultrasonography (USG) is a commonly used technique for diagnosing NAFLD, exhibiting a sensitivity and specificity of 84.8% and 93.6%, respectively [3]. These values suggest that USG's diagnostic accuracy is comparable to biopsy, the gold standard examination, and is proven to be effective in detecting moderate to severe fatty liver [4].

NAFLD is seen as a liver manifestation of the metabolic syndrome due to its connection with metabolic comorbidities such as dyslipidemia, Type 2 Diabetes Mellitus (T2DM), and obesity [5]. The global prevalence of NAFLD is approximately 25.24%, with a higher prevalence in Asia at 27.37% [6]. A study reveals that the prevalence of NAFLD increases approximately twofold to 55.48% in individuals diagnosed with T2DM [7]. Diabetes mellitus, a metabolic disorder characterized by chronic hyperglycemia, affects approximately 90% of diabetes cases, with type 2 diabetes being the most common. This condition initiates insulin resistance, leading to compensatory increases in insulin production. However, over time, production decreases, resulting in the development of T2DM [8]. Globally, the incidence of type 2 diabetes mellitus remains substantial, affecting approximately 537 million individuals aged 20-79. In Asia, the number of diabetes mellitus cases reaches 90 million, and in Indonesia, it is estimated at around 19.5 million people [9]. T2DM patients frequently use Fasting Plasma Glucose (FPG), a screening tool known for its cost-effectiveness and ease of administration, for diagnosis.

Previous research in China revealed that FPG is an independent risk factor for the onset of NAFLD in nonobese individuals with normal blood lipid levels [10]. Similarly, a study in Sri Lanka emphasized the importance of FPG as an indicator for NAFLD in women from South Asia. Nonetheless, it is essential to acknowledge that the research's limitation lies in its exclusive focus on adult women as the study participants [11].

Meanwhile, a study conducted in Indonesia aimed to establish a link between HbA1c and lipid profiles as indicators for T2DM and dyslipidemia, respectively, with Alanine Aminotransferase (ALT) levels serving as an indicator for NAFLD. The findings showed no significant association, indicating a negative correlation between ALT levels and HbA1c [12]. However, liver enzymes such as ALT are considered less suitable for inclusion in the diagnostic criteria for NAFLD, particularly when predicting the occurrence of NASH, compared to ALT [13]. In contrast, USG emerges as a more precise diagnostic method, exhibiting sensitivity and specificity comparable to the gold standard, biopsy. Given the high prevalence of NAFLD, the potential worsening of NAFLD pathophysiology, variations in samples, variables, and research outcomes, coupled with a limited number of relevant studies, researchers are motivated to delve into the relationship between FPG and NAFLD, particularly when assessed through USG at UNS Hospital.

METHODS

This study utilized an analytical observational approach with a cross-sectional design, focusing on the medical records of patients diagnosed with T2DM. The study included T2DM patients either hospitalized or attending the outpatient clinic at the internal medicine department of UNS Hospital from 2021 to 2023; meeting specified inclusion and exclusion criteria. Inclusion criteria involved:

1. Patients aged 18 years or older;
2. Patients who had undergone hepatic USG;
3. Patients with FPG data (within a maximum interval of 3 months from the hepatic USG examination).

Patients with autoimmune conditions were excluded from the study.

A simple random sampling technique was employed, with a sample size of 93 T2DM patients. The variables under investigation included FPG as the independent variable and the occurrence of NAFLD as the dependent variable. The data will be subjected to chi-square tests to examine the association between FPG and the incidence of NAFLD. Ethical clearance for this research was obtained from Moewardi Surakarta Regional Hospital, protocol number 941/V/HREC/2023.

RESULTS

Sample Characteristics

We collected information on sex, age, FPG, and abdominal USG results for each sample. To categorize patients as having or not having NAFLD, researchers required hepatic ultrasound data. This hepatic USG data was part of the 2D abdominal USG information, which included details on the gallbladder, spleen, pancreas, kidneys, urinary bladder, prostate, and paraaortic lymph nodes. Age groups were differentiated into ≥ 51 years and <51 years, considering the increased prevalence of NAFLD in post-menopausal women [14], as the average age of menopause for women is 51 years [15].

Table 1. Distribution of Research Sample.

Demographic Data	Frequency	Percentage
Age		
<51	21	22,58
≥ 51	72	77,42
Sex		
Male	47	50,54
Female	46	49,46
Fasting Blood Glucose		
Controlled (≤ 130 mg/dL)	33	35,48
Uncontrolled (>130 mg/dL)	60	64,52
Ultrasound		
NAFLD	48	51,61
Mild-moderate	45	48,39
Severe	3	3,22
Not NAFLD	45	48,39

Table 1 illustrates that T2DM is more prevalent among patients aged 51 years or older. The data suggests a nearly equal distribution of male and female T2DM patients in the sample. Of the 93 samples, 60 (64.52%) exhibited uncontrolled fasting plasma glucose, while the others had fasting plasma glucose within the controlled range. FPG is considered controlled in patients with DM when it is between 80 and 130 mg/dL [16]. Among the 48 patients diagnosed with fatty liver, three have reached a severe grade, and the remaining 45 are categorized as mild to moderate. The data indicate that a considerable proportion of the samples have been diagnosed with fatty liver.

Table 1. Demographic Data of T2DM Patients.

Demographic Data	Range	Mean ± Standard deviation	Median
Age	23 - 86	58,08 ± 11,993	58
Fasting Blood Glucose	53 - 363	161,67 ± 65,141	146

The research sample's age ranged from 23 to 86 years, computed from the examination date, with a mean ± standard deviation of 58.08 ± 11.993 and a median age of 58 years. Regarding FPG levels, the samples ranged from 53 to 363 mg/dL, with a mean ± standard deviation of 161.67 ± 65.141 and a median of 146.

Table 1. Demographic Analysis of Research Subjects.

Demographic Data	NAFLD Patients		Not NAFLD		p
	n	%	n	%	
Age					
<51	12	57,14	9	42,86	0,564
≥ 51	36	50,00	36	50,00	
Sex					
Male	29	61,70	18	38,30	0,049
Female	19	41,30	27	58,70	

The amount of data is expressed in n

Note: p = significance of correlation test with Chi-Square

According to the chi-square test, the findings suggest no statistically significant association between age and NAFLD ($p > 0.05$). Conversely, when considering sex, a significant correlation with the incidence of NAFLD is observed ($p < 0.05$).

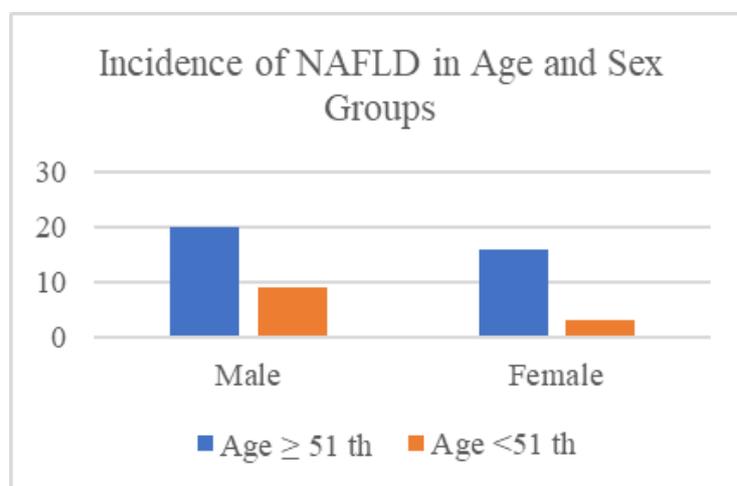


Figure 1. Incidence of NAFLD in Age and Sex Groups

Referring to Figure 1, the ratio of females to males in the incidence of NAFLD among those aged 51 years or older is 0.8 (16:20). In contrast, for the age group younger than 51 years, the ratio stands at 0.33 (3:9).

Table 1. Demographic Analysis of Research Subjects.

Demographic Data	NAFLD Patients		Not NAFLD		p
	n	%	n	%	
FPG					
Un-controlled (> 130 mg/dL)	33	55,00	27	45,00	0,378
Controlled (≤130 mg/dL)	15	45,45	18	54,55	

The amount of data is expressed in n

Note: p = significance of correlation test with Chi-Square

As per the Chi-Square test results, there is no statistically significant correlation between FPG and the incidence of NAFLD in patients with T2DM ($p > 0.05$). However, based on the data presented in Table 4, the group with uncontrolled FPG (33 samples) has more NAFLD patients than the group with controlled FPG (15 samples).

DISCUSSION

Diabetes is more prevalent in adults aged 45 years and older [17]. The data reveals that most samples fall into the age group of 51 years or older. Regarding sex distribution, the samples are pretty evenly split, with a nearly equal male-to-female ratio (47:46). The analytical test concludes that there is no significant correlation between age and the occurrence of NAFLD ($p = 0.378$). On the other hand, sex demonstrates a significant association with the incidence of NAFLD ($p = 0.049$).

Data presented in Figure 1 illustrates that the incidence of NAFLD in the age group of 51 years or older and among females is lower compared to males, with a ratio of 0.8. In contrast, in the age group younger than 51 years, the ratio decreases to 0.3. It is consistent with prior research indicating a lower prevalence of NAFLD in women during reproductive years, gradually increasing post-menopause. In males, the prevalence tends to rise with age, peaking between 50 and 60 years [14].

The discussion entails an exploration that draws connections and comparisons between the research outcomes, the theories under examination, and the findings of prior studies. The discussion can conclude by outlining the research limitations and offering recommendations for future investigations.

The primary objective of this study is to ascertain whether a relationship exists between fasting blood sugar levels and the occurrence of NAFLD in individuals with type 2 diabetes mellitus (T2DM). Based on the analysis, the conclusion is drawn that there is no statistically significant correlation between fasting blood sugar and the incidence of NAFLD ($p = 0.378$). Nevertheless, the percentage of NAFLD patients in the group with uncontrolled fasting blood sugar, consisting of 33 samples (68.75%), surpasses that in the controlled fasting blood sugar group, which comprises 15 samples (31.75%).

Similar research has yet to be conducted in Indonesia, but there are studies with comparable findings. A prior study in Algeria involved 426 samples, dividing them into 213 NAFLD patients and 213 control samples. Regardless of obesity, the study found a higher prevalence of prediabetes (Fasting Blood Sugar levels between 1 and 1.25 g/L) in NAFLD compared to the control group ($p = 0.001$). There was also a significant difference in BMI < 30 ($p = 0.002$). However, in obese NAFLD patients (BMI ≥ 30), the difference was not significant compared to obese controls ($p = 0.32$). This is explained by the strong predisposition of obesity to diabetes [18].

Another study reported a significant association between FPG and NAFLD. The research concluded that there is an independent nonlinear relationship between FPG and an increased risk of NAFLD in the Chinese population without obesity and normal blood lipid levels ($p < 0.0001$) [10]. A study in Sri Lanka also highlighted that FPG is a crucial indicator for the occurrence of NAFLD in South Asian women in the adult female population. This study involved 34 adult Sri Lankan women. Among the participants, 11 were categorized as fatty liver grade 0 (NAFL 0), 13 as fatty liver grade 1 (NAFL 1), and 10 as fatty liver grade 2 (NAFL 2), with no participants falling into the NAFL 3 category. The analysis results demonstrated a significant increase in FPG between NAFL 0 and NAFL 1 ($p = 0.011$) and between NAFL 0 and NAFL 2 ($p = 0.003$). However, between NAFL 1 and NAFL 2, the results were not significant ($p = 0.26$) [11].

Our study's data suggest that the majority of the samples have been diagnosed with fatty liver. Out of the total 93 samples from T2DM patients, 48 were diagnosed with fatty liver, with three in severe grade and the remaining 45 falling into the mild to moderate grade. Excluding FPG values, this observation can clarify the link between T2DM and NAFLD. However, since abdominal ultrasound examinations are typically based on indications, it is reasonable to observe that most samples were diagnosed with fatty liver, especially with the cross-sectional research method employed in this study.

In our study, no significant association was found between FPG and T2DM. Several factors that could explain the lack of a significant association between FPG and NAFLD include 1) potential sample selection bias due to the inability to adjust for confounding factors such as obesity, dyslipidemia, diabetes medications, and medications causing steatosis; 2) the non-prospective nature of the study, resulting in inconsistent data (abdominal ultrasound examinations were performed based on indications and may not represent the entire T2DM population); 3) the presence of other predisposing solid factors leading to nonsignificant results.

The incidence of NAFLD is higher among patients with T2DM. Some researchers have demonstrated a relationship using variables like FPG and abdominal ultrasound. In this study, there was no significant association between FPG and NAFLD. However, the increased number of NAFLD patients in the uncontrolled FPG group in this research supports the findings of previous studies.

CONCLUSIONS

According to the study, no significant correlation was observed between FPG and NAFLD. The incidence of NAFLD rises in patients with T2DM exhibiting uncontrolled FPG. Additional research is required to substantiate this conclusion. Despite this, the study's findings indicate that early detection and prevention of NAFLD are essential, and one approach is to control FPG in patients with diagnosed T2DM.

Author Contributions

Conceptualization, M.A.N.L. and P.D.P.; methodology, M.A.N.L.; validation, M.A.N.L.; formal analysis, M.A.N.L.; resources, M.A.N.L.; data curation, M.A.N.L.; writing—original draft preparation, M.A.N.L.; reviewing, P.D.P., H.B.D., and P.N.A.; visualization, M.A.N.L.; supervision, P.D.P., H.B.D., and P.N.A.; project administration, M.A.N.L.

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Institutional Review Board Statement

The study was conducted after obtaining ethical clearance from Moewardi Surakarta Regional Hospital, protocol number 941/V/HREC/2023.

Informed Consent Statement

Patient consent was waived because the data used is secondary data from medical records, so researchers do not have direct contact with patients for research needs.

Data Availability Statement

Links

https://docs.google.com/document/d/1vtmjZYnwBUaJeD98U_xR0_sJw9wjjFhIiutEJWFULUs/edit?usp=sharing

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Conflicts of Interest

The authors declare no conflict of interest.

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