

CHARACTERISTICS OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) PATIENT IN DIABETES MELLITUS AT THE PROF I.G.N.G NGOERAH DENPASAR BALI CENTRAL GENERAL HOSPITAL

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ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is a common disease worldwide, including in Indonesia, due to an imbalanced lifestyle. The increase in NAFLD is also caused by the increasing number of diabetes mellitus (DM). This is due to the relationship between the risk factors and pathophysiology of NAFLD and DM. The incidence of NAFLD is increased by 2-3 times in patients with DM. However, data on NAFLD are rarely found in Indonesia. The purpose of this study was to determine the characteristics of patients with NAFLD in patients with DM. This study is a quantitative observational study using descriptive-analytical methods with total sampling techniques and a cross-sectional approach. The results showed that there were 86 NAFLD samples, of which 26 were diagnosed with DM, with the most frequent age range of 46-65 years (53.5%). The most common gender was male (61.6%). Most of the samples had a body mass index (BMI) above normal (65.1%), but there was a difference between NAFLD with DM (80.8%) and without DM (58.3%). The SGOT and SGPT levels of the samples were the same, namely more normal (62.8%). However, between NAFLD with DM and without DM, different results were obtained, where NAFLD with DM tended to have high SGPT levels (53.8%) while NAFLD without DM tended to be normal (70%). The conclusions of the study are BMI and SGPT levels can be used to distinguish between patients with NAFLD with DM and NAFLD without DM but age, gender, and SGOT levels are not significantly different.

Keywords: NAFLD., DM., Liver Function Test., SGOT., SGPT

ABSTRAK

Non-alcoholic fatty liver disease (NAFLD) merupakan salah satu penyakit yang cukup banyak di seluruh dunia termasuk Indonesia akibat pola hidup tidak seimbang. Peningkatan NAFLD juga diakibatkan Diabetes Melitus (DM) yang terus bertambah. Hal ini disebabkan adanya hubungan faktor risiko dan patofisiologi antara NAFLD dengan DM. Peningkatan kejadian NAFLD mencapai 2-3 kali pada pasien penderita DM. Meskipun demikian, data mengenai NAFLD atau DM pada NAFLD jarang ditemukan di Indonesia. Tujuan penelitian ini untuk mengetahui karakteristik pasien NAFLD pada penderita DM. Penelitian ini merupakan penelitian kuantitatif *observational* menggunakan metode deskriptif analitik dengan teknik *total sampling* dan pendekatan *cross-sectional*. Hasilnya didapatkan 86 sampel NAFLD dimana 26 orang terdiagnosis DM dengan rentang usia terbanyak 46-65 tahun (53.5%). Jenis kelamin terbanyak adalah laki-laki (61.6%). Sebagian besar sampel memiliki BMI diatas normal (65.1%), namun terdapat perbedaan antara NAFLD dengan DM (80.8%) dan tanpa DM (58.3%). Didapatkan juga persentase kadar SGOT dan SGPT sampel sama yaitu lebih banyak normal (62.8%). Namun antara NAFLD dengan DM dan tanpa DM, didapatkan kadar SGPT berbeda dimana NAFLD dengan DM cenderung memiliki kadar SGPT tinggi (53.8%) sedangkan NAFLD tanpa DM cenderung normal (70%). Dapat disimpulkan lebih banyak pasien NAFLD tanpa disertai DM daripada NAFLD dengan DM. Didapatkan pula BMI dan kadar SGPT dapat menjadi parameter pembeda antara pasien NAFLD dengan DM tanpa DM. Sedangkan usia, jenis kelamin, dan kadar SGOT tidak terlalu signifikan perbedaannya.

Kata kunci : NAFLD., DM., Tes fungsi hati., SGOT., SGPT

INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) is a liver condition that can affect people who consume little or no alcohol. To be considered "non-alcoholic" the daily alcohol intake limit is 20 grams for women and 30 grams for men.¹ Diagnosis of NAFLD requires the presence of steatosis hepatitis in both histological and radiological examinations, along with the exclusion of secondary causes of hepatic fat accumulation such as alcohol consumption, the use of steatogenic drugs, hereditary diseases such as Wilson's disease, viral liver diseases such as hepatitis B and C, autoimmune hepatitis and malnutrition, hemochromatosis, and biliary diseases.² Liver function tests are often used to aid in the diagnosis of NAFLD. Alanine aminotransferase (ALT)/Serum Glutamate Pyruvate Transaminase (SGPT) and aspartate aminotransferase (AST)/serum glutamate oxalate transaminase (SGOT) are two tests that often increase in NAFLD patients, but significant increases do not always occur so they cannot be used to diagnose NAFLD. Other tests such as Gamma-glutamyl transferase (GGT), triglycerides, and Alkaline phosphatase (ALP) are also often found to be increased but not all.³ Fatty liver can be caused by various factors including age, genetics, gender, knowledge level, and certain medical conditions like obesity, diabetes mellitus (DM), hypertension, hyperlipidemia, hypertriglyceridemia, and decreased HDL cholesterol.⁴

Diabetes mellitus (DM) is a chronic metabolic disease that occurs when the pancreas does not produce or properly use insulin. DM and non-alcoholic fatty liver disease (NAFLD) are two conditions that are closely linked in terms of risk factors and pathophysiology. The bidirectional relationship between DM and NAFLD can lead to an increase in the progression of NAFLD, the development of DM, and a worsening prognosis. The most common mechanism that connects the two diseases is related to oxidative stress, lipotoxicity, and inflammation, which eventually leads to insulin resistance.⁵ The mortality rate is significantly higher in individuals with both NAFLD and DM compared to those with NAFLD or DM alone. The combination of NAFLD and Diabetes leads to a higher risk of various complications, which is the primary cause of the increased mortality and morbidity rates associated with this condition.⁶

In recent years, the prevalence of chronic metabolic diseases such as DM and NAFLD has increased worldwide due to sedentary lifestyles and high-sugar and fat diets. The prevalence of NAFLD worldwide is 24%, and in Asia, it reaches 27%.⁷ In Indonesia, the prevalence of NAFLD is estimated to be 30,6% and is expected to continue

increasing. DM is one of the major factors contributing to the rise in NAFLD incidence. Indonesia has the seventh-highest number of DM sufferers in the world, with 10.7 million people affected as of 2020. People with NAFLD have a 2-3 times higher risk of developing DM than those without it. However, data on NAFLD or NAFLD sufferers with DM is still scarce in Indonesia.⁸

This study aims to examine the characteristics of NAFLD sufferers with DM, especially those at RSUP Prof. Dr. I.G.N.G Ngoerah Denpasar, Bali. The study is expected to provide valuable insights into the characteristics of NAFLD in DM and serve as a basis for further research. Ultimately, the findings could help improve healthcare strategies.

1. OBJECT AND METHOD

This study is a quantitative observational study that uses a cross-sectional method to determine the characteristics of NAFLD patients with diabetes. An analytical descriptive technique is employed to analyze the accessible population, which includes all NAFLD patients at RSUP Prof. Dr. I.G.N.G Ngoerah Denpasar, Bali, between 2020-2022. Samples will be taken from the accessible population, based on inclusion and exclusion criteria. The inclusion criteria require patients to have a diagnosis of Fatty Liver Disease based on abdominal ultrasound results recorded in the medical record at RSUP Prof Ngoerah in 2020-2022. On the other hand, patients are excluded from the study if they have a history of consuming alcohol of more than 20 mg/day for women and 30 mg/day for men, have other secondary causes of fatty liver, or if the required data is incomplete.

Total sampling is used for this study, considering the number of samples is less than 100 people. The data is taken from the medical record sheet after obtaining research permission from the relevant hospital and ethics committee. The data is then processed using Statistical Product and Service Solutions (SPSS) version 26 software to obtain characteristics based on age, gender, BMI, SGOT levels, and SGPT levels. This study has been approved by the ethics committee of the Faculty of Medicine, Udayana University with the letter of ethical fitness number 691/UN14.2.2.VII.14/LT/2023.

RESULT

Based on the data collected, 117 people were diagnosed with Fatty Liver Disease at RSUP Prof Ngoerah Bali in the period 2020-2022. Of these 117 people, 86 were diagnosed with NAFLD and met the inclusion and exclusion criteria.

Table 1. Distribution of Sample Characteristics Based on Age and Body Mass Index (BMI)

Variable	Frequency (n)	Percentage (%)	Mean ±SD
Age			
< 26	3	3.5	
26-45	33	38.4	48.09 ± 12.7
45-65	46	53.5	
> 65	4	4.6	
BMI			
Underweight (<18,5)	4	4.7	
Normal (18,5-24,9)	26	30.2	
Overweight (25-29,9)	26	30.2	27.7 ± 5.9
Obese (30-34,9)	21	24.4	
Extremely obese (>35)	9	10.5	

Based on the age data in Table 1, most NAFLD patients were aged 45-65 years, with 46 people (53.5%) and an average age of 48 years for the entire sample. Table 1 also shows the BMI status of NAFLD patients, which is dominated by normal and overweight BMI, with 26 people

each (30.2%). If the samples with BMI above normal are added together, 56 people have BMI above normal. The average BMI value of the entire NAFLD sample was found to be 27.7 with a standard deviation of 5.9.

Table 2. Distribution of Sample Characteristics Based on Diabetes History, Gender, SGOT Levels, and SGPT Levels

Variable	Frequency (n)	Percentage (%)
DM History	26	30.2
Gender		
Female	53	61.6
Male	33	38.4
SGOT Levels		
Normal	54	62.8
Increase	32	37.2
SGPT Levels		
Normal	54	62.8
Increase	32	37.2

Table 2 shows that out of 86 samples with Non-Alcoholic Fatty Liver Disease (NAFLD), 26 people also have Diabetes Mellitus (DM), accounting for 30,2% of the total samples. The data also reveals that more males (53

people, or 61,6%) suffer from NAFLD than females. Furthermore, Table 2 displays the levels of liver function tests, SGOT and SGPT, of NAFLD patients, where 54 people (62,8%) had normal SGOT and SGPT levels

Table 3. Difference in Distribution of DM and Non-DM Sample Characteristics Based on Age and Body Mass Index

Variable	DM History, N (%) or Mean±SD		P-value
	DM	Non-DM	
Age			
< 26	0 (0)	3 (5)	0.383
26-45	8 (30.8)	25 (41.7)	
45-65	16 (61.5)	30 (50)	
> 65	2 (7.7)	2 (3.3)	
Mean ± SD	51 ± 11	47±13	
BMI			
Underweight (<18,5)	0 (0)	4 (6,7)	0.013
Normal (18,5-24,9)	5 (19,2)	21 (35)	
Overweight (25-29,9)	9 (34,6)	17 (28,3)	
Obese (30-34,9)	5 (19,2)	16 (26,7)	
Extremely obese (>35)	7 (26,9)	2 (3,3)	
Mean ± SD	30.6 ± 6.6	26.4 ± 5.2	

On this research, the comparison between patients with NAFLD with DM and NAFLD without DM can be seen in Table 3 and Table 4. If viewed by age, both patients with NAFLD with DM and without DM are dominated by the age of 46-65 years, which is 16 people (61.5%) in NAFLD with DM and 30 people (50%) in NAFLD without DM. The average age of patients with NAFLD with DM is 30.6 years and the average age of patients with NAFLD without DM is

26.4 years. Table 3 also presents the BMI status between patients with NAFLD with DM and without DM. In patients with NAFLD with DM, the most common BMI status is overweight, which is 9 people (34.6%). Whereas in NAFLD without DM, patients who are also overweight are dominated, namely as many as 17 people (28.3%). The average BMI of patients with DM is 30.6 and the average BMI of patients without DM is 26.4.

Table 4. Difference in Distribution of DM and Non-DM Sample Characteristics Based on Gender, SGOT Levels, and SGPT Levels

Variable	DM N (%)	Non-DM N (%)	P-Value
Gender			
Female	17 (65.4)	36 (60)	0.637
Male	9 (34.6)	24 (40)	
SGOT Levels			
Normal	13 (50)	41 (68.3)	0.106
Increase	13 (50)	19 (31.7)	
SGPT Levels			
Normal	12 (46.2)	42 (70)	0.036
Increase	14 (53.8)	18 (30)	

The data presented in Table 4 shows that both male and female patients suffer from Non-Alcoholic Fatty Liver Disease (NAFLD) with and without Diabetes Mellitus (DM). However, the majority of patients with NAFLD and DM are males, with 9 people (34.6%) while for those with NAFLD without DM, 24 people (40%) are males. The study also reveals that patients with NAFLD and DM have higher levels of serum glutamic pyruvic transaminase (SGPT) than those without DM. In fact, 14 people (53.8%) with NAFLD

and DM had increased SGPT levels. In contrast, the number of patients with normal and increased serum glutamic oxaloacetic transaminase (SGOT) levels was the same, with 13 people (50%) in each category. On the other hand, patients with NAFLD without DM had more normal liver function tests. In fact, 41 people (68.3%) had normal SGOT levels and 42 people (70%) had normal SGPT levels.

DISCUSSION

According to a recent study conducted at Prof. Dr.I.G.N.G Ngoerah General Hospital Denpasar, out of 86 patients diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD), 26 patients (30.2%) were also found to have Diabetes Mellitus (DM). This finding is consistent with a systematic review that suggests the prevalence of DM in patients with NAFLD ranges from 30% to 80%.⁷ The study conducted at Prof. Dr.I.G.N.G Ngoerah General Hospital Denpasar in 2017-2018 found that 2 out of 11 patients with NAFLD also had DM, accounting for 15.4%.⁹ This is in line with the theory that DM and NAFLD, with risk factors and pathophysiology influence each other, resulting in the prevalence of DM and NAFLD increasing together every year.¹⁰

Based on age characteristics, the age group with the highest number of people suffering from NAFLD is between 46 and 65 years old, accounting for 53.5% of cases. However, the number of cases decreases in the age group of individuals who are over 65 years old, accounting for only 4.6% of cases. These findings are consistent with a meta-analysis that suggests that the prevalence of NAFLD increases with age and peaks around the age of 60, after which it begins to decrease. The decrease in prevalence above 60 years of age is likely due to the poor nutritional status that often occurs at this age.¹¹ The age range with the fewest NAFLD sufferers is less than 26 years old. This has been discussed in the theory that the peak age of NAFLD prevalence occurs at the age of 50-60 years in men and over 60 years in women, and the prevalence of NAFLD will decrease further at a young age.¹² If compared between samples with and without DM, both are dominated by the 46-65 age group, with 61.5% in NAFLD patients with DM and 50% in NAFLD patients without DM. However, after analysis, the difference was found to be not significant, which may be due to the limited sample size. Although the difference is very small, if viewed from the results of the average calculation, there is a tendency for NAFLD patients with DM to be older than NAFLD patients without DM. This is in line with a retrospective study that obtained similar results to this study.¹³

Based on the study, it was found that 61.8% of NAFLD patients were male. This could be attributed to the fact that men are more susceptible to the condition due to their waist-to-hip ratio (WHR). Men tend to have higher amounts of visceral adipose tissue, which increases their risk of developing insulin resistance and consequently, NAFLD. On the other hand, estrogen - which is more abundant in women - has been found to protect against fatty liver by inhibiting insulin resistance and reducing triglyceride synthesis.¹⁴ The comparison between samples with NAFLD DM and samples with NAFLD without DM revealed that gender wasn't a significant parameter. The percentage of male NAFLD patients with DM was 65.4%, while male NAFLD patients without DM was 60%. The chi-square test also indicated a p-value of 0.637, which means that the difference isn't significant. Therefore, it can be concluded that gender isn't a significant parameter in

comparing NAFLD patients with DM and NAFLD patients without DM.

According to BMI classification, the majority of samples fall into the normal and overweight categories, both at 30.2%. Only a small percentage, 4.7%, of samples fall under the underweight category. This indicates that 65.1% of NAFLD samples have a BMI above the normal range. On average, the BMI value is calculated as 27.7, which falls under the overweight classification. This supports the theory that people with higher BMIs are more susceptible to fatty liver disease, as long-term imbalances between energy intake and expenditure cause excess energy to be stored as triglycerides in the body, leading to fatty liver. Obesity is a major risk factor for fatty liver disease. Due to the bidirectional relationship between metabolic diseases and fatty liver, a new term called Metabolic-associated Fatty Liver Disease (MAFLD) has been coined, where obesity or overweight is one of the criteria for diagnosing fatty liver patients with MAFLD.¹⁵ In addition, obesity is also associated with the progression of fatty liver disease and extrahepatic complications, including cardiovascular disease and kidney disease, so it is a special concern for NAFLD patients.¹⁵ This result is similar to a study that was also conducted at Prof. Dr.I.G.N.G Ngoerah Denpasar General Hospital in 2017-2018, where the percentage of NAFLD patients with a BMI above normal was found to be 61.5%.⁹ The study conducted in China in 2018, which analyzed the relationship between BMI and the incidence of fatty liver, also found an average BMI in NAFLD patients of 26.82, with the highest percentage based on BMI classification being overweight.¹⁶

Comparing the samples of patients NAFLD with DM and patients NAFLD without DM reveals that those with NAFLD and DM tend to have a higher Body Mass Index (BMI) than those with NAFLD alone. In the NAFLD with DM group, patients who are classified as overweight are the most common, accounting for 34.6% of cases. If we add together all patients with NAFLD and DM who have a BMI above normal, the percentage will be 80.8%. On the other hand, in patients with NAFLD without DM, the highest percentage of BMI classification is normal, which is 35%, and the percentage of patients with a BMI above normal is 58.3%. Furthermore, the percentage of patients who are extremely obese differs significantly between the two groups. Out of the nine extremely obese patients, seven of them have NAFLD with DM. When looking at the average BMI, patients with NAFLD and DM have a higher BMI of 30.6 kg/m², while those with NAFLD alone have an average BMI of 26.4 kg/m². After processing the data with the Fisher exact test, a p-value of 0.013 was obtained. This indicates that the difference in BMI between patients with NAFLD with DM and those with NAFLD alone is statistically significant. Therefore, it can be concluded that BMI can be used as a distinguishing characteristic between the two groups. This conclusion is consistent with a retrospective study that reported similar results. The study suggests that NAFLD and DM are conditions that are closely related to obesity, thus, obesity is more likely to

occur in individuals who have NAFLD and DM together than those who only have NAFLD.¹³

The study discovered that more patients with NAFLD had normal SGOT levels, at 62.8%, than samples with high SGOT levels, at 31.7%. One possible explanation for this finding is that SGOT may not be sensitive enough to detect liver damage, as it is found in various organs including the liver, heart muscle, skeletal muscle, kidneys, brain, pancreas, lungs, leukocytes, and red blood cells. In NAFLD patients, SGOT levels may only slightly increase, which is considered insignificant.¹⁷ From previous studies, it has also been found that there is a less significant increase in SGOT in patients with NAFLD, but there is still a tendency to increase. In that study, the average SGOT of patients with NAFLD was higher than those without NAFLD.¹¹ In patients with DM, the percentage of patients who experienced an increase in SGOT levels was 50%, while in patients without DM, the percentage of high SGOT levels was only 31.7%. This result was then processed with the chi-square test and a p-value of 0,106 was obtained, which means that although there is a tendency for patients with NAFLD with DM to have higher SGOT levels than patients with NAFLD without DM, the difference is not significant or meaningful. In a study in 2021, it was also found that an increase in SGOT was more common in patients with NAFLD with DM than NAFLD without DM, but the difference was not too significant.¹⁸

According to the findings of this study, 37.2% of patients with NAFLD had high levels of SGPT, while 62.8% had normal SGPT levels. This can be attributed to a population study which suggests that NAFLD can occur without an increase in SGPT levels as the normal range of this liver enzyme is too high. In contrast, only a slight increase in SGPT levels is observed in NAFLD cases. Although the increase is insignificant, SGPT levels are more likely to increase than SGOT levels in liver disease as SGPT levels are predominantly found in the liver.¹⁹ In patients with NAFLD with DM, high SGPT levels were found in 53.8% of cases, while in NAFLD without DM, high SGPT levels were found in only 30% of cases. This data was then processed using the chi-square test and a p-value of 0.036 was obtained. From this, it can be concluded that in this study, a significant difference was found in SGPT levels between patients with NAFLD with DM and NAFLD without DM, where the SGPT levels in patients with NAFLD with DM tended to be higher. This result can be explained by the theory that an increase in SGPT levels is associated with decreased hepatic insulin sensitivity and the risk of DM because SGPT plays a role in increasing hepatic gluconeogenesis and inflammation in the pathogenesis of DM.²⁰

CONCLUSIONS AND SUGGESTIONS

Based on a study conducted at Prof. Dr.I.G.N.G Ngoerah General Hospital, Denpasar Bali between 2020-2022, it has been observed that there are more patients with Non-alcoholic Fatty Liver Disease (NAFLD) without Diabetes Mellitus (DM) than with DM. Men tend to be more affected than women, and the most common age range for <http://ojs.unud.ac.id/index.php/eum> doi:10.24843.MU.2024.V13.i12.P18

patients is 45-65 years. The study also found that patients with NAFLD generally have a BMI above normal. Additionally, BMI and SGPT levels are found to be differentiating parameters between patients with NAFLD with DM and without DM. However, other characteristics such as gender, age, and SGOT levels do not show significant differences between the two groups.

The authors of the study recommend conducting further research with a larger population and more variables to determine additional characteristics that can differentiate between patients with NAFLD with DM and those without DM. Further research on fatty liver disease is also suggested, especially in regards to the new terminology, MAFLD, which could potentially group at-risk patients more effectively than NAFLD criteria.

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