International Journal of Public Health Excellence (IJPHE)
Vol. 4, Issue 1, June-December 2024, pp. 044~050
Journal Homepage: https://ejournal.ipinternasional.com/index.php/ijphe
ISSN: 2809-9826, DOI: 10.55299/ijphe.v4i1.922

Description of HbA1c Levels in Fatty Liver Disease Patients in a West Jakarta Private Hospital in 2018-2019

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Article Info

Article history:

Received June 13, 2024
Revised July 06, 2024
Accepted July 08, 2024

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ABSTRACT

Fatty liver disease is a chronic disease that is very often found in the community and is often called "silent" liver disease because there are no specific symptoms in patients. The incidence of fatty liver disease in Indonesia is quite high by 30 percent and this disease can develop into liver cirrhosis. The high incidence of fatty liver disease can be caused by various factors such as obesity, dyslipidemia, hypertension, unhealthy lifestyles and insulin resistance. Insulin resistance can be characterized by an increase in HbA1c levels in the blood. This study aims to determine the description of HbA1c levels in patients with fatty liver disease. This research is an observational descriptive study using a cross-sectional approach by using medical record data of fatty liver disease patients who have been on radiologic examination and doing HbA1c examination. Fatty liver disease affects more male sex groups by 55.4 percent, with the most age range at 51-60 years by 34.9 percent. Diabetes HbA1c levels (59%) are more than prediabetes (25.3%) and normal HbA1c levels (15.7%). Abnormal HbA1c levels (prediabetes and diabetes) were found to be higher in men (47 % vs 47,3%). The most accompanying diseases in patients with fatty liver disease are diabetes mellitus (51.8%), hypertension (33.7%), dyslipidemia (26.5%), dyspepsia (28.9%), and hyperuricemia (15.7%). Fatty liver disease patients were also found to have metabolic syndrome by 54.2% which was dominated by female sex by 53.3% with 91.1% having 3 components of metabolic syndrome and 8.9% having 4 components of metabolic syndrome.

Keywords: *Fatty Liver Disease, HbA1c, Patients in Jakarta Private Hospital*

1. INTRODUCTION

Fatty liver disease (FLD) is a condition where there is a buildup of excess fat in the liver. In recent years FLD has received a lot of attention because of its association with the obesity epidemic and metabolic syndrome. Fatty liver disease is one of the most common chronic liver diseases. Fatty liver disease has high morbidity and mortality rates and increases health care costs over 5 years by around 26% 1. This disease is often called " silent" liver disease because there are no specific symptoms in sufferers [1]. If this disease is not treated, it can progress to fibrosis in 30-40% of patients and liver cirrhosis in 15% of patients within approximately 5 years 1 0, 1 2. Fatty liver disease also increases the risk of developing cardiovascular disease [2]. Chronic kidney disease is also found in 20-50% of FLD patients 1 2. Other complications of FLD include liver cancer or hepatocellular carcinoma (HCC), colorectal cancer, metabolic bone diseases (vitamin D deficiency, osteoporosis) and other metabolic diseases (lipodystrophy, glycogen storage disorders) 1 2. FLD -related deaths in the United States increased 15% at an average of 2% per year from 2007–2016 34. Fatty liver disease can be caused by alcohol (Alcoholic fatty liver disease/AFLD) and non-alcoholic (Non-alcoholic fatty liver disease/NAFLD). Non-alcoholic fatty liver disease (NAFLD) is subdivided into primary (related to insulin resistance) and secondary (not related to insulin resistance, due to medical conditions, medications) [3].

The prevalence of NAFLD in the general population in Europe and the Middle East by ultrasound is 20–30% 3, 4, 1 2 and in Western countries, 17–46% of adults are diagnosed with NAFLD 5. This is in line with the prevalence of metabolic syndrome which increases the risk factors for developing NAFLD in both adults, adolescents and children 6. In Indonesia itself, there are studies which state that FLD occurs in 30% of the population 7, 1 1 [4].

Insulin resistance is an important component of metabolic syndrome. Glycated hemoglobin (HbA1c) is used to measure average blood sugar over several weeks to several months. HbA1c can also be used as a surrogate marker of metabolic syndrome in high-risk individuals [5]. HbA1c also serves as a marker of insulin resistance 8, 9. Until now there is no clarity between the relationship between HbA1c levels and the incidence of NAFLD. Some studies say there is a significant relationship between HbA1c levels and the incidence of NAFLD and some say the opposite [6].

HbA1c research in FLD patients in Indonesia is still limited, and there are still many studies outside that are not clear about the relationship between HbA1c levels in FLD patients, therefore this research was carried out. It is hoped that this research can add to existing references [7].

2. METHODS

This research is a descriptive observational study with a cross- study design sectional. This research was conducted at the hospital West Jakarta Swasta. The target population in this study is patients with FLD and the accessible population in this study is patients with FLD in West Jakarta private hospitals in 2018-2019. The sample in this study was a population that met the inclusion criteria, sampling was carried out using a total sampling technique [8]. The sample size in this study was 83 respondents with the inclusion criteria being patients who were diagnosed with FLD and had supporting radiology data, were aged over 18 years and had HbA1c data. After data collection, data processing and data analysis are carried out using data analysis software [9].

3. RESULTS AND DISCUSSION

Table 1 shows the characteristics of FLD patients, which are dominated by men at 55.4%. FLD patients at the West Jakarta Private Hospital were the youngest 21 years old and the oldest 66 years old with a mean of 46 (±10.89) years and a median of 47 years. The highest number of patients was in the 51-60 year range (34.9%). HbA1c levels in a sample of 83 people, obtained a mean of 7.18 (±1.74)%, median 6.7%, max 12.8%, and min 4.3%. There were 49 people with diabetic HbA1c levels (59%). In table 2 of 46 male samples, it was found that prediabetes HbA1c levels in men were higher than women (18.1%) and diabetes HbA1c levels were higher in women (30.1%). Various comorbidities were also found in FLD patients in table 3. There were 14 comorbidities found in FLD patients [10]. The most common comorbidities found were diabetes mellitus, hypertension, dyspepsia, dyslipidemia and hyperuricemia. In table 4, it is also found that the number of FLD patients with metabolic syndrome was 45 people (54.2%). Number of metabolic syndrome components in FLD patients presented in table 5. In table 6, it was found that more FLD patients with metabolic syndrome were female (54.5%) [11].

DISCUSSION

Demographic Features of FLD Patients

Of the 83 samples studied, it was found that FLD sufferers were more common in men, namely 46 people (55.4%). This is in accordance with cohort research conducted by Hamaguchi (2005) which found 78% of men and 22% of women 14. A cohort study by Tsuneto (2010) found an incidence of 19.9/1000 people/year with 22.3 for men and 18.6 for women 15.. A cross-sectional descriptive study by Mukesh (2019) in Nepal on 385 patients, obtained similar results where 209 patients were male (54.3%) 35 [12]. More men suffer from FLD than women because there is a hypothesis about the protective effect of the hormone estrogen. In menopausal women the number is almost the same as in men because the protective effect of the hormone estrogen has disappeared, the levels of which decrease in menopausal women 16. However, research was found that said the incidence of FLD was 4.2% higher in women than men 19 [13]. This difference in results could be due to differences in sample size, sample characteristics and also the theory that women are more at risk of developing metabolic syndrome than men 31 [14].

Based on the research results, the highest number of FLD patients were 29 people aged 51-60 years (34.9%) followed by 24 people in the 41-50 year age range (28.9%). These results are in accordance with cross-sectional research conducted by IB Prasetya (2017) at Cipto Mangunkusumo Hospital which found that most patients were over 40 years old with an average of 58 years 13. A cohort study by William CD (2011) in America found that the average age of patients diagnosed with FLD was 49 - 62 years 17. The high incidence rate in this age range is due to decreased physical activity and food intake that is high in fat, which can lead to obesity and dyslipidemia, which are risk factors for FLD 7, 16 [15].

From research There was an increase in HbA1c levels in FLD sufferers, namely 13 people with normal HbA1c levels (15.7%), 21 people with prediabetic HbA1c levels (25.3%) and 49 people with diabetic HbA1c levels (59%). This is in accordance with a cross-sectional study by Han Ma (2013) of 949 people who found an increase in HbA1c levels in FLD patients 18. A cohort study by Changxi Chen (2020) found that increasing HbA1c levels was directly proportional to the incidence of FLD 20. Increased HbA1c levels in FLD patients can be due to insulin resistance which is a component of FLD and can also be caused by oxidative stress which can affect the strength of erythrocytes so that they are easily lysed, thus affecting HbA1c levels 1 8, 20 [16].

Description of HbA1c Levels in FLD Patients Based on Gender

In this study, it was found that abnormal HbA1c levels (prediabetes and diabetes) were higher in 39 men (47%) than 31 women (37.3%). The results of this study are in accordance with a cohort study of 2811 people in Southern China by Changxi Chen (2020) which found that abnormal HbA1c levels in FLD patients were higher in men, especially at the age of 40-59 years 20. In this study, it was found that diabetes HbA1c levels in women (30.1%) were higher. These results are in accordance with research by Nadya M (2015) which found that women with diabetes HbA1c levels were higher than men (57.14% vs 42.85%). Abnormally high HbA1c levels in men can be caused by a bad lifestyle such as consuming foods high in carbohydrates or smoking habits. High HbA1c levels can also be caused by insulin resistance and oxidative stress 18. The higher number of women compared to men with diabetes HbA1c levels who suffer from FLD could be due to the loss of the protective effects of the hormones estrogen and progesterone and also the larger number of women who have metabolic syndrome compared to men [17].

Comorbidities in FLD Patients

The most common comorbidity was diabetes mellitus, numbering 43 people (51.8%). Cross-sectional descriptive research by IB Prasetya, found 33%-50% of FLD patients suffering from diabetes mellitus 13. Meanwhile, cross-sectional research by Nadya M at Fatmawati General Hospital in 2013-2014 found 20 people (28.5%) FLD patients with diabetes mellitus 22. These results are very different because most patients who have their HbA1c levels checked are patients who are suspected of having high blood sugar or have been diagnosed with diabetes mellitus. However, if we look at all FLD patients At the West Jakarta Private Hospital in 2018-2019, with or without HbA1c data, 55 people (23.9%) had diabetes mellitus. This is no different when compared with research by Nadya M in 2013-2014 [18]. The large number of FLD patients who are accompanied by diabetes mellitus is due to increased intrahepatic gluconeogenesis resistance and increased insulin resistance due to decreased adiponectin levels 1 1, 21. The high rate of diabetes mellitus in FLD patients can be caused by increased oxidative stress and insulin resistance. 18, 23 [19].

The second most common comorbidity after diabetes mellitus is hypertension. There were 28 FLD patients with hypertension (33.7%). Many studies report that hypertension is a risk factor for the occurrence of FLD, one of which is research by Lonardo (2018), where hypertension is included in the metabolic syndrome component which influences the occurrence of FLD, even though the risk is the lowest among the metabolic syndrome components. another 24. Several studies also report that FLD can increase the risk of hypertension, this is because FLD can cause changes in the cardiovascular system such as causing arteriosclerosis in blood vessels which can increase blood pressure 25. Research conducted by Michopoulos in Greece in 2016 using a cross-sectional method found that hypertension is considered a precursor for the development of FLD. The high incidence of hypertension in FLD is also due to disruption of the renin, angiotensin and aldosterone systems which function to regulate blood pressure in the body 36 [20]. Cross-sectional descriptive research conducted by Nadila in 2015 at RSUP. Dr. M. Djamli Padang received 75% of FLD patients have hypertension 33. The differences in results are due to the lack of complete medical record data held by researchers [21].

Other comorbidities besides hypertension and diabetes mellitus were dyslipidemia in 22 people (26.5%). This is in line with a 2013 cohort study conducted by Mahaling which found hypertriglyceridemia (67.14%) and HDL cholesterol abnormalities (62.85%) 28. Cross-sectional descriptive research conducted at RSUP. Dr. M. Djamli Padang in 2015 by Nadila found that 50% of patients suffered from dyslipidemia 33. The differences in results obtained by researchers were due to incomplete data on lipid profile examinations in the medical records of FLD patients. Dyslipidemia is characterized by high levels of triglycerides and low LDL density lipoprotein) and low HDL (high lipoprotein density). Dyslipidemia can be caused by the process of converting glucose into free fatty acids which are stored in the liver in the form of triglycerides, which is known as the process of de-novo lipogenesis 29 [22]. On FLD There is an excessive buildup of triglycerides in hepatocytes, so that there will also be an increase in the export of triglycerides into the blood which causes high levels of triglycerides in the blood. A total of 24 people (28.9%) of FLD patients with HbA1c data had dyspepsia. This is in accordance with research in 2017 by Karn et al. who reported a 2-fold increase in risk in FLD sufferers of experiencing dyspepsia 26 [23].

FLD patients, as many as 13 people (15.7%). This is in accordance with a retrospective cohort study by Chao Yang (2017) which reported that hyperuricemia increased the risk of FLD compared to normouricemia (29% vs 12.9%). The increased risk was more pronounced in women than in men (20.6% vs. 8.3%) 27 [24].

Metabolic syndrome in FLD patients

In this study, 45 (54.2%) FLD patients had metabolic syndrome. The results of this study are not much different from research by Ki Won Moon (2004) which found that 56% of FLD patients had metabolic syndrome 30. A descriptive cross-sectional study by Mukesh (2019) in Nepal found that 57.6% of FLD patients met the criteria for metabolic syndrome based on NCEP-ATP III, out of 385 FLD patients with ultrasound confirmation 35. Cross-sectional observational research conducted at RSUP Dr. Kariadi within a period of 1 year (2009-2010) by Gabriella found 72% of FLD patients who met the criteria for metabolic syndrome 32 [25]. This difference in results is due to incomplete patient data in the medical record, especially waist circumference data [26]. The high number of FLD patients is due to the fact that FLD is one of the clinical manifestations of metabolic syndrome, some also say that FLD is the liver component of metabolic syndrome 30. The high numbers also indicate that metabolic syndrome is closely related to FLD and also type 2 DM 31. This is also due to the presence of insulin resistance that occurs in the body, both in metabolic syndrome and in FLD 3, 14 [27].

Based on the number of components, there were 41 FLD patients with metabolic syndrome (91.1%) with 3 components and 4 people (8.9%) with 4 components. A cross-sectional descriptive study of 385 patients by Mukesh (2019) in Nepal found that at least 91.4% of FLD patients had one component of the metabolic syndrome and only 10.6% had all five components of the metabolic syndrome 35. Research conducted by Nadila (2015) found (30%) patients with 3 components disturbed, (35%) patients with 4 components disturbed, and (35%) patients with 5 components disturbed 33. Other results from research by Gabriella (2012) which found 36.1% of patients with 3 components were disturbed, 41.7 patients with 4 components were disturbed and 22.2% of patients with 5 components were disturbed. This difference could be caused by incomplete medical record data and the small number of samples 32 [28]. The results of research by Gabriella (2012) also did not find any relationship between the number of metabolic syndrome components that were disturbed and the degree of fatty liver assessed using ultrasound 32, 33.

FLD patients with metabolic syndrome were more female than male, namely 24 female (53.3%) and 21 male (46.7%). These results are not different from a cohort study of 304 patients conducted by Marchesini, G. (2003) which found more women (60%) than men (31%) 31. There are more women than men because women tend to experience obesity, hypoHDL, increased waist circumference and hyperglycemia more easily than women. male 31. A cross-sectional observational study conducted by Gabriella (2012) obtained different results, namely that there were more males (66.7%) than females (33.3%) 32. This difference could possibly occur because the number of male samples is larger so bias could occur [29].

Research Limitations

In this research there are several limitations even though it has been attempted and carried out according to scientific procedures, including:

1. Selection bias

Data collection using medical records at the West Jakarta Private Hospital meant that not all FLD patients in the community could be collected.

2. Information bias

In this study, this may have happened because it used medical record data, the data of which was collected by health workers at the hospital, which could result in errors in the collection [30].

3. Confounding bias

The factors that influence FLD examined in this study are age, gender, comorbidities, and HbA1c levels, while there are many other factors that can influence the occurrence of FLD, such as activity, diet patterns, smoking habits, and alcohol consumption [31].

4. CONCLUSION

1. Diabetes HbA1c levels (59%) were higher than prediabetes HbA1c levels (25.3%) and normal HbA1c (15.7%) in FLD patients. In this study, it was found that abnormal HbA1c levels (prediabetes and diabetes) were higher in 39 men (47%) than 31 women (37.3%).
2. Fatty liver disease is more common in the male group than in the female group at 55.4%, with the highest age range being 51-60 years at 34.9%.

3. The most common comorbidities in FLD patients in private hospitals West Jakarta are diabetes mellitus (51.8%), hypertension (33.7%), dyslipidemia (26.5%), dyspepsia (28.9%), and hyperuricemia (15.7%). FLD patients at the West Jakarta Private Hospital were also found to have metabolic syndrome as much as 54.2%, dominated by female gender as much as 53.3% with 91.1% having 3 components of metabolic syndrome and 8.9% having 4 components of metabolic syndrome.

SUGGESTION

1. For researchers

Research can be carried out using a cohort research method so that research bias can be minimized, and subjects suffering from FLD can be differentiated based on the degree of disease

2. For society

The public needs to be educated so they can understand about FLD which can occur at any age, gender and can turn into cirrhosis, liver cancer and other diseases that increase morbidity and mortality.

3. For research sites

More complete and more accurate recording of medical record data at the research site.

4. For further research

Carry out a physical examination or anthropometric measurements so that weight and height data can be obtained to calculate BMI and waist circumference for metabolic syndrome criteria. More in-depth research is needed to assess risk factors.

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