DISTRIBUTION PATTERNS AND RISK FACTORS OF DYSLIPIDEMIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY IN BOGOR, INDONESIA

ABSTRACT

Objective: Type 2 diabetes mellitus (T2DM) patients tend to have abnormal lipid profiles, explaining the association between elevated cholesterol and triglyceride levels in diabetic patients and coronary heart disease. This study aims to evaluate how the common risk factors for dyslipidemia affect the lipid profile of diabetic patients and to determine which factors can be used as predictors for the occurrence of dyslipidemia in T2DM patients.

Methods: A total of 238 diabetic patients (63 male and 175 female; age: 31–70 years) were enrolled in this cross-sectional study. All of them had undergone regular examinations in cohort studies on risk factors for non-communicable diseases conducted by the Ministry of Health in Bogor between December 2017 and January 2018.

Results: The result found that age differences did not affect lipid profile levels, and the females had higher mean values of body mass index (p<0.001), total cholesterol (TC) (p<0.05), and high-density lipoprotein (HDL) (p<0.001) than the males. The most common occurrences of dyslipidemia were high TC level (57.1%), followed by high low-density lipoprotein (LDL) level (47.1%), high triglyceride level (37.4%), and low HDL level (16.4%). Being overweight was found to be the best predictor of dyslipidemia.

Conclusion: The results of this study suggest that in T2DM patients, sex affects TC and HDL levels, whereas age does not exert a significant effect on the lipid profiles. In addition, poor glycemic control, hypertension, and obesity may serve as predictors of dyslipidemia in T2DM patients.

Keywords: Type 2 diabetes, Dyslipidemia, Cardiovascular disease.

INTRODUCTION

Diabetes has become a global concern due to its increasing incidence. The number of patients with diabetes is expected to increase from 425 million in 2017 to 693 million by 2045. The leading cause of morbidity and mortality for patients with type 2 diabetes mellitus (T2DM) is cardiovascular diseases (CVDs) [1]. T2DM is associated with an increased risk of macrovascular diseases such as atherosclerosis, coronary heart disease, and peripheral arterial disease [2]. Independently, diabetes may bring about a two-fold increase in the risk of macrovascular disease [3] as well as increase the effects of other risk factors that cause macrovascular diseases such as smoking, hypertension, and hypercholesterolemia [4]. The mortality rate associated with vascular abnormalities in people with diabetes mellitus is significantly higher than that of non-diabetic individuals [5]. According to the American Heart Association, at least 60% of the people with diabetes aged >65 years die of heart disease, whereas 16% die of stroke [6]. The overall cardiometabolic risk of diabetes is driven by a complex interplay between several non-modifiable (age, sex, and genetics) and modifiable (hypertension, hyperlipidemia, and hyperglycemia) factors and the components of the metabolic syndrome commonly associated with type 2 diabetes [1]. Therefore, patients with T2DM tend to have abnormal lipid profiles, which include increased total cholesterol (TC), increased cholesterol low-density lipoprotein (LDL), increased triglyceride (TG), and decreased cholesterol high-density lipoprotein (HDL) [7]. This explains the association between coronary heart disease and elevated cholesterol and triglyceride levels observed in patients with diabetes [2, 8]. The impairment of sugar metabolism that occurs in patients with T2DM is strongly associated with impaired fat metabolism.

Several known factors that contribute to this include insulin deficiency or resistance, adipocytokines, and hyperglycemia [9].

Indonesia has a high prevalence of diabetes. In 2015, it was the 7th country with the highest T2DM prevalence in the world with a 6% prevalence rate of diabetes-associated deaths. Although dyslipidemia plays an underlying role in diabetes, how its incidence is influenced by other risk factors is not widely known. Rather, unique genetic, cultural, and environmental factors shape the geographic patterns [10]. According to the WHO, the overall prevalence of dyslipidemia in Indonesia in 25-year-old adults

Table 1: Extraction parameters

| Variables               | Sex                      | p  |
|-------------------------|--------------------------|----|
|                         | Male (n=63)               | Female (n=175) |
| Age                     | 53.56±9.11               | 52.85±9.15 | 0.527 |
| Body weight (kg)        | 66.90±11.05              | 63.28±12.40 | 0.022* |
| Body mass index         | 25.65±4.12               | 28.07±4.77 | 0.000* |
| Fasting plasma glucose  | 142.08±55.56             | 152.76±81.81 | 0.718 |
| glucose (mg/dL)         |                          |                  |
| 2-h plasma glucose      | 207.12±105.80            | 228.28±103.23 | 0.061 |
| (mg/dL)                 |                          |                  |
| HbA1c (%)               | 7.20±2.33                | 6.80±2.40 | 0.055 |
| Systole (mmHg)          | 141.61±23.48             | 139.29±21.62 | 0.479 |
| Diastole (mmHg)         | 88.68±11.91              | 88.12±12.94 | 0.734 |

*p<0.05
RESULTS AND DISCUSSION

The prevalence of dyslipidemia in terms of TC, TG, LDL, and HDL showed that the most elevated indices of dyslipidemia were high TC levels (57.1%), followed by high LDL levels (47.1%), high TG levels (37.4%), and low HDL levels (16.4%). In terms of the pattern of dyslipidemia, subjects with two types of lipid abnormalities were the highest (35.3%), followed by three types of abnormalities (21.0%), one type of abnormality (26.9%), and all four types of abnormalities (2.6%). The number of subjects who did not have lipid abnormalities was 64 (26.9%).

Dyslipidemia risk factor

Table 4 showed that being overweight increased the risk of dyslipidemia in the form of abnormalities in the level of TC, TG, and LDL. In addition, being hypertensive increased the risk of abnormalities in the level of TC and LDL. The least predictor of dyslipidemia was poor glycemic control, which increased the risk of abnormalities only in the level of TG.

DISCUSSION

An examination of the biomedical parameters of the diabetes subjects in this study showed that there were no statistical differences in the glycemic characteristics of FPG, OGTT, and HbA1c between the male and female groups. In line with the results of this study, studies in Turkey, in patients at a high risk for diabetes in the US, and in cynomolgus monkeys with impaired FPG, indicate that sex is not associated with glycemic control differences in terms of age, FPG, 2-h PG, HbA1c, and the systolic and diastolic BPs between the male and female groups. However, significant differences were seen in the body weight and BMI, the latter being higher in the females. Although both were significantly different, the BMI levels in both groups fall into the overweight category.

Pattern of dyslipidemia in study subjects

The lipid profiles were stratified in terms of age group and sex. The results in Table 2 showed that there were no statistically significant lipid level differences within each age group. In terms of sex, there were statistically significant differences in TG and HDL level (Table 3). The mean TC in the female group was higher than the male group (p=0.039) while the mean HDL in the female group was also higher compared to the male group (p=0.000).

MATERIALS AND METHODS

This study is a cross-sectional study. We analyzed the database of cohort studies on risk factors for non-communicable diseases carried out by the Ministry of Health in Bogor. This study was approved by the Ethical Committee of the Faculty of Medicine, Universitas Indonesia, and informed consent was obtained from each participant. We collected data on 238 diabetes subjects (31–70 years old) who had received regular examinations in the Ministry of Health cohort study. The data were obtained between December 2017 and January 2018. The diagnosis of diabetes was based on the criteria of the American Diabetes Association as follows: Glycosylated hemoglobin (HbA1c) level ≥5.6%, or a fasting plasma glucose (FPG) level ≥126 mg/dL, or a 2-h plasma glucose level ≥200 mg/dL during a 75-g oral glucose tolerance test (OGTT), or a random plasma glucose ≥200 mg/dL in patients with classic symptoms of hyperglycemia (i.e., polyuria, polydipsia, polyphagia, and weight loss) or hyperglycemic crisis. Dyslipidemia was defined as a TC level ≥200 mg/dL, or a triglyceride level ≥150 mg/dL, or a low-density lipoprotein cholesterol (LDL-C) ≥100 mg/dL, or a high-density lipoprotein cholesterol (HDL-C) ≤40 mg/dL. Poor glycemic control was defined as HbA1c >7%.

Hypertension was defined as taking antihypertensive medications or having a systolic blood pressure (BP) of ≥140 mmHg and/or a diastolic BP of ≥90 mmHg. Overweight was defined as body mass index (BMI) ≥25.

We compared the mean lipid profile data based on sex and the age groups 30–39, 40–49, 50–59, and ≥60. The mean significance test for the age groups was done by ANOVA for normally distributed data and the Kruskal–Wallis test for data that are not normally distributed. The t-test was used to evaluate the sex group for normally distributed data and the Mann–Whitney test for data that are not normally distributed.

We calculated the odds ratios (ORs) for poor glycemic control, hypertension, and overweight by dyslipidemia on each lipid profile (high TC, high TG, high LDL-C, and low HDL-C). Differences with a p≤0.05 were considered statistically significant. All statistical analyses were performed using the SPSS Statistics software (IBM SPSS Statistics version 24 for Windows; IBM, New York, NY, USA).

RESULTS AND DISCUSSION

Subject characteristics

The characteristics of the 238 subjects were divided into male and female sex groups as shown in Table 1. There were no significant differences in the characteristics in terms of age, FPG, 2-h PG, HbA1c, and the systolic and diastolic BPs between the male and female groups. However, significant differences were seen in the body weight and BMI, the latter being higher in the females. Although both were significantly different, the BMI levels in both groups fall into the overweight category.

Lipid profile characteristic based on age and sex

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Levels of lipid profiles based on age group indicate that age does not affect the lipid profile of patients with diabetes. Research on other patients with diabetes showed that the relationship between the age of diabetic subjects with elevated TC, HDL, and LDL values significantly had a negative correlation with a very low correlation coefficient [20]. Another study in elderly subjects showed that HDL level is not correlated with age [21].

The most common pattern of dyslipidemia among the subjects in this study was combined dyslipidemia. Patients with diabetes tend to have high triglycerides, an abnormal blood lipid profile consisting of slightly elevated low-density lipoprotein cholesterol (LDL-C), and moderately decreased high-density lipoprotein cholesterol (HDL-C) [7]. The condition is called atherogenic dyslipidemia and is commonly found in patients with obesity, metabolic syndrome, insulin resistance, and T2DM. It is also an important marker of increased CVD risk [22].

The numbers of patients with diabetes with HDL ≤40 mg/dL were not as much as other lipid abnormalities. In the atherogenesis process, LDL has the most important role while HDL works to reduce the risk. HDL serves to facilitate the excess of cholesterol efflux from cells in the periphery and turning back the cholesterol to the liver for excretion into bile. HDL may also bring enzymes that further can reduce oxidized lipids [23]. Thus, inadequate levels of HDL-C are related to more atherogenic forms of LDL and it commonly seen in T2DM to foil the natural homeostatic process, and contribute to atherogenesis [23]. HDL mean levels in this study at various age levels or different sex were above the standard level (40 mg/dL). Therefore, it may be considered that the subjects in this study have some protection against the formation of atherogenic dyslipidemia.

The OR shows that being overweight is the best predictor of the incidence of dyslipidemia in diabetes because it can significantly increase the risk of abnormalities in TC by 2.280 times, TG by 2.176 times, and HDL by 1.938 times compared to the values in normal-weight people. Based on data from the WHO in 2016, the prevalence of overweight in Indonesia was 24.4% (male 20.7% and female 28.1%) [24]. The prevalence of overweight in female was higher than males, which is consistent with the results of this study. The selection of overweight as a limitation of BMI in this study is based on the high prevalence of overweight in Indonesia compared to the prevalence of obesity (5.7%). Overweight and obesity are one of the main causes of metabolic syndrome that includes insulin resistance, T2DM, and dyslipidemia, all of which are also risk factors for CVD [25]. Another study suggests that overweight school children were 2.4–7.1 times more likely to have elevated TC, LDL cholesterol, and TG compared to normal weight school children [26]. Moreover, overweight adolescents who remained overweight in adulthood were 2.4, 3, and 8 times more likely to have abnormal LDL cholesterol, TG, and HDL cholesterol concentrations than those who remain lean [27].

Hypertension can increase the risk of TC abnormalities by 2.666 and LDL by 2.400 times higher in subjects with normal BP. Research on working-age Japanese males showed that there is a link between hypertension and increased levels of TC, LDL, and non-HDL [28]. Another study conducted in Bangladesh using T2DM patients showed a link between hypertension and an increased risk of abnormal TC levels by 1.50 and HDL by 1.67 times higher [29]. Poor glycemic control can increase the risk of abnormalities 2.176 times higher than in subjects with good glycemic control. Glycemic control can be used as a predictor of the incidence of dyslipidemia [29].

The major limitation of the present study is that the data used were restricted to the Bogor area only. As such, it cannot represent the overall Indonesian situation. With Indonesia being the biggest archipelago country with various tribes and cultural customs, follow-up research studies that utilize larger data are needed to establish the prevalence rate in the whole of Indonesia.

CONCLUSION

Based on the results of this study, we can conclude that in T2DM patients, sex affects the TC and HDL level, whereas age grouping did not show significant differences in any lipid profiles. Poor glycemic control, hypertension, and overweight may serve as predictors of dyslipidemia in T2DM.

ACKNOWLEDGMENTS

This study was funded PITTA Grants by Universitas Indonesia with the data obtained from Directory General of Non-Communicable Disease, Indonesian Ministry of Health.

CONFLICTS OF INTEREST

The author has no conflicts of interest to declare.

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