Risk of Cardiovascular Complication Among Type 2 Diabetes Mellitus Patients in Medan, Indonesia. A Cross-sectional Study

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ABSTRACT

Background: Cardiovascular disease (CVD) is a disease associated with impaired heart and blood vessel function. The occurrence of Diabetes Mellitus (DM) is due to an imbalance in blood glucose that could cause damage to large and small blood vessels and increase platelet aggregation, contributing to atherosclerosis and cardiovascular disease. It could be attributed to high blood pressure, smoking, diabetes, lack of movement, obesity, high cholesterol, unbalanced diet. CVD can be prevented, especially in at-risk groups, with risk assessment utilizing the Framingham Risk Score (FRS).

Objective: The study aimed to analyze the risk of CVD according to the Framingham Risk Score (FRS) in type 2 DM patients.

Methods: The data were collected with the Framingham Risk Score, which consisted of sub-variables of age, total cholesterol, HDL cholesterol, systolic blood pressure (SBP), history of DM, and history of smoking, which were assessed by gender. It was a cross-sectional analytic study with consecutive sampling on 252 respondents, namely DM patients who came for treatment or control to the health centers in Medan and fulfilled the inclusion and exclusion criteria. The data were then analyzed with SPSS.

Results: The respondents consisted of 197 women (78.2%) and 55 men (21.8%). The results were predominated with high risk patients (139, 55.2%), followed by those with medium risks (80, 31.7%), and low risks (33, 13.1%). Chi-square test yielded a significant association between each sub-variable of CVD risk factors and the risks based on FRS in type 2 DM patients.

Conclusion: Each sub-variable of CVD risk factors and the risks on FRS among type 2 DM patients. In future studies, it is recommended to include that a larger number of samples in the community with a balanced proportion of men and women.

Keywords: Cardiovascular disease, Framingham Risk Score (FRS), Diabetes Mellitus, Complications.

1. BACKGROUND

Type 2 Diabetes mellitus (DM) is a chronic disease with the number of patients increasing from year to year along with the growing population. In 2019, DM was the 9th of the top 10 diseases that caused the highest mortality in the world, following a significant increase of 70% since 2000 and is responsible for the largest rise of deaths among the top 10, increasing 80% from 2000 (1). Based on a report from the IDF, around 415 million people in the world have DM, meaning that 1 in 11 people have DM, and one in two people does not know that one has DM. It is predicted that by 2040, the number of people with DM in the world will be 642 million, inferring that one in 10 people in the world will have DM. In Indonesia, the number of people with DM is around 10 million and the country itself occupies the 7th position with the largest number of people with DM in the world (2).

DM reduces a person’s life expectancy by as many as 10 years. The leading cause of death and disability in diabetic patients is cardiovascular disease (CVD). People who have DM have a higher prevalence of CVD compared to those who do not. In a previous study with a total subject of 29,863 patients (5,501 patients with DM and 24,362 patients without), the patients with DM had a 10%, 53%, 58%, and 112% higher risks for coronary heart disease, myocardial infarction, stroke, and heart failure respectively (3). There is a fairly high rate of CVD incidence and mortality in diabetic patients, where the patients have a two to three times higher risks of developing CVD (4). Based on
the high risks of CVD, WHO made a chart of cardiovascular disease risk assessment for the following 10 years which refers to the Framingham Heart Study which has been modified to be simpler. The risk factors include age, gender, smoking behavior, systolic blood pressure (SBP), diabetes mellitus (DM), and blood cholesterol. There are 2 sets of charts, where the first chart is used if blood cholesterol can be measured, and the other chart is used when blood cholesterol cannot be measured (5).

2. OBJECTIVE

This study aimed to analyze the risk of CVD according to the Framingham Risk Score (FRS) in type 2 DM patients in Medan, thus the efforts for prevention can be maximized and reduce the risks of CVD based on the risk levels.

3. PATIENTS AND METHODS

Study Design and ethical considerations

The current study is an analytical and cross-sectional research. It has been approved by the ethical clearance with approval number 902/KEPK/USU/2022. The study was held from September to December 2021. The sample included diabetic patients from primary health centers spread across the city of Medan.

Participants

The samples were selected by consecutive sampling, rounding up to 252 respondents who met the inclusion criteria, namely DM patients who came for treatment or control at the health centers and were willing to participate in the study. The exclusion criteria were patients who had history of heart diseases before DM and those who have had strokes.

Study Procedure

Assessment of risk factors for CVD in 10 years using the Framingham Risk Score (FRS) consisted of the sub-variables age, total cholesterol, HDL cholesterol, systolic blood pressure (SBP), history of DM, and history of smoking assessed by gender. The data were then grouped into 3 CVD risk groups, namely <10% low, 10–19% moderate, and 20% high risks and a demographic questionnaire was provided. Primary data were obtained by taking clinical histories of age and smoking status, blood pressure measurements, total cholesterol and HDL cholesterol values from laboratory examination using a Pentra 400 with Spectrophotometer Colorimeter + Fully Automatic Method. The results of the measurements were then calculated and compared with the controlled normal values in type 2 DM patients.

Statistical analysis

Data analysis was carried out using chi-square test (p > 0.005) on the Statistical Package for Social Science (SPSS) software.

4. RESULTS

Table 1 shows the CVD risk assessment with the sub-variables based on gender the majority of respondents are women (197, 78.2%), and having average age of 55.91 years. The mean total cholesterol was 232.91 mg/dl, HDL cholesterol 48.35 mg/dl, and SBP 145.41 mmHg. As many as 118 (59.9%) people had DM for less than 5 years and there was no family history of DM for 121 (61.5%) people.

None of the female patients had a history of smoking. In contrast, all of male patients admitted to having smoking histories. In male respondents, the mean age was 58.60 years, total cholesterol 236.2 mg/dl, HDL cholesterol 83.35 mg/dl, and SBP 149.4 mmHg. Whereas in female respondents, the mean age was 55.91 years, total cholesterol 232.91 mg/dl, HDL cholesterol 48.4 mg/dl, and SBP 145.4 mmHg. The majority of the male patients have had DM for 5 -10 years and <5 years, accounting to 24 (43.6%) and 22 (40.0%) people respectively, while more than half (118; 59.9%) of the female counterparts had DM for less than 5 years. Both the male (34; 61.8%) and female (121, 61.5%) patients predominantly had no family history of DM.

Table 1. Characteristics of Cardiovascular Disease Risk Assessment with Framingham Risk Score Based on Gender (N=252)

| Characteristics          | Male     | Female   |
|--------------------------|----------|----------|
| Gender                   | N (%)    | N (%)    |
| Male                     | 55 (21.8%) | 197 (78.2%) |
| Female                   | 197 (78.2%) | 55 (21.8%) |
| Average Age (years)      | 58.60    | 55.91    |
| Cholesterol (mg/dL)      |          |          |
| Normal                   | 11 (24.4%) | 48 (23.2%) |
| Borderline high          | 12 (26.7%) | 78 (37.7%) |
| High                     | 22 (48.9%) | 81 (39.1%) |
| Average                  | 236.2    | 232.91   |
| HDL Cholesterol (mg/dL)  |          |          |
| Optimal                  | 16 (35.6%) | 79 (38.2%) |
| Near optimal             | 15 (33.3%) | 68 (32.9%) |
| Low                      | 14 (31.1%) | 60 (29.0%) |
| Average                  | 83.35    | 48.35    |
| Average SBP (mmHg)       | 149.38   | 145.41   |
| Duration of DM (years)   |          |          |
| <5                       | 22 (40.0%) | 118 (59.9%) |
| 5-10                     | 24 (43.6%) | 60 (30.5%) |
| >10                      | 9 (16.4%) | 19 (9.6%) |
| Familial History of DM   |          |          |
| Father                   | 11 (20%) | 39 (19.5%) |
| Mother                   | 8 (14.5%) | 31 (15.7%) |
| Father and mother        | 2 (3.6%) | 6 (3.0%) |
| None                     | 34 (61.8%) | 121 (61.5%) |
| Smoking history           |          |          |
| Yes                      | 55 (100%) | 0 (0%) |
| No                       | 0 (0%) | 197 (100%) |

Table 2. Characteristics of Respondents (N=252)

| Characteristics          | Mean | Median | SD    | Min | Max |
|--------------------------|------|--------|-------|-----|-----|
| Gender                   | 1.78 | 2.00   | 0.414 | 1   | 2   |
| Age                      | 56.60| 55.00  | 8.875 | 35  | 83  |
| Total Cholesterol        | 233.63| 229.00| 45.685| 136 | 399 |
| HDL Cholesterol          | 47.83| 45.50  | 15.828| 22  | 202 |
| SBP                      | 146.28| 145.00| 23.875| 90  | 220 |

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Table 2. Characteristics of Respondents (N=252)
The averages of the participants’ age were 56 ± 8.875 years, total cholesterol 233.6 ± 229 mg/dL, HDL cholesterol 47.8 ± 15.8 mg/dL, and SBP 146.28 ± 23.875 mmHg (Table 2). The risks of CVD in 10 years were divided into 3 categories, the most to the least prevalent group were those (139, 52.2%) with high risks of CVD, medium risks (80, 31.7%), and low risks (33, 12.1 %). The largest number of patients with predicted high risks in CVD were female (92, 46.7%). Similar results could be seen in male patients, with most of them (47, 85.5%) possessed high risks of CVD and 47 men (33.8%) (Table 3).

The relation between CVD risk factors and risk levels based on FRS in type 2 DM patients are presented in Table 4. The confidence interval was set at 95%, with p<0.05 indicating statistically significant data. Gender (p=0.0001), age (p=0.0001), systolic blood pressure (p=0.0001), and family history of type 2 diabetes (p=0.006) are the sub-variables related to the risks of CVD. Whereas total cholesterol (p=0.368), HDL cholesterol (p=0.805), and duration of type 2 DM (p=0.778) do not have significant association with risks of CVD.

### Table 3. CVD Risk Assessment with Framingham Risk Score Based on Gender in Type 2 DM Patients (N=252)

| Characteristics | Male | Female | Total |
|----------------|------|--------|-------|
| Low Risk | 2 | 6 | 47 |
| Medium Risk | 31 | 74 | 92 |
| High Risk | 44 | 92 | 136 |

The occurrence of DM is due to an imbalance in blood glucose that could cause damage to large and small blood vessels and increase platelet aggregation, contributing to atherosclerosis. Increased blood viscosity will then increase blood pressure, leading to stroke or heart disorders. People with diabetes also possess risks of complications such as heart attack and stroke as high as two to three times compared to the individuals without. The occurrences of heart attack or stroke are known as cardiovascular events, ones of the most common complications in diabetic (7). More than three-quarter of the participants in this study were female with a total of 197 (78.2%) people, while the rest were male (55, 21.8%). The average age of the male patients was around 58 years, while female patients was around 55 years. The group with high risks of CVD prediction in 10 years based on gender tend to be male (47, 85.5%), although the highest number seen were female (92, 46.7%) as the percentage of female patients was actually higher than that of male patients. This is in accordance with previous studies that the highest incidence of CVD is in men aged > 45 years (8).

The mean total cholesterol in the male group has similar level to that in the female group, 236.24 and 232.91 mg/dL, respectively, with similar trend in both total cholesterol levels, peaking in high levels (22, 48.9% and 81, 39.1% respectively). Meanwhile, the opposite trend could be seen in HDL cholesterol levels, as both male and female patients mostly had optimal levels (16, 35.6% and 79, 38.2% respectively). However, the mean HDL cholesterol of the male group (83.35 mg/dl) was much higher than that of the female group (48.35 mg/dl). The finding was in line with previous studies which indicated that the elevated levels of conventional lipids indices, including total cholesterol (TC), low-density lipoprotein

### 5. DISCUSSION

Diabetes Mellitus is one of the Non-Communicable Diseases (NCD), which is a global problem. According to the World Health Organization (WHO) in 2018, there were 422 million people in the world suffering from diabetes mellitus, an increase of about 8.5% in the adult population, and it was estimated that there would be 2.2 million deaths due to diabetes mellitus occurring before the age of 70 years, especially in countries with low and middle economic status. Indonesia is the fourth out of the top ten countries in the world with the highest DM prevalence, accounting to 8.6% of the total population. In 2018, the largest number of DM patients were of 55 to 64 years old (6.3%) and 65 to 74 years old (6.03%) (6).

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### Table 4. The Relationship among CVD Risk Factors and Risk Levels based on the Framingham Risk Score in Type 2 DM Patients (N=252)

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cholesterol (LDL-C), and triglycerides (TG), and the reduced level of high-density lipoprotein cholesterol (HDL-C) contributed to the increased risk of CVD incidence (9). However, as HDL had been acknowledged so, there were actually studies stating that the levels of HDL serum hardly correlates with its quality, rendering its predictive value of cardiovascular risks inaccurate (10).

In contrast to optimal levels of HDL cholesterol, the mean SBP in these two groups were classified as high, with 149.38 mmHg in male and 145.41 mmHg in female participants. These data showed that on average, the participants had hypertension along with DM. Previous researches had also reported prevalent hypertension among their samples as a major risk factor for cardiovascular disease, raising the risks to as many as ten folds higher compared to those without hypertension (11, 12).

As many as 24 (43.6%) of the male group had suffered from DM for 5-10 years, while more than half (118, 59.9%) of the female group only had DM for less than 5 years. All male were active smokers, in contrast to the female respondents did not have any history of smoking. More than half of both the male (34, 61.8%) and female (121, 61.5%) patients had no familial history of DM. A research conducted by in 2015 stated that DM could increase the risk of CVD because in people with type 2 DM with insulin resistance, there was an increase in C-reactive protein (CRP) which was an inflammatory mediator. CRP would then attract LDL cholesterol and combine with macrophages to form foam cells which was the beginning of the atherosclerosis process (13).

Smoking is one of the well-known risk factors that contribute to various diseases including type 2 diabetes. Nicotine and other chemical compounds found in cigarettes can reduce insulin sensitivity. Nicotine can increase the levels of the catecholamine hormones, which include noradrenaline and adrenaline. The release of adrenaline will cause an increase in heart rate, blood pressure, respiration and blood glucose. Based on the results of a research on subjects who had smoking habit and a control group, the individuals who smoked >10 cigarettes a day had a 7.15 times higher risk of suffering from type 2 DM compared to light smokers. It was also disclosed that there was a 5 times increased risk of type 2 DM in smokers over 20 years (14).

The majority of male respondents (47, 85.5%) had a high risk of CVD, as with the female (92, 46.7%) counterparts. The incidence of CVD is associated with many factors, including high-density lipoprotein (HDL) cholesterol levels, total cholesterol levels, SBP, familial history of DM, history of diabetes, smoking history, old age, and obesity (15). The relationships between CVD risk factors and risk levels based on FRS in type 2 DM patients were assessed by chi-square test, yielding significant results, namely gender (p = 0.0001), age (p = 0.0001), systolic blood pressure (p = 0.0001), and familial history of type 2 DM (p = 0.006). The results were in line with previous studies, where risk factors such as gender, age, the incidence of hypertension and a family history of DM indicate a higher risk for patients suffering from cardiovascular disease (16). However the studies also yielded significant association with total cholesterol and HDL cholesterol levels in contrast to the results of the current study.

For the gender category, Chi-square test yielded a p value = 0.0001. Thus, it could be concluded that there is a very significant relationship (p <0.0001) between gender and the incidence of CVD in type 2 DM patients. However, the current study had samples with imbalanced gender proportion, inferring the need for further studies with a more balanced one. The incidence of hypertension with p = 0.000 showed a significant relationship with the risk of CVD in type 2 DM patients. This is due to increased oxidative stress and activity of oxygen radical species that will mediate blood vessel damage due to angiotensin-II activation, thereby aggravating the endothelial dysfunction and increasing the risk of CVD (17).

Patients with diabetes often have unhealthy and uncontrolled cholesterol levels, including high LDL cholesterol and triglyceride levels as well as low HDL cholesterol levels. This condition often occurs in patients with early coronary heart disease (18). Theoretically, everyone who suffers from type 2 diabetes is at risk for chronic complications (5-10 years from onset), one of which is coronary heart disease (CHD). However, the people who are at the highest risk are the patients who have had DM for a long period, uncontrolled glucose levels, and histories of hypertension and kidney damage.

The Framingham Heart Study discovered a method to predict the incidence of cardiovascular disease in the next 10 years, namely the Framingham Risk Score. The method is performed by calculating 5 predictors, namely age, smoking history, HDL cholesterol levels, total cholesterol levels, and SBP. FRS is often considered the reference standard but it has limited accuracy as it tends to overestimate the risks in low-risk populations as well as underestimate in high-risk populations. The use of FRS in this study was limited by the sub-variable assessment which required laboratory results, namely total cholesterol and HDL cholesterol as they can be a hassle to be carried out by the general population alone. Thus it is necessary to consider a simpler risk assessment measuring instrument which can be utilized by the community or risk groups with guidance from health providers.

6. CONCLUSION

The risk of cardiovascular disease complications based on the Framingham Heart Study in patients with type 2 Diabetes Mellitus in Medan were mostly high. There were significant association among CVD risk levels with gender, age, systolic blood pressure, and familial history of DM. Furthermore, it is recommended to study a larger sample size with balanced gender proportion using a simpler cardiovascular disease risk assessment instrument that has been adapted to the Indonesian community.

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