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Risk Factors of Chronic Kidney Disease (CKD) in Type 2 Diabetes Mellitus (DM) Patients at Dr. Soetomo General Academic Hospital, Surabaya

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A B S T R A C T

Introduction: Type 2 diabetes mellitus (DM), categorized as a non-communicable disease, has become a global health concern. This study aimed to identify the risk factors for chronic kidney disease (CKD) in type 2 DM patients at Dr. Soetomo General Academic Hospital, Surabaya.

Methods: This was a case-control study. The samples were collected using consecutive sampling methods from the medical records Dr. Soetomo General Academic Hospital, Surabaya. The total samples were 158 patients consisting of 79 cases and 79 controls. Independent variables were a history of uncontrolled HbA1c levels; hypertension; high triglyceride (TG) levels; low high-density lipoprotein (HDL) levels, high low-density lipoprotein (LDL) levels, and being overweight. The dependent variable was CKD. Samples were analyzed using the Chi-Square test and logistic regression.

Results: From six independent variables that were analyzed, two variables had significant results based on the Chi-Square test. Logistic regression was performed and showed the significant results between risk factors of CKD and type 2 DM patients at Dr. Soetomo General Academic Hospital, Surabaya, were a history of hypertension (OR = 3.801, 95% CI = 1.875-7.706) and a history of low HDL levels (OR = 3.356, 95% CI = 1.650-6.827). The highest risks were a history of hypertension followed by a history of low HDL levels.

Conclusion: Type 2 DM patients at Dr. Soetomo General Academic Hospital, Surabaya, with a history of hypertension and low HDL, had a greater risk of developing CKD.

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Introduction

Type 2 diabetes mellitus (DM), categorized as a non-communicable disease, has become a global health concern. The prevalence of DM has been increasing over the years. According to the data from International Diabetes Federation (IDF), approximately 463 million people aged 20-79 had DM in 2019 and are estimated to become 578.4 million in 2030.[1] Type 2 DM is estimated to play a role in contributing to 90% of DM worldwide.[1]

Type 2 DM may lead to further complications, including damage to the kidneys and cause chronic kidney disease (CKD).[2] This can increase morbidity and mortality in type 2 DM patients. Data obtained from a global survey showed that in 1990, approximately 408.6 thousand patients died due to CKD, and 46.3 thousand died due to CKD caused by DM.[3] In 2013, it increased with approximately 956.2 thousand patients dying due to CKD, and 173.1 thousand patients died due to CKD caused by DM.[3]

It is important to understand the risk factors of type 2 DM to prevent the incidence and further progression of CKD. One of the risk factors is uncontrolled HbA1c levels, which can affect kidney function by disrupting the metabolism pathways in glycolysis, Krebs cycle, and oxidative phosphorylation.[4] Hypertension impacts kidney damage by increasing intraglomerular pressure, microvascular disruption, inflammation and causing loss of kidney function.[5] Thus, elevated triglyceride (TG) levels are known to correlate with a higher incidence of CKD, but the complete mechanism still cannot be explained.[6] Microvascular complications caused by TG elevation are suspected of causing impaired renal function.[6] High-density lipoprotein (HDL) has antioxidant, anti-inflammatory, and protective effects, which means low HDL will reduce its protective function.[7] The negative effect of oxidized low-density lipoprotein (LDL) in vessels can be prevented by HDL.[7] Low HDL levels can lower the glomerulus filtration rate (GFR) and increase the risk of albuminuria.[7]

Type 2 DM patients usually have elevated LDL levels followed by increasing oxidized LDL, which causes inflammation, oxidative stress, and fibrosis in the kidney.[8,9] Being overweight is known to increase CKD risk. This is related to the rise of leptin levels, mechanical stress, and fat deposition in renal sinuses, causing toxic effects, hypertrophy of the glomerulus, death of podocytes, and compressed blood vessels in the kidneys.[10]

Several studies have been conducted associated with the risk factors of CKD. However, each study had different variables, designs, places, and sample amounts. Therefore, this study aimed to identify the risk factors for CKD among patients with type 2 DM at Dr. Soetomo General Academic Hospital, Surabaya. Through this study, the results obtained were expected to give additional information. Hence, the incidence of CKD can be reduced, and preventive steps can be taken by knowing the risk factors.

Methods

The case-control study approach was used in this observational analytical research. The population of this study were patients with type 2 DM. The samples were gathered using secondary data from medical records Dr. Soetomo General Academic Hospital, Surabaya, in 2016-2020. The samples were chosen by consecutive sampling. The inclusion criteria were that patients must be at least 18 years old, and the exclusion criteria were patients without complete data in the medical records. This study obtained ethical approval from Ethical Committee for Health Research Dr. Soetomo General Academic Hospital, Surabaya.

This study consisted of a case group, type 2 DM patients, and a control group, type 2 DM patients with CKD. Each group consisted of 79 patients. Therefore, the total sample was 158 patients. The independent variables in this study were a history of uncontrolled HbA1c levels, a history of hypertension, a history of high TG levels, a history of low HDL levels, a history of high LDL levels, and a history of being overweight. The dependent variable was CKD. This study used Chi-Square test analysis to determine the significant difference between each risk factor and CKD. Logistic regression analysis was used to analyze all dependent variables, which were significant from the previous Chi-Square test to the dependent variable. The samples were analyzed using IBM SPSS statistics version 25.

Results

Table 1. Characteristic of risk factors between case and control groups

Variables	Case		Control	
	n	%	n	%
History of uncontrolled HbA1c levels				
HbA1c ≥ 7%	58	73.4%	52	65.8%
HbA1c < 7%	21	26.6%	27	34.2%
History of hypertension				
BP ≥ 140/90 mmHg	59	74.7%	31	39.2%
BP < 140/90 mmHg	20	25.3%	48	60.8%
History of high TG levels				
TG ≥ 150 mg/dl	48	60.8%	38	48.1%
TG < 150 mg/dl	31	39.2%	41	51.9%
History of low HDL levels				
HDL < 40 mg/dl	46	58.2%	20	25.3%
HDL ≥ 40 mg/dl	33	41.8%	59	74.7%
History of high LDL levels				
LDL ≥ 100 mg/dl	65	82.3%	65	82.3%
LDL < 100 mg/dl	14	17.7%	14	17.7%
History of being overweight				
BMI ≥ 25 kg/mm²	28	35.4%	24	30.4%
BMI < 25 kg/mm²	51	64.6%	55	69.6%

Source: Research data, processed

Based on Table 1, the characteristics of type 2 DM patients in the case and control group, the majority were uncontrolled HbA1c levels, high LDL levels, and no history of being overweight. There was a difference in the majority

of patient characteristics between the two groups for the history of hypertension, history of high TG levels, and history of low HDL levels; 58 (73.4%) and 52 (65.8%) patients, respectively. The majority of samples in the case group had a history of hypertension (74.7%), a history of high TG levels (60.8%), and a history of low HDL levels (58.2 %). Meanwhile, in the control group, the majority did not have a history of hypertension, high TG levels, or low HDL levels.

Table 2. Chi-Square test analysis between risk factors and CKD

Variables	OR	95% CI	p
History of uncontrolled HbA1c levels	1.434	0.725-2.837	0.299
History of hypertension	4.568	2.316-9.008	0.000
History of high TG levels	1.671	0.888-3.141	0.110
History of low HDL levels	4.112	2.091-8.085	0.000
History of high LDL levels	1.000	0.442-2.263	1.000
History of being overweight	1.258	0.647-2.447	0.498

Source: Research data, processed

From Table 2, It could be known whether the risk factors were significant for CKD or not from the p-value. Results were said to be significant when the p-value < 0.05. The Chi-Square test analysis showed no significant difference for the history of uncontrolled HbA1c levels, high TG levels, high LDL levels, and being overweight since the p-value was < 0.05. As a consequence, these dependent variables were considered insignificant risk factors. The p-value for the Chi-Square analysis related to hypertension history using the Chi-Square test was p = 0.000 (OR = 4.568, 95% CI = 2.316-9.008), meaning it was significant. Thus, type 2 DM patients who had a history of hypertension had 4.568 times greater risk of suffering CKD compared to those who did not. Significance was also earned for the history of low HDL levels in this study. Its Chi-Square p-value = 0.000 (OR = 4.112, 95% CI = 2.091-8.085), meaning type 2 DM patients with a history of low HDL levels were at 4.112 times more likely to suffer CKD.

Table 3. Analysis of the history of hypertension and history of low HDL levels using logistic regression

Variables	OR	95% CI	p
History of hypertension	3.801	1.875-7.706	0.000
History of low HDL levels	3.356	1.650-6.827	0.001

Source: Research data, processed

Discussion

This study demonstrated that individuals with type 2 DM did not significantly increase their risk of CKD by having a history of uncontrolled HbA1c levels. These results were in line with a study by Nazzal, *et al*. (2020), which stated there was no relationship between HbA1c and the incidence of CKD.[11] Even so, this study was contrary to a study by Jitraknatee, *et al*. (2020), which found significant results of uncontrolled HbA1c levels with HbA1c ≥ 7% related to developing CKD (OR = 3.32, 95% CI = 2.20–5.01).[12] The study involved 1,094 patients based on a cross-sectional study design.[12] The sample size and the study design might impact differences in the study results. In its early stages, CKD is often asymptomatic and only detected when other symptoms or complications appear.[13] This could cause type 2 DM patients with decreased kidney function but not yet manifested symptoms and complications were undiagnosed. Several factors, including the age at which DM was first diagnosed and the duration of suffering, also affected the risk of a person suffering from CKD.[14]

From logistic regression analysis in this study, it can be interpreted that type 2 DM patients with a history of hypertension were more likely to develop CKD (OR = 3.801, 95% CI = 1.875-7.706). The results were in accordance with a study by Maulana, *et al*. (2018) at Sultan Agung Hospital and Semarang Hospital, which stated that hypertension was a risk factor associated with terminal-stage CKD in diabetic patients (OR = 17.47, 95% CI = 2.06-147.77).[15] Nazzal, *et al*. (2020) showed a significant relationship between type 2 DM patients with a history of hypertension and the incidence of CKD (OR = 5.7, 95% CI = 2.2–15.2).[11] Similarly, *Palo, et al.* (2021) stated that there was a significance between patients with a history of hypertension for more than five years with CKD (OR = 4.24, 95% CI = 1.23-10.05).[16] Guidelines by the Indonesian Endocrinology Society (PERKENI) recommended maintaining blood pressure < 140/90 mmHg in diabetic patients.[17]

The Chi-Square test analysis showed no significance between the history of high TG levels and CKD in type 2 DM patients. These results were different from a study by Xie, *et al*. (2019), which found that increasing TG levels had a significant impact on the incidence of CKD (OR = 1.81, 95% CI = 1.28–2.57).[18] The study used a cross-sectional study design located in 15 major cities in China and involved 2,484 patients.[18] When further analysis was performed, it was found that elevated TG levels were associated with CKD in both diabetic patients and non-diabetic patients.[18] Another study by Shimizu, *et al*. (2015) in Kyushu and Okinawa with a cohort study design involving 1,824 patients found that elevated TG levels were connected with CKD.[19] The difference, especially in sample size, research design, and geographic area, could deliver different outcomes.

A history of low HDL levels was deemed to be another significant risk factor in this study based on logistic regression analysis (OR = 3.356, 95% CI = 1.650-6.827). The study of Ikawati, *et al*. (2018) at Dr. Kariadi Central General Hospital Semarang and Semarang General Hospital support this, which also got significant results (OR = 3.120, 95% CI = 1.080-9.040).[20] From a study by Bramlage, *et al*. (2019), it was also known that patients with type 2 DM along with CKD had lower HDL levels (men = 40

mg/dl; women = 46.4 mg/dl) compared to those who did not suffer from CKD (men = 42 mg/dl; women = 50 mg/dl).[21] Kawachi, *et al*. (2019) found low HDL levels related to CKD progression and low kidney survival rate.[22]

Based on the Chi-Square test result, the history of high LDL levels was insignificant to cause CKD. This is similar to a study by Zaman, *et al*. (2018) that did not get a significant difference.[23] Ikawati, *et al*. (2018) at Dr. Kariadi Central General Hospital Semarang and Semarang General Hospital also got insignificant results.[20] High LDL levels often show poor clinical outcomes that vary and mainly cause vascular disorders.[24] This insignificant result could be caused by external factors, such as lifestyle modification of the patients by maintaining nutritional intake and exercise, and patients who were given treatment such as statins.[24]

History of being overweight in type 2 DM patients was not a significant risk factor for CKD based on the Chi-Square test analysis. The results were in accordance with a study by Rini, *et al*. (2015) at Dr. Soedarso General Hospital Pontianak, which stated that type 2 DM patients who were overweight with a body mass index (BMI) ≥ 25 kg/m^2 were not significantly correlated to CKD.[25] However, Pinto, *et al*. (2021) found that people with obesity had a 1.81 times higher risk of developing CKD (OR = 1.81, 95% CI = 1.52-2.16).[26] The experimental research using rats by Salim *et al.* (2018) showed that a high-fat diet, which results in obesity, could damage the kidney by contributing to glomerulosclerosis, tubular defects, inflammation, and other histopathological changes in the kidney.[27] Chang, *et al*. (2018) explained that the measured BMI did not fully represent the variation in the composition of each body. Therefore, BMI was not accurate enough to determine its effect on CKD.[28]

Strength and Limitations

Through this study, risk factors for type 2 DM patients in developing CKD at Dr. Soetomo General Academic Hospital, Surabaya, were identified. Hence, risk factors management could be taken. From risk factors that had been analyzed, it could be known which risk factor that had greatest impact for developing CKD. Still, there could be bias in data that were collected since this was retrospective study and external variables were not included in this study.

Conclusion

In this study, from six independent variables analyzed, two variables showed significant results, meaning patients with type 2 DM at Dr. Soetomo General Academic Hospital, Surabaya, were at risk for CKD if they had a history of hypertension and low HDL. The risk factors that had the greatest impact sequentially were a history of hypertension followed by a history of low HDL.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Ethical Clearance

This study had received ethical clearance from Ethical Committee for Health Research Dr. Soetomo General Academic Hospital, Surabaya (no. 0719/LOE/301.4.2/XII/2021) on 8 December 2021.

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