Conference Paper

Risk Factors Associated with End-Stage Renal Disease in Type 2 Diabetes Mellitus Patients

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Abstract

Diabetes Mellitus is a chronic disease and has various complications, including diabetic nephropathy. This complaint is found in 20-40% of diabetes patients and a primary cause of end-stage renal disease. Identifying risk factors has an important role in the implementation of various health promotion and disease prevention activities. This research aims to know the risk factors which related to end-stage renal disease. This is an analytic descriptive study with a case control approach. The study involves 23 people in the test group and 46 in the control group. Bivariat analysis showed risk factors for end-stage renal disease are duration of DM (p-value:0.028), diet pattern (p-*value*: 0.000; OR: 13.5), hypertension (p-*value*: 0.036; OR: 2.9), smoking (p-*value*: 0.027; OR: 3.3), alcohol consumption (p-*value*: 0.034; OR: 0.3). While sex (p-*value*: 0.222), history of renal disease in the family (p-*value*: 0.09), activities (p-*value*: 0.149/0.457), dyslipidemia (p-*value*: 0.561) and HbA_{1c} (p-*value*: 0.246) are not risk factors of end-stage renal disease. The risk factors correlated with end-stage renal disease is duration of DM suffered, smoking habit, drinking alcohol, diet pattern, hypertension. It is recommended that nurses develop a nursing care standardization focused on preventive effort to minimize complication, especially end-stage renal disease.

Keywords: Diabetes Mellitus, End-stage Renal Disease, Risk factors

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1. Introduction

Diabetes Mellitus (DM) is a metabolic disease characterized by high glucose level in the blood (hyperglycemia) caused by disturbance in insulin secretion or insulin resistance or both [1]. Type 2 DM is the most widely found which is around 90% of all DM and often occurred in the age of 40 years and above [2].

DM is one of many chronic diseases with increasing prevalence each year. World Health Organization (WHO) estimated that type 2 DM patients in Indonesia will increase to triple fold and at 2030 will reach 21.3 millions [3]. Patients with type 2 DM have risks of complications in various organs. Issues encountered by type 2 DM are complicated in relation with acute and chronic complications. One of the microvascular complications is diabetic nephropathy which is chronic progressive and irreversible with end-stage

renal disease as the worst outcome. This condition requires care which is expensive. The increase in the incidence of type 2 DM will significantly increase the incidence of nephropathy [4]. Diabetic nephropathy is a renal disease caused by diabetes mellitus [5]. DM is the primary cause of end-stage renal failure in The USA [6].

Diabetic nephropathy were found in 20-40% of diabetes patients and a primary cause of end-stage renal disease [7]. End-stage renal disease is often found in DM patients after they have DM for 10-20 years [8]. Epidemiology study conducted by Craig, et al [9] showed that in 40 years, only 10% DM patients with nephropathy survived and 70% of DM patients without nephropathy survived. The above fact showed that end-stage renal disease caused by diabetic nephropathy is an important cause of death among DM patients. End-stage renal disease as final stadium of renal disease, occurred when approximately 90% nephron mass were destructed. In this condition, the value of glomerular filtration rate is only 10%. In this condition, serum creatinine and urea nitrogen level in the blood will increase sharply as a result from the decrease of the glomerular filtration rate [10].

Several cross-sectional and longitudinal studies identified risk factors related to the development of diabetic nephropathy, such as: hypertension, blood glucose level, cholesterol level, smoking, older age, insulin resistance, sex, race (black), and high protein diet [11]. [12] also found risk factors which accelerate the progressivity of renal disease, i.e. hyperglycemia, hypertension, dyslipidemia, smoking, high fat and high protein diet. Another study conducted by Yokota, Kimura and Inenaga (1994) about risk factors for progressivity acceleration in diabetic nephropathy found impacts of hypercholesterolemia and smoking. Bhattacharya [13] concluded that factors which increase risks of diabetic nephropathy are genetics component, hypertension, the increase of GFR value, blood, and race. Another study about factors which influence the progressivity of DM complications is lifestyle. Lifestyle has a role in the development and progressivity of a chronic disease. Lifestyle includes smoking habit, lack of activities, poor diet, alcohol consumption, and drug abuse [14]. Lifestyle modification may be implemented through client empowerment approach, starting with enhancement of the client's knowledge concerning his/her illness. As part of a team, a nurse may plan, arrange, and coordinate care with other health workers, giving care, education, and health promotion [15]. Identifying risk factors also has an important role in the implementation of various health promotion and disease prevention activities. DM is a chronic disease and has various complications, therefore, identifying risk factors is needed in order to be able to modify those risks [16].

2. Methods

The design of this study is analytic descriptive with case control (retrospective study) approach. Sample taken using consecutive sampling technique matched by age. The aim is to identify risk factors related to end-stage renal disease cases in Hasan Sadikin Hospital Bandung.

23 respondents of case group and 46 respondents of control group were recruited according to inclusion and exclusion criteria. The instrument used a questionnaire containing risk factor data, International Physycal Activity Questionnaire, and Diit Pattern questionnaire. Each instrument has been tested for validity and reliability. Statistical analysis used were univariate, bivariate with chi-square categorical data and Mann Whitney test for numerical data.

This research has passed the process of ethics committee from Faculty of Nursing University of Indonesia and Hasan Sadikin Hospital, Bandung

3. Results

There were a higher percentage of male (60.9%) in the case-group while in the control-group female has higher percentage, i.e. 24 persons (52.2 %). In the case-group, there were 4 persons with history of renal disease in the family (17.4%), while in the control-group, there were only 2 persons (4.3%). Most respondents in the case-group have academy or university degree, which were 11 persons (47.8%) similar to the control-group, where the education level of the respondents mostly is academy or university graduated, which were 15 persons (32.6%). In the case-group, most respondents did not work, which were 17 persons (73.9%), similar to the control-group, where most respondents did not have any occupation, i.e. 27 persons (58.7%). Most respondents have strenuous activities in the case-group which were 11 persons (47.8%) while in the control-group, most respondents have light activities which were 19 persons (41.3%). Smoking habit distribution showed that the case-group and the control-group have similar number or smokers which were 11 persons (47.8%) and 12 persons (52.2%) respectively. There were only 3 (13.0%) respondents in the case-group have alcohol drinking habit while in the control-group, all respondents which were 46 persons (100%) never consumed any alcoholic drink. Diet pattern distribution showed that most respondents in the case-group have unhealthy diet pattern which were 19 persons (82.6%), in contrast with the control-group, where the highest proportion which were 34 persons (73.9 %) have healthy diet pattern. There were a greater proportion of hypertension history prior to

Table 1: Respondents distributions according to sex, education, occupation, complication, family history, activity level, smoking habit, alcohol drinking habit, diet, hypertension, dyslipidemia, and blood glucose level control in Hasan Sadikin Bandung (n case = 23, n control = 46)

No	Variable	Case (n = 23)	Control (n = 46)		
		N	%	n	%
1	Sex				
	- Male	14	60,9	22	47,8
	- Female	9	39,1	24	52,2
2	Renal disease history in the family				
	- Yes	4	17,4	2	4,3
	- No	19	82,6	44	95,7
3	Education				
	- Elementary school	5	21,7	11	23,9
	- Junior High School	4	17,4	7	15,2
	- High School	3	13	13	28,3
	- University	11	47,8	15	32,6
4	Occupation				
	- Not working	17	73,9	27	58,7
	- Civil servant/Army/Police	6	26,1	13	28,3
	- Others	0	0	6	13
5	Activities				
	- Light activities	8	34,8	19	41,3
	- Moderate activities	4	17,4	16	34,8
	- Strenuous activities	11	47,8	11	23,9
6	Smoking habits				
	- Yes	11	47,8	10	21,7
	- No	12	52,2	36	78,3
7	Alcohol drinking habit				
	- Yes	3	13	0	0
	- No	20	87	46	100
8	Diet pattern				
	- Healthy	4	17,4	34	73,9
	- Unhealthy	19	82,6	12	26,1
9	Hypertension				
	- Yes	16	69,6	20	43,5
	- No	7	30,4	26	56,5
10	Dislipidemia				
	- Yes	13	56,5	34	73,9
	- No	5	21,7	12	26,1
	- No data	5	21,7	0	0
11	HbA1c				
	- Well (< 7)	2	8,7	19	41,3
	- Not well (> 7)	7	30,4	27	58,7
	- No data	14	60,9	0	0

end-stage renal disease in the case-group which were 16 persons (69.9%) compare to the control-group, which were 26 persons (56.5%). Dyslipidemia distributions showed that in the case-group, 13 (56.5%) persons have dyslipidemia history, and in the control-group there were also a high proportion of dyslipidemia history, which were 34 (73.9%) persons. Glycosylate hemoglobin level were not well in 7 (30.4%) respondents in the case-group, and the same condition were found in the control-group, where a higher proportion of the respondents, i.e. 27 (58.7%) persons did not have a well controlled glycosylate hemoglobin level.

Table 2: Respondents distributions according to age, duration of having DM, duration of having renal disease, duration of smoking, amount of cigarette smoked, and duration of alcohol consumption in type 2 DM patients (n case = 23, n control = 46)

Group	Mean	Median	SD	Min-Max	95% CI
Age					
-Case	58.2	58	6.7	43 - 69	55.3 - 61,0
-Control	58.7	59.5	7.7	41 - 70	56.4 - 61,0
Duration of DM					
-Case	10,0	7,0	8,8	1-35	6,2 - 13,8
-Control	5.8	4	5.2	1-35	4.3 – 7.4
Duration of renal disease	2.1	1	2.4	1-35	1.1 – 3.2

From the data above, we can see that the mean age of patients in the case-group was 58.2 (CI: 55.3 – 61.0) years old with SD 6.7 years, where the youngest participant was 43 years old and the oldest participant was 69 years old. Mean age in the control-group was 58.7 (CI: 56.4 – 61.0) years old with SD 7.7 years, where the youngest participant was 41 years old and the oldest participant was 70 years old. The above table also showed that mean duration of having DM in the case-group was 10 (CI: 6.2 – 138) years, while in the control-group was 5.3 (CI: 4. 3 – 7.4) years. Mean duration of having renal disease in type 2 DM patients was 2.1 (CI: 1.1 – 3.2) years, with SD 2.4 years.

Table 3: The association of duration of DM with end-stage renal disease in type 2 DM patients (n case=23, n control=46)

Group	Mean	Median	SD	P Value
(years)				
- Case	10	7	8.8	0.028
- Control	5.83	4	5.2	

The table above showed that mean duration of DM in the case-group was 10 years with SD 8.8, while mean duration of DM in the control-group was 5.8. Nonparametric statistical test (Mann-Whitney test) showed p-value= 0.028, which means with alpha value of 5% there was a relation between duration of DM with end-stage renal disease.

Table 4: Associations of sex, activities, diet pattern, smoking habit, alcohol consumption, hypertension, dyslipidemia, blood glucose control with end-stage renal disease in type 2 DM patients

Variable	Case		Control		P-Value	OR (95% CI)
	N	%	N	%		
Sex						
- Male	14	60.9	22	47.8	0.222	1.7
- Female	9	39.1	24	52.2		(0.6 – 4.7)
Family history						
- Yes	4	17.4	2	4.3		4.6
- No	19	82.6	44	95.7	0.09	(0.78 – 27.5)
Activity						
- Light activity	8	34.8	19	42.2		
- Moderate activity	4	17.4	15	33.3	0.457	0.6(0.2-2.3)
- Strenuous activity	11	47.8	11	24.4	0.149	2.4(0.7-7.7)
Smoking habit						
- Yes	11	47.8	10	21.7		3.3
- No	12	52.2	36	78.3	0.027	(1.1 – 9.7)
Alcohol consumption						
- Yes	3	13	0	0		0.3
- No	20	87	46	100	0.034	(0.2 – 0.4)
Diet pattern						
- Unhealthy	19	82.6	12	26.1	0	13.5
- Healthy	4	17.4	34	73.9		(3.8 – 47.6)
Hypertension						
- Yes	16	69.6	20	43.5	0.036	2.9
- No	7	30.4	26	56.5		(1.0 – 8.6)
Dyslipidemia						
- Yes	13	56.5	34	73.9	0.561	0.9
- No	5	21.7	12	26.1		(0.3 – 3.1)
HbA1c						
- Well (< 7%)	2	8.7	19	41.3	0.246	2.5
- Not well (> 7%)	7	30.4	27	58.7		(0.5 – 13.2)

Table 4 showed that risk factors for end-stage renal disease are: diet pattern (p-*value*: 0.000; OR: 13.5), hypertension (p-*value*: 0.036; OR: 2.9), smoking (p-*value*: 0.027; OR: 3.3), alcohol consumption (p-*value*: 0.034; OR: 0.3). While sex (p-*value*: 0.222), history of renal disease in the family (p-*value*: 0.09), activities (p-*value*: 0.149/0.457), dyslipidemia (p-*value*: 0.561) and HbA_{1c} (p-*value*: 0.246) are not risk factors of end-stage renal disease.

4. Discussion

In this research, there were more male with end-stage renal disease compare to female respondents. However, it is not statistically significant. This is in line with the previous studies. A study by [17] also concluded that sex is not a factor that influenced severe nephropathy (p = 0.181). Another research by [18] stated that there were a difference in the incidence of end-stage renal disease in different countries. In Sweden, ratio female and male were 1:1.7, while in The USA 1:1.4. It appears that end-stager renal disease was more likely to be found in males compare to females. Some researchers thought that there may be an influence of hormonal factors such as testosterone and estrogen. However, other researchers assumed that other than cell degradation, lifestyle such as smoking and drinking alcohol were more often to be found in males compare to females, and these factors were the actual cause of the increased risk for end-stager renal disease.

Statistic test showed that duration of having DM is not a risk for renal failure (p=0.083). This finding is similar to a study by [11], where Chi Square test gave a p value=0.276, which means there was no significant association between duration of DM with end-stage renal disease. However, there was another study conducted in Dr. Kariadi Hospital Semarang which showed that there was a significant association between duration of DM with complications [19]. Several literature explained that approximately 35-45% patients with type 1 were found to have diabetic nephropathy after 15-20 years, while 20% of type 2 DM patients were most likely to develop diabetic nephropathy 5 to 10 years after diagnosis [2]. Another explanation for why duration of DM does not have a significant relation with end-stage renal disease is inaccuracy in the recording of the first onset of DM. Delay in establishing diagnosis of DM may be due to unawareness of the patients that they had DM. Respondents with end-stage renal disease were commonly unaware that they have DM, therefore they came to the hospital with complications. Small sample size may also allow “chance” to influence the analysis.

Bivariate analysis for history of renal disease in the family gave p-value=0.09 and OR=2.469, which means that patients with history of renal disease in their family were 2.469 times more likely to develop end-stage renal disease compare to patients without history of renal disease in their family. This is not contradictory with studies done by [13] and [20] which convey that genetic factor is one of the important factors which may cause end-stage renal disease in type 2 DM patients. One genetic component which may have contribution is angiotensin converting enzyme (ACE) gene type. Results from

19 studies showed that there is a possible association between ACE gene type and diabetic nephropathy. ACE gene is a potential vasoconstrictor which convert angiotensin-I (Ang-I) into angiotensin-II (Ang-II). Mutant D allele in ACE gene may increased the level of angiotensinn-II, and high level of angiotensin-II can cause renal damage [20].

Bivariate analysis for activity variable resulted dummy OR value. OR for activity (1) is 0.6, which means that patients with moderate activity have 0.6 times higher risk compare to patients with light activity. OR for activity (2) is 2.4, which means patients with strenuous activity have 2.4 times higher risk compare to patients with moderate activity. A study by [21] showed that activity level is a factor strongly related to BMI (p=0.035), but it is not directly related to HbA1c. [22] in [21] stated the same thing; there was no significant difference of HbA1c level between intervention group and control group after 12 weeks of training activity. This finding is contradictory with other arguments and studies, such as [23] which said that regular physical activities improve blood glucose level and may prevent development of type 2 DM. Physical activities protect DM patients from fat accumulation effect. Training activities recommended for type 2 DM patients were aerobic training such as jogging, cycling, swimming, aerobic calisthenics, etc.

Bivariate analysis gave evidence that there was a significant association between diet pattern with end-stage renal disease (p-value=0.000); OR=10.178, which means that patients with unhealthy diet have 10.178 times higher risk of having end-stage renal disease compare to patients with healthy diet pattern. This finding is in line with several other studies, such as Diabetes Control and Complication Trial (DCC) which showed that lifestyle is related to normal HbA1C level. An example of healthy lifestyle is adherence to a consistent meal schedule and compliance to recommended diet pattern [24]. A prospective study with intervention to lifestyle such as diet pattern showed that there was a difference in the incidence of type 2 DM which were 4.3 cases in the intervention group and 7.4 in the control group out of 100 people each year (p = 0.0001) [25]. Diet pattern is related to meal pattern and the amount of food consumed by diabetes patients where the amount of protein, carbohydrate, and fat, and meal time were adjusted for diabetes patients to avoid hyperglycemia as well as hypoglycemia. Healthy diet pattern recommended for Diabetes patients was DASH diet, where diet pattern adjusted would be food consists of vegetables (4-5 servings/day), fruits (4-5 servings/day, low-fat or non-fat milk (2-3 servings/day), meat, fowl, or fish (2 servings/day). [24] convey that healthy lifestyle to stabilize blood glucose level consist of having meal in consistent times every day, reduce or avoid beverages with sugar of artificial sweetener, and consistently having snack during night time.

Bivariate analysis showed that there is an association between smoking habit with end-stage renal disease (OR=3.3; 95% CI: 1.1 – 9.9), which means that the risk of end-stage renal disease in patients with smoking habit is 3.3 times higher than those who did not smoke. [26] explained in their study that there is a relation between smoking with type 2 DM nephropathy (OR=1.61; 95% CI: 1.01 to 2.58), whereas from 61% patients with smoking habit, 26% had micro albuminuria and 14% had severe nephropathy. Another study conducted by [17] showed a significant result of the effect of smoking to advanced nephropathy or end-stage renal disease (OR=1.464; p-value=0.011). A cross sectional study by dilakukan [27] about the relation between smoking, drinking alcohol, and chronic renal failure found a relation between smoking and development of chronic renal failure (OR=2.1; 95% CI: 0.78 –1.51). A different study about relation between smoking habit with chronic renal failure showed an increase in the odds ration each year of the increase in the number of cigarette smoked and conversely, the OR went down since the year of smoking stopped [27]. In contrary, a study by [28] concluded that there was no relation between the decreases of GFR with diabetic nephropathy. However, smoking were assumed to have association with the increase in micro albuminuria. The mechanism of renal failure in relation to smoking remains uncertain. However, smoking may cause damages such as renal atherosclerosis, systemic and hemodynamics damage, and disturbs the function of renal endotelial cells [27].

Bivariate analysis found a relation between hypertension and end-stage renal disease (p= 0.036; OR=2.9; 95% CI: 0.1 – 8.6), where DM patients with hypertension have 2.9 times higher risk of end-stage renal disease compare to those without hypertension. This study is in line with several other previous studies such as Oklahoma Indian Diabetes Study about type 2 DM which stated that hyperglycemia and hypertension were related to the increase of end-stage renal disease risk [29]. [17] did a regression test and found a p-value < 0.004 in the systolic pressure but there were no significant result in the diastolic pressure (OR= 1.034; p-value=0.048). A retrospective study about the risk of end-stage renal disease also add to association between hypertension to end-stage renal disease [13]. There was a slight difference in a study by [11] in Semarang. It describes that one of the risk factors associated with end-stage renal disease was diastolic hypertension (OR=15.03; 95% CI: 2.25-100.43). Another study by [29] also found a similar result, the increase in the diastolic pressure above 95 mmHg have the risk of renal failure 9.81 times higher than individuals with diastolic pressure < 95 mmHg. Hypertension occurred in one third of diabetes patients, and it is believed that hypertension in type 2 DM has a relation with diabetic nephropathy, directly as well as indirectly, like causing renal vascular disease. In general, hypertension

affect the perfusions of the body systemically, causing damages to organs especially kidney. Systolic hypertension is known to contribute to major arteriosclerosis of the blood vessels, increase in the plasma volume, increase in the peripheral resistance, and decrease of renin activity [30].

Bivariate analysis found no significant relation between blood glucose control with renal failure (p=0.246; OR=2.5) which means that patients with poor blood glucose control were at risk of 2.5 times higher to have end-stage renal disease, but the relation was not statistically significant. A well known study stated that a tight monitoring of blood glucose level reduces the risk of nephropathy and other complications, but the relation between the risk of nephropathy and hyperglycemia was not linear with HbA1c cut-off [29]. Diabetes Control Complication Trial (DCCT) stated that a tight blood glucose monitoring lowers the progressivity of diabetic nephropathy to terminal renal failure [9]. The result in this study was not statistically significant may be because we were not able to find a complete data of blood glucose control in the medical records of end-stage renal disease patients.

Bivariate analysis showed a relation between alcohol drinking habit with end-stage renal disease (p-value=0.034; OR = 0.3 95% CI: 0.2 – 9.9). Patients with alcohol drinking habit have 0.3 risk of end-stage renal failure compare to those who have not alcohol drinking habit. However, the result was not statistically significant (95% CI includes 1), because of the small number. A study by [27] found a relation between alcohol drinking habit with end-stage renal disease (OR=1.99). According to the study, only heavy drinkers showed significant relation with end-stage renal disease, they were the ones who consumed at least 4 standard drink every day. Alcohol consumption have relation with the increase risk of type 2 DM, especially in individuals with history of DM in the family [31]. Calories contained in alcohol hamper body weight decrease in many ways. Alcohol contains high calories (7 calories per gram) and human body processed alcohol in similar way to the process of fat. Drinking alcohol also diminishes self-control and people tend to consume more calories as a result [24].

5. Conclusion

Sex is not a risk factor for end-stage renal disease. History of renal disease in the family is also note a risk factor of end-stage renal disease, but bivariate analysis showed OR=4.6 which means that patients with history of renal disease were at risk 4.6 higher to have end-stage renal disease. Duration of DM is not a risk factor for end-stage renal disease. Hypertension is not a risk factor end-stage renal disease, but bivariate

analysis showed OR=2.9 which means that patients with hypertension have a 2.9 times higher risk of end-stage renal disease compare to patients without hypertension. Blood glucose control is not a risk factor for end-stage renal disease, but bivariate analysis showed OR=2.5, which means that patients with poor blood glucose control have 2.5 times higher risk of end-stage renal disease compare to those with well blood glucose control. Dyslipidemia is not a risk factor for end-stage renal disease. Diet pattern is a risk factor for end-stage renal disease, bivariate analysis showed OR=13.5 which means that patients with unhealthy diet pattern have 13.5 times higher risk of end-stage renal disease compare to those with healthy diet pattern. Smoking habit is not a risk factor for end-stage renal disease, but bivariate analysis showed OR=3.3, which means that patients with smoking habit have 3.3 times higher risk of end-stage renal disease compare to those who did not smoke. Alcohol drinking habit is not a risk factor for end-stage renal disease. Activity is not a risk factor for end-stage renal disease.

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Conflict of Interest

The authors have no conflict of interest to declare.

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