The risk factors of Chronic Kidney Disease in type 2 Diabetes Mellitus

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Abstrak

Latar belakang*: Penderita Diabetes melitus (DM) yang tidak ditangani dengan baik akan menimbulkan komplikasi Nefropati Diabetika sebagai penyebab utama dari Gagal Ginjal terminal. Tujuan penelitian ini adalah untuk menentukan faktor risiko Gagal Ginjal pada pasien DM tipe 2.*

Metode: *Desain penelitian ini adalah potong lintang yang meneliti faktor risiko Gagal Ginjal pada pasien rawat jalan DM tipe 2 di bagian penyakit dalam RSUD kota Bekasi mulai tanggal 01 September 2015 sampai dengan 30 September 2015. Data primer dikumpulkan melalui kuesioner terstruktur. Sampel dalam penelitian ini berjumlah 246 purposive individual sampling (107 pria dan 139 wanita). Analisis data mempergunakan SPSS versi 21 dan EPISTAT versi 3.3*

Hasil: *Faktor risiko gagal ginjal yang terkait dengan perjalanan penyakit DM tipe 2 adalah: umur saat didiagnosis DM 36-54 tahun (ORa=2.41; p=0.01); menderita DM 6-10 tahun dan lebih dari 10 tahun setelah didiagnosis (ORa=4.30; p=0.000 vs ORa=18.54; p=0.000). Dibandingkan dengan kadar glukosa darah awal 201-300 mg/dl, responden dengan kadar gula darah awal 401-500 mg/dl dan lebih dari 500 mg/dl masing-masing berisiko Gagal Ginjal 5.63 kali dan 11.11 kali (p=0.000 vs p=0.000). Kadar glukosa darah tertinggi >500 mg/dl berisiko Gagal Ginjal 5.86 kali dibandingkan dengan 201-300 mg/dl (p=0.000).*

Kesimpulan: *Usia pada saat didiagnosis DM, lamanya menderita DM setelah didiagnosis, kadar glukosa darah awal dan kadar glukosa darah tertinggi >500 mg/dl merupakan faktor-faktor risiko Gagal Ginjal.* **(Health Science Journal of Indonesia 2018;9(1):19-24)**

Kata kunci: *Faktor risiko, progresi DM tipe 2, Gagal Ginjal*

Abstract

Background: A condition when Diabetes Mellitus patients does not get an adequate medical treatment, will cause Diabetic Nephropathy, which is a major cause of a terminal Chronic Kidney Disease (CKD). The objective of this study is to determine risk factors of CKD in patients with type 2 DM.

Methods: Design of this study was a cross sectional, that investigated risk factors of CKD in outpatients who suffered type 2 DM at Department of Internal Medicine of Bekasi General Hospital from the 1st of September to the 30th of September, 2015. Primary data was collected through structured questionnaires. Sample in this study was 246 purposive individual sampling (107 male and 139 female). The data analysis used SPSS version 21 and EPISTAT version 3.3.

Results: The risk factors of CKD related to progressive of Diabetes Mellitus type 2 disease were: age at first diagnosed of DM 36-54 years (ORa=2.41; p=0.01), suffering DM 6-10 years and more than 10 years after being diagnosed (ORa=4.30; p=0.000 vs ORa= 18.54; p=0.000). Referring to initial blood glucose levels of 201-300 mg/dl, the respondents with initial blood glucose levels of 401-500 mg/dl and more than 500 mg/dl had the risk of CKD 5.63 times and 11.11 times respectively (p=0.000 vs p=0.000). The highest blood glucose levels >500 mg/dl had the risk of CKD 5.86 times compared with 201-300 mg/dl (p=0.000).

Conclusion: Age at first diagnosed of DM, duration of suffering DM post diagnosed, initial blood glucose levels, and the highest blood glucose levels >500 mg/dl were the risk factors of CKD. **(Health Science Journal of Indonesia 2018;9(1):19-24)**

Keywords: Risk factors, progressive of type 2 DM, CKD

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia in the long term due to impaired of insulin secretion, impaired work mechanism of insulin or both. Management of DM requires sustainable medical care with strategy of decreasing risk factors and controlling blood sugar levels.[1,2] According to Kidney Disease Death Rate by Countries, DM mortality rate in Indonesia was 29.5 per 100.000 population and rank number 92 out of 192 countries.[3] If DM patients are not treated properly, it will result in Diabetic nephropathy[4] that represents a major cause of a terminal CKD.[5,6] Incidence of CKD in Indonesia in recent years has tended to increase. Mortality rate due to kidney disease in Indonesia is 21.54 per 100.000 population and rank number 54 out of 183 countries.[7]

Risk factors of CKD consists of the modifiable and non-modifiable factors. The non-modifiable risk factors include age at first diagnosed of having DM, years of suffering from diabetes, initial blood glucose levels and highest blood glucose levels.[8] From previous study at Kandou Hospital in Indonesia was known that there was a significant relationship between long-suffering DM with CKD. Percentage of CKD patients with type 2 DM who suffered DM <10 years were 30% and >10 years: 70%.[9]

A clinical studied during 5-7 years revealed that controlling blood glucose levels intensively would reduce disease progressive of DM and prevent complications of DM (Diabetic Nephropathy and CKD), both in patients with type 1 and type 2 DM.[10] The meaning by controlling blood glucose levels was pre-prandial blood glucose level of 90-130 mg/dl and post prandial <180 mg/dl.[10] Since the previous study, it has been known that some risk factors influence the progressive of type 2 DM to develop CKD. The aim of this study was to determine the risk factors of CKD in patients of type 2 DM so that the progressive of type 2 DM disease to become CKD can be controlled. The benefit of this study is in the prevention program of diabetics to resolve the complications of CKD

METHODS

Design of the study was cross sectional that investigated risk factors of CKD in outpatients with type 2 DM at Department of Internal Medicine of Bekasi General Hospital from the 1st of September to the 30th of September, 2015. The study applied purposive individual sampling that comprises 107 males and 139 females diabetics. The inclusion criteria of respondent in this study encompasses (1) out patients of type 2 DM at RSUD Bekasi Hospital (2) Indonesian citizens (3) the age was ≥ 17 years old (4) have no complication diseases of type 2 DM except CKD. The study tools were questionnaires with nominal, ordinal, and numerical data. The questionnaires consist of the independent variables include gender, age, age at diagnosed DM for the first time, duration of suffering DM after being diagnosed, the initial blood glucose level when diagnosed DM, the highest blood glucose level during suffering DM and also whether the respondents suffering CKD (dependent variable).

By DM in this study using the current WHO diagnostic criteria for diabetes: fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl) or 2 h post prandial plasma glucose ≥ 11.1mmol/l (200 mg/dl).

Definition of operational of CKD in this study refers to the National Kidney Foundation criteria. According to the National Kidney Foundation, criteria for CKD meets one of these criteria: (1) kidney damage occured over three months with structural and functional abnormalities accompanied with or without decreasing of glomerular filtration rate (GFR); (2) Glomerular filtration rate (GFR) less than 60 ml/min/1.73m2 for 3 months with or without kidney damage.

The characteristics of demographic were age, gender, age at diagnosed of DM and duration of suffering DM. The variable of age was classified into: (1) 17-35; (2) 36–54 and (3) >55 years old. Duration of suffering DM based on questionnaire was categorized into 3 subcategorized: (1) 5 years (2) 6- 10 years (3) > 10 years. The characteristics of disease consist of initial blood glucose level and the highest blood glucose level. The blood glucose level (mg/dl) was classified into four categories: (1) 201 – 300; (2) 301 – 400; (3) 401 – 500; (4) >500.

The data were edited at the time of data entry and then analyzed using SPSS version 22 and EPISTAT version 3.3. Furthermore univariate analysis of the description of the demographic characteristics and DM characteristics were conducted . Bivariate analysis was then performed with statistical tests of Odds Ratio to determine the relationship between demographic characteristics as well as the progression of the disease and blood glucose levels of patients with type 2 DM towards CKD.

This study was approved by the Ethics Commitiee for research, Faculty of Medicine, Christian University of Indonesia with letter number 205/FK UKI/07.2015.

RESULTS

Table 1 showed a description of the sociodemographic characteristics of patients. The average age of patients was 54.11 years. The highest number of patients (50.81%) was in group of age ≥55 years and the female group (56.50%). The average age at diagnosed DM was 45.37 years. The majority of patients at the time of DM diagnosed had the ages of 36-54 years (58.54%) and suffered DM for 6-10 years after being diagnosed. (41.06 %). Initial blood glucose levels at the time of diagnosis of DM were mostly (38.62%) in the range of 301-400 mg/dl, while the majority of respondents (36.18%) have the highest blood glucose levels of 301-400 mg/dl.

Table 1. Distribution of respondents by sociodemographic characteristics of type 2 DM disease and others

Variabel	Respondent		
	N	%	Average
Gender			
Female	139	56.50	
Male	107	43.50	
Age (y)			
17 – 35	9	3.66	
36 – 54	112	45.53	54.11
≥55	125	50.81	
Age at diagnosed of DM (y)			
17 – 35	32	13.01	
36 – 54	144	58.54	45.37
≥55	70	28.45	
Duration of suffering DM (y)			
1 – 5	96	39.02	
6 – 10	101	41.06	7.25
>10	49	19.92	
Initial blood glucose level (mg/dl)			
201 – 300	78	31.71	
301 – 400	95	38.62	356.15
401 – 500	55	22.36	
>500	18	7.31	
The highest blood glucose level (mg/dl)			
201 – 300	28	11.38	
301 – 400	89	36.18	404.30
401 – 500	85	34.55	
>500	44	17.89	

Table 2 showed the description of the risk of CKD in DM characteristics of the respondents and blood glucose level. The lowest ratio of CKD were the group of age at diagnosed DM ≥ 55 year, suferring DM 1-5 years, initial blood glucose levels 201-300 mg/dl and the highest blood glucose levels 201-300 mg/dl.

Referring to the lowest ratio, this study revealed that the high risk significantly of CKD was age of diagnosed of DM 36-54 y (OR=2.60), duration of suffering DM 6-10 years and more than 10 years after being diagnosed (OR=4.41 vs OR= 21.70), initial blood glucose level 401-500 mg/dl (OR=5.51) and more than 500 mg/dl (OR=12.05) and the highest blood glucose level >500 mg/dl (OR=6.05).

Furthermore, age at diagnosed of DM 17–35 years, initial blood glucose level 301–400 mg/dl, the highest blood glucose level 301–400 mg/dl and 401–500 mg/dl were not significantly on the risk of CKD.

Table 3 (final model) revealed that the patients on age at diagnosed 36-54 years had the risk of CKD 2 times higher compared to age at diagnosed DM ≥ 55 year group significantly. (95% CI=1.21–6.12; p=0.01).

The longer of suffering DM and the higher initial blood glucose level will enhance the risk of CKD. The patients who had blood glucose levels >500 mg/dl after being diagnosed DM had risk of CKD 6 times compared to patients with blood glucose 201-300 mg/dl.(95% CI=1.71-17.86; p=0.01).

DISCUSSION

The present study revealed that there was a relationship between age at DM diagnosed with CKD. The patients on age at diagnosed DM 36-54 years had the risk of CKD 2 times higher compared to age at diagnosed DM ≥ 55 years significantly. The younger a person when diagnosed of diabetes, the more likely the occurrence of CKD. The study result of Baltimore Longitudinal Study of Aging showed that increasing of age will decline in average creatinine clearance of 0.75 ml/min/year either without kidney disease or other comorbidities. Over 30 years old, GFR will decline 1 ml/min/1.73m^2. Comorbidities (DM) will accelerate the decline in GFR and thus increase the risk of CKD.[11,12]

Tefera G study involving 700 patients with type 2 DM found that there was relationship between age at diagnosed of DM with CKD. The respondents who were diagnosed with diabetes aged 41-48 years had 4.4 times higher risk of suffering CKD (p=0.05; 95% CI=1.0-19.6) compared with the 25-32 year age group.[13]

Table 2. The risk factors of CKD in DM characteristics of the respondents and blood glucose level

Variable	CKD		Non CKD		Crude	95% CI (p value)
	n	%	n	%	OR	
Gender						
Female	35	25.18	104	74.82	1	
Male	29	27.10	78	72.90	1.10	0.62-1.96 (0.73)
Age (yo)						
17–35	0	0	9	100	NA	
36–54	36	32.14	76	67.86	1	
≥55	28	22.40	97	77.60	0.61	0.34-1.09 (0.09)
Age at diagnosed of DM (yo)						
≥ 55	11	15.71	59	84.29	1	
17–35	6	18.75	26	81.25	1.24	0.41-3.71 (0.69)
36–54	47	32.64	97	67.36	2.60	1.25-5.40 (0.008)
Duration of suffering DM (yo)						
1–5	7	7.29	89	92.71	1	
6–10	26	25.74	75	74.26	4.41	1.81-10.73 (0.00)
>10	31	63.27	18	36.73	21.70	8.35-57.42 (0.00)
Initial blood glucose level (mg/dl)						
201–300	9	11.54	69	88.46	1	
301–400	21	22.11	74	77.89	2.18	0.93-5.07 (0.07)
401–500	23	41.82	32	58.18	5.51	2.29-13.25 (0.00)
>500	11	61.11	7	38.89	12.05	3.72-39.01 (0.00)
The highest blood glucose level (mg/dl)						
201–300	5	17.86	23	82.14	1	
301–400	11	12.36	78	87.64	0.65	0.20-2.06 (0.52)
401–500	23	27.06	62	72.94	1.71	0.58-5.02 (0.45)
>500	25	56.82	19	43.18	6.05	1.94-18.86 (0.00)

OR = Odds Ratio;   95% CI = 95% Confidence Interval

Table 3. The relationship between the risk factors of type 2 DM and CKD

Variable	CKD		Non CKD		Adjusted	95% CI (p value)
	n	%	n	%	OR	
Age at diagnosed of DM (y)						
≥55	11	15.71	59	84.29	1	
36–54	47	32.64	97	67.36	2.41	1.21-6.12 (0.01)
Duration of suffering DM (y)						
1–5	7	7.29	89	92.71	1	
6–10	26	25.74	75	74.26	4.30	1.61-9.11 (0.01)
>10	31	63.27	18	36.73	18.54	7.81-51.18 (0.00)
Initial blood glucose level (mg/dl)						
201–300	9	11.54	69	88.46	1	
401–500	23	41.82	32	58.18	5.63	1.96-7.54 (0.00)
>500	11	61.1	7	38.89	11.11	3.18-37.21 (0.00)
The highest blood glucose level (mg/dl)						
201–300	5	17.86	23	82.14	1	
>500	25	56.82	19	43.18	5.86	1.71-17.86 (0.01)

From the variable of duration of suffering diabetes after being diagnosed, it was known that there was a relationship between duration suffering DM with CKD. The longer a person suffers from DM, the greater the probability of the occurrence of CKD. Within 1-2 years after the appearance of clinical symptoms of DM, morphologic changes occur in the kidney. This change causes hyperfiltration serum proteins into the urine, mainly albumin. Ekstracelullar matrix accumulation leads to expansion of mesangium. Mesangium expansion associated with the occurrence of mesangium sclerosis. This leads to chronic glomerulosclerosis and increase the risk of CKD.[14]

Khalid Al-Rubeaan et al found a relationship between long-suffering DM with CKD. Respondents who suffer diabetes 5-9 years had 1.57 times higher risk of suffering CKD (95% CI=1.34-1.82; p<0.001;). While respondents suffered from diabetes >10 years had a higher risk of 2.45 times to suffer CKD (95% CI=2.11-2.83; p<0.001).[15]

Our study revealed that there was significant correlation between the initial blood glucose level >400 mg/dl with the incidence of CKD. This study conformed to the previous study (Valmir Jose Filho Crestani et al) that conducted with study design of a cohort involving 65 patients and stated that there was a relationship between initial blood glucose levels with CKD (RR=2.53; 95% CI=1.95-6.72).[16,17]

When blood glucose level reaches >500 mg/dl, the excess blood glucose will enter the cells through GLUT-1 glomerulus. This situation activates the polyol pathway, PKC (Protein Kinase C) pathway, hexosamine pathway thereby increasing the accumulation of AGEs (Advanced Glycosilation End-Products) pathway, which result in damage to the capillaries glomerulus.[18] Our study result conformed to research by Adam T. Whalley et al stated that there was a relationship among the highest blood glucose levels with CKD (OR=1.28; 95% CI=1.16 to 1.41; p<0.001).[19]

In conclusion, the risk factors of CKD were age at diagnosed of DM, duration of suffering DM after being diagnosed, the initial blood glucose level and the highest blood glucose level more than 500 mg/dl. Based on these risk factors, everyone who have family history of DM or have tendency to suffer DM should perform early detection of increasing blood glucose levels and risk factors. Thus the progress of CKD can be controlled

Acknowledgments

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