

The Relationship between Type 2 Diabetes Mellitus with Chronic Kidney Disease In Indonesian Population In 2014-2015 (Data Analysis of IFLS 5)

Hubungan Diabetes Melitus Tipe-2 dengan Penyakit Ginjal Kronis pada Penduduk Indonesia Tahun 2014-2015 (Analisis Data IFLS 5)

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ABSTRAK

Penelitian *Global Burden of Disease* pada tahun 2010 mengungkapkan bahwa kasus penyakit ginjal kronis mengalami peningkatan dan menjadi masalah kesehatan serius. Data Riskesdas tahun 2013 mengungkapkan bahwa proporsi penderita gagal ginjal kronis usia ≥ 15 tahun berdasarkan diagnosis dokter sebesar 0,2% dan 0,6%. Penelitian ini bertujuan menganalisis hubungan diabetes mellitus tipe 2 dan penyakit ginjal kronis pada penduduk di Indonesia. Desain penelitian ini adalah *cross-sectional* dan menggunakan data sekunder, yaitu Indonesia Family Life Survey ke-5 (IFLS5). Jumlah minimal sampel dalam sebanyak 792 orang dengan teknik *total sampling* dimana ditemukan sebanyak 34.012 orang yang memenuhi kriteria inklusi dan eksklusi. Analisis bivariat hubungan antara diabetes mellitus tipe 2 dan penyakit ginjal kronis dalam penelitian ini. Penelitian ini menunjukkan prevalensi penyakit ginjal kronis pada populasi Indonesia pada tahun 2014 - 2015 adalah 1%. Hasil uji *chi-square* dari hubungan antara diabetes mellitus tipe 2 dan penyakit ginjal kronis pada penduduk Indonesia menunjukkan POR = 2,48 (*p-value*=0,0002; 95% CI 1,422-4,071). Analisis multivariat dengan uji regresi logistik dihasilkan POR 1,88 (95% CI 1,124-3,168; *p-value*=0,016) setelah status merokok dan riwayat kolesterol tinggi dikontrol. Penderita diabetes melitus tipe 2 diharapkan melakukan upaya pengobatan yang tepat untuk mencegah komplikasi penyakit ginjal kronis

Kata Kunci: Penyakit ginjal kronis, diabetes melitus tipe 2, IFLS-5, Indonesia

ABSTRACT

The *Global Burden of Disease* research in 2010 reveal that cases of chronic kidney disease increase and became a serious health problem. Indonesia Basic Health Research data in 2013 reveal that the proportion of patients with chronic kidney failure aged ≥ 15 years old based on doctor's diagnosis was 0,2% and 0,6% kidney stones. The study aimed to analyze the relationship between type 2 diabetes mellitus and chronic kidney disease in the population of Indonesia in 2014-2015. This design of research used cross-sectional and secondary data from the Indonesia Family Life Survey (IFLS) 5. The minimum sample size in this study was 792 people with technique used total sampling, which found 34,012 people who meet the inclusion and exclusion criteria. The prevalence of chronic kidney disease in Indonesia population in 2014 - 2015 was 1%. The result of chi-square test of the relationship between type 2 diabetes mellitus and chronic kidney disease in the Indonesian population showed POR=2.48 (95%CI 1.422-4.071; *p-value* =0.0002). Multivariate analysis with logistic regression tests POR 1.88 (95% CI 1.124 - 3.168; *p-value* = 0.016) after smoking status and history of high cholesterol were controlled. Patients with type 2 diabetes mellitus expects to make appropriate treatment efforts to prevent complications of chronic kidney disease.

Key words: chronic kidney disease, type 2 diabetes mellitus, IFLS-5, Indonesia

Introduction

Chronic kidney disease is a structural or functional abnormality of the kidney for 3 months manifestation by kidney damage (pathological abnormalities, signs of kidney damage in urine or blood, or imaging abnormalities) or a GFR value < 60 mL/min / 1.73m^2 (with or without damage kidney).¹ The *Global Burden of Disease* research in 2010 reveal that cases of chronic kidney disease increase and became a serious health problem. Chronic kidney disease is the 27th leading cause of death in the world in 1990 and increases to 18th in 2010.² Indonesia Basic Health

Research data in 2013 reveal that the proportion of patients with chronic kidney failure age ≥ 15 years base on doctor's diagnosis is 0.2% and 0.6% live from kidney stones.³ IFLS5 data (5th Indonesia Family Life Survey) shows a greater proportion of chronic kidney disease, which is 1%, or 1 out of 100 Indonesians suffer from chronic kidney disease.

The most common cause of CKD is diabetes.⁴ Diabetes mellitus (DM) is a chronic disease that requires good glycemic control and strategies to reduce risk factors. A kidney is an organ in the body that is potentially

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affected by diabetes mellitus. Globally, the percentage of type 2 diabetes is greater than 90%.⁵ The prevalence of some degree of CKD among adults with type 2 diabetes is 40%.⁴ Until now, research on the relationship between diabetes mellitus and kidney disease with IFLS5 data has never been done so the researchers are interested in this topic.

Method

This research used a cross-sectional study design and secondary data, namely the 5th Indonesia Family Life Survey (IFLS 5). IFLS is an on-going longitudinal survey. The population in IFLS5 was same as in IFLS1, all households in 13 provinces in Indonesia.⁶ The minimum sample size in this study was used to hypothesis testing for difference two proportions.⁷ For study type 2 diabetes mellitus and chronic kidney disease in the Indonesian population, minimum sample size was 792 people for 2 proportions.^{8,9} The sampling technique in this study used total sampling in which found as many as 34,012 people who met the inclusion and exclusion criteria will be included as a sample. The inclusion criteria of respondents were all residents in Indonesia, both living in urban and rural areas. Respondents were excluded if they were diagnosed with kidney disease before being diagnosed with diabetes mellitus, history of hypertension, and history of high cholesterol. This was to ensure exposure occurs before the outcome. Besides, respondents who had missing data would be excluded from this study.

The independent variable was type 2 diabetes mellitus (T2DM). The categorization of type 2 diabetes mellitus was divided into yes T2DM and non-T2DM. Type 2 diabetes mellitus if ever diagnosed by health workers (doctor, paramedic, nurse, or midwives) had diabetes mellitus and was diagnosed with diabetes when they are ≥ 30 years old.^{10,11} Whereas non-T2DM, if it had never been diagnosed with diabetes mellitus during life until the study was conducted. Also, those who answered did not know, had missing data and were diagnosed at age <30 years were excluded from the study sample. Diagnosed T2DM was self-reported by the respondent, so the laboratory diagnosis conducted can vary among them could be HbA1c, random blood sugar, and fasting blood sugar. The dependent variable in this study was the occurrence of chronic kidney disease. Chronic kidney disease (CKD) was divided into chronic kidney disease and non-chronic kidney disease. It was chronic kidney disease if it had been diagnosed by a healthcare provider (doctor, paramedic, nurse, or midwives) and kidney

disease duration ≥ 1 year.^{12,13} It was non-CKD if the patients had never been diagnosed with kidney disease until the study was conducted. Those who answered did not know, had missing data, and were diagnosed with kidney disease <1 year, would be excluded from the study sample. The covariate variables in this study were age, sex, smoking status, history of hypertension, and history of high cholesterol (total or Low-Density Lipoprotein/LDL). Data analyzed using univariate, bivariate, and multivariate. The magnitude of risk in the bivariate analysis was measured through the prevalence odds ratio (POR) and analyzed using chi-square with 95% confidence intervals. Multivariate analysis was performed by the logistic regression test. No ethical issue in this research because secondary data was using pseudonyms or replacements can protect the subject's identity.

Result

Out of 34,012 respondents, 1% had chronic kidney disease, 2.1% had type 2 diabetes mellitus, 3.92% had a history of high cholesterol and 12.04% had a history of hypertension. The proportions of respondents in this study were mostly female (52.34%), aged less than 60 years (88.44%), and non-smokers (63.31%).

In table 1, it presented that type 2 diabetes mellitus variable had a significant relationship with chronic kidney disease. Respondents with type 2 diabetes mellitus had a 2.48 times greater risk of having chronic kidney disease compared to respondents without type 2 diabetes mellitus. Other variables that might become potential confounders in this study were gender, smoking status, history of high cholesterol, and history of hypertension. The results of a multivariate analysis used logistic regression tests was presented in Table 2. Respondents with type 2 diabetes mellitus had a 1.74 times greater risk to suffer from chronic kidney disease compared those without type 2 diabetes after age, sex, smoking status, history of high cholesterol, and history of hypertension were controlled.

The interaction test between the main independent variables (type 2 diabetes mellitus) and the covariate variables (age, sex, smoking status, history of high cholesterol, and history of hypertension) on chronic kidney disease was presented in Table 3. From table 3, there was no interaction variable on the relationship between type 2 diabetes mellitus and chronic kidney disease in the Indonesian population because $p\text{-value} > 0.05$. Next, to

Table 1. Bivariate Analysis to Identify The Relationship of Independent Variables, Covariate Variables to The Dependent Variable

Variable	Chronic Kidney Disease				Total	POR	95% CI	p-value
	Yes (n=341)		Non (n=33671)					
	N	%	n	%				
Type 2 Diabetes Mellitus								
Yes	17	2.38	696	97.62	713	2.48	1.422 – 4.071	0.0002
Non	324	0.97	32975	99.03	33348	1.00	Reference	
Age (mean=38;SD=16.05)								
= 60 years old	47	1.20	3884	98.80	3931	1.18	0.879 – 1.676	0.1964*
<60 years old	294	0.98	29787	99.02	30081	1.00	Reference	
Gender								
Man	201	1.24	16010	98.76	16211	1.58	1.268 – 1.981	<0.0001
Women	140	0.79	17687	99.06	17801	1.00	Reference	
Smoking status								
Smoker	131	1.21	10697	98.79	10825	1.51	1.203 – 1.900	<0.0001
Ex-smoker	37	2.24	1617	97.76	1654	2.84	1.974 – 4.043	
Non smoker	173	0.80	21360	92.20	21533	1.00	Reference	
History of high cholesterol								
Yes	29	2.18	1303	97.82	1332	2.31	1.51 – 3.398	<0.0001
No	312	0.95	32368	99.05	32680	1.00	Reference	
History of hypertension								
Yes	61	1.49	4034	98.51	4095	1.60	1.191 – 2.123	0.0009
No	280	0.94	29637	99.06	29917	1.00	Reference	

* not significant (p-value> 0.05)

Table 2. Full Model Relationship between Type 2 Diabetes Mellitus and Chronic Kidney Disease, In Indonesian Population In 2014-2015

Variable	POR	95% CI	p-value
Type 2 Diabetes Mellitus	1.74	(1.029 – 2.941)	0.039
Age	0.96	(0.697 – 1.341)	0.840
Gender	1.26	(0.923 – 1.733)	0.143
Smoking status			
Smoker	1.33	(0.965 – 1.839)	0.000
Ex-smoker	2.17	(1.422 – 3.336)	0.081
History of high cholesterol	1.84	(1.219 – 2.792)	0.004
History of hypertension	1.41	(1.039 – 1.910)	0.027

Table 3. Interaction Test between Type 2 Diabetes Mellitus and Covariate Variable with Chronic Kidney Disease, In Indonesian Population, In 2014-2015

Variable Interactions	p-value	Remarks
Type 2 diabetes mellitus*age	0.132	Not an interaction
Type 2 diabetes mellitus*gender	0.595	Not an interaction
Type 2 diabetes mellitus* status smoking	0.980	Not an interaction
Type 2 diabetes mellitus*history of high cholesterol	0.335	Not an interaction
Type 2 diabetes mellitus* history of hypertension	0.787	Not an interaction

evaluated whether a covariate variable was a confounder or not by calculating the difference POR between POR crude (before covariate variable l leaves

the model) and POR adjusted (after covariate variable leaves the model). When the difference POR of independent variable > 10%, then the variables out of the model was a confounding variable,^[14] so it should be put back in the analysis (table 4).

Table 4. Confounding Test between Type 2 Diabetes Mellitus and Covariate Variable with Chronic Kidney Disease, In Indonesian Population, In 2014-2015

Variable	POR crude	POR adj	ΔPOR%	Remarks
Full Model	1.74			
Without age	1.74	1.73	0.58	Not Confounding
Without gender	1.73	1.74	0.57	Not Confounding
Without history of hypertension	1.74	1.88	2.28	Not Confounding
Without smoking status	1.88	2.02	11.88	Confounding
Without history of high cholesterol	1.88	2.31	32.82	Confounding

Based on the table 4, we knew that there were 2 confounding variables in this study, namely smoking status and history of high cholesterol. Based on the results of the interaction test and confounding test, the final model obtained in this study was as follows:

Based on table 5, respondents with type 2 diabetes mellitus had a 1.88 times greater risk of having chronic kidney disease compared to respondents without type 2 diabetes mellitus after smoking status and history of high cholesterol were controlled (p-value = 0.016; 95% CI 1.124 - 3.168).

Table 5. Final Model Relationship between Type 2 Diabetes Mellitus and Chronic Kidney Disease, In Indonesian Population, In 2014-2015

Variable	POR	95% CI	p-value
Type 2 Diabetes Mellitus	1.88	(1.124 – 3.168)	0.016
Smoking status			
Smoker	1.55	(1.236 – 1.953)	0.000
Ex-smoker	2.61	(1.816 – 3.747)	0.000
History of high cholesterol	2.03	(1.353 – 3.036)	0.001

Discussion

Diagnosed T2DM was self-reported by the respondent, so the laboratory diagnosis conducted can be vary among them could be HbA1c, random blood sugar, and fasting blood sugar. Random blood sugar could not be as an ideal standar for T2DM diagnosis so the result obtained can be overestimate.

The proportion of kidney disease based on analysis of the 5th IFLS data was around 1%, which means that 1 out of 100 people was at risk of having chronic kidney disease. The proportion of kidney disease in the 5th data IFLS was greater than the Indonesia Basic Health Research data in 2013 on chronic kidney disease and kidney stones where 0.2% and 0.6% respectively.

The bivariate analysis results in this study proved the relationship between type 2 diabetes mellitus and chronic kidney disease in the Indonesian population. Respondents with type 2 diabetes mellitus had a 2.48 times greater risk of suffering from chronic kidney disease than respondents without type 2 diabetes mellitus (p-value = 0.0002; 95% CI 1.422-4.071). The results of this study were in line with Aljabri (2019), where there was a significant relationship between type 2 diabetes mellitus and chronic kidney disease (p < 0.0001).¹⁵

Multivariate analysis proved that the relationship of type 2 diabetes mellitus and chronic kidney disease in the Indonesian population was influenced by smoking status, and history of high cholesterol. Respondents with type 2 diabetes mellitus had a 1.88 times greater risk of having chronic kidney disease compared to respondents without type 2 diabetes mellitus after smoking status and history of high cholesterol were controlled (p-value = 0.016; 95% CI 1.124 - 3.168). The results of this study were in line with Adebamowo(2016), where there was an impaired kidney function among those with type 2 diabetes was 1.50 (95% CI: 1.17-1.91; p-value = 0.001) compared

to those without type 2 diabetes after controlled age, sex, hypertension, BMI, and lipid (HDLc, LDLc, and triglycerides). Impaired kidney function in this research used eGFR measurement at a onetime point as to diagnosed criteria for CKD.¹⁶

Diabetes at all stages affects the kidneys. In early diabetes, the pathogenesis of glomerular hyperfiltration is well known a maladaptive response that initiating and sustaining the development of kidney damage during developing diabetes which is a joint effect of hemodynamic, vasoactive, metabolic, tubular, and pro-growth actions. At the glomerular level, there will be an increase in the plasma flow rate and hydraulic pressure in the glomerular capillaries associated with changes in systemic arterial pressure and efferent/afferent arteriolar resistance. Hyperfiltration in diabetic patients would irreversibly injure some glomeruli which change blood flow to nephrons which function and even accelerate the rate of filtration in other glomeruli which worsens the loss of nephrons, hypofiltration, and ESRD.¹⁷ In people with diabetes mellitus whose blood sugar that is not well controlled, the endothelial wall that is an insulator between blood and tissue is easily damaged, triggering the leakage of capillaries, broken embankments, and protein get into the urine. After that, there would be symptoms of kidney damage.¹⁸

Kidney filter damage arises due to high blood sugar levels (generally above 200 mg/dl), diabetes that lasts for years, and is exacerbated by high blood pressure (systolic blood pressure more than 130 mmHg and diastolic above 80 mmHg). The longer they had diabetes, the longer high blood pressure lasts, and the easier the kidneys to get damaged.¹⁸ Smoking also had a connection with the occurred of complications in people with diabetes. A common complication in people with diabetes who smoke is kidney disease, which is referred to as nephropathy, which increases the risk of albuminuria.¹⁹ The toxic content of cigarettes would be poisoning the entire body. Cigarettes can damage the kidneys both directly and indirectly. Cigarettes increase blood pressure, which worsens the kidneys. Nicotine and smoking are very bad for the blood vessels of the kidneys filter and increase the tendency to leak.¹⁸ Besides, aging coupled with chronic diseases, such as high blood pressure (hypertension) or diabetes, are likely to cause irreversible kidney damage. Sugar poisoning due to diabetes will cause nephron damage, which is called diabetic nephropathy. Many diabetics often lowers HDL cholesterol, high triglyceride, and high LDL cholesterol. The target LDL cholesterol in adult diabetics is less than 100mg/dl, lower is better. A

greater LDL value might be acceptable for someone without diabetes, but it is too high for many diabetics. High blood sugar associated with diabetes can accelerate changes in a chemical known as LDL cholesterol oxidation. The oxidation of LDL cholesterol plays a role in causing inflammatory damage and causes atherosclerosis. And the buildup of atherosclerosis in the kidneys can cause chronic kidney disease.²⁰

Conclusions

The results of this study prove there is a relationship between type 2 diabetes mellitus and chronic kidney disease in the Indonesian population. Multivariate analysis with logistic regression tests POR 1.88 (95% CI 1.124 - 3.168; p-value = 0.016) after controlling smoking status and history of high cholesterol. Respondents with type 2 diabetes mellitus have a 1.88 times greater risk of having chronic kidney disease compare to respondents without type 2 diabetes mellitus after controlling smoking status and history of high cholesterol. The relationship influence by smoking status and history of high cholesterol. Patients with type 2 diabetes mellitus expects to make appropriate treatment efforts to prevent complications of chronic kidney disease. Whereas for those without type 2 diabetes mellitus, they expect to make prevention efforts by implementing a healthy lifestyle by not smoking and controlling the consumption of food which triggers an increase in cholesterol in the blood which can ultimately lead to chronic kidney disease. Besides, it expects from health facilities to give proper education to people with type 2 diabetes mellitus to prevent chronic kidney disease.

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