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Title

Early Detection of Chronic Kidney Disease In Diabetes Population And Hypertension In Project Sunrise in East Jakarta

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Abstract

Background: Hypertension and diabetes are two of the most prevalent causes of chronic kidney disease (CKD). Screening for kidney disease in primary health facilities in patients with diabetes and hypertension plays a significant role in the early detection of CKD. Dipstick proteinuria is the easiest and widely used method to detect proteinuria in epidemiologic studies, and it is relatively cheaper and easier than examining the urinary ACR, however, some patients with negative proteinuria might have increased urinary albumin-to-creatinine ratio (ACR).

Methods: This is a cross-sectional multicenter descriptive study conducted in four district's community health centers in East Jakarta. Subjects are patients aged > 45 in community health centers and were not enrolled in their respective community health center's Chronic Disease Management Program (Program Pengelolaan Penyakit Kronis). Patients were classified as diabetic, hypertensive, diabetic and hypertensive, and no known history of both diseases. Subjects were then examined for proteinuria using a dipstick examination. Patients with negative proteinuria were then examined for urine ACR. Data analysis was performed in this study with a univariate analysis to describe the characteristics of each variable.

Results: There were 400 subjects included in this study. The majority of subjects were female (76%) and a large proportion of patients was aged 51-69 years (40%). Subjects have hypertension (51%), diabetes (17%), both diabetes and hypertension (26%), and no known history of both (4%). In the group of diabetes patients with negative proteinuria, urinary ACR 30-300 mg/g were found in 4 subjects (16.7%), whereas in patients with both hypertension and diabetes and negative dipstick proteinuria, urinary ACR 30-300 mg/g was found in 12 subjects (30.8%).

Conclusion: Examination of ACR in subjects with negative dipstick proteinuria shows some subjects have increased ACR. This data should prompt further investigations in the prevalence of albuminuria and reduced glomerular filtration rate in patients with risks of CKD in primary health care settings.

Keywords: CKD, urinary albumin-creatinine-ratio, hypertension, diabetes, proteinuria

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BACKGROUND

Chronic kidney disease (CKD) is a major contributor to world health problems. The increasing prevalence of CKD will be one of the causes of death from 20 diseases worldwide.[1] CKD is defined as kidney damage or decreased glomerular filtration rate of <60 ml/minute/1.73 m^2 in three consecutive months, with abnormalities found in the histopathological examination and/or imaging examination, and marked with an albumin-to-creatinine ratio (ACR) of > 30 mg/g.[2] Increased prevalence of CKD and increased risk of death in CKD is found in many low and medium-income countries.[3] From the 11th Report of Indonesian Renal Registry in 2018, the incidence of end-stage renal disease (ESRD) needing renal replacement therapy were 30,831, which is significantly higher than the reported 25,446 patients of the previous year.[4]

Experts recommend screening people with risk factors and this has a big impact especially for highly-populated nations.[5] Hypertension and diabetes are two of the most prevalent causes of CKD.[6] Screening for kidney disease in primary health facilities in patients with diabetes and hypertension plays a significant role in early detection of CKD.[7] Prodjosudjadi W et al. reported that about 3% from 9,412 patients were found to have persistent proteinuria, and proteinuria, along with high systolic blood pressure and diabetes mellitus, is a predictor of decreased glomerular filtration rate.[8]

Dipstick proteinuria is the easiest and widely used method to detect proteinuria in epidemiologic studies, and it is relatively cheaper and easier than examining the urinary ACR.[9] However, 24% of patients with a negative result in dipstick proteinuria examination have an ACR >30 mg/g.[10] In this study, we screened the population within The Sunrise Project, a pilot program aimed at early detection of chronic kidney disease in primary health facilities in the East Jakarta initiated by the Health Office of Jakarta in collaboration with the Indonesian Society of Nephrology and Fresenius Medical Care Indonesia. This project was held in four districts in East Jakarta.

METHODS

This is a cross-sectional multicenter study conducted in four East Jakarta community health centers (Pusat Kesehatan Masyarakat), namely Jatinegara Community Health Center, Cakung Community Health Center, Matraman Community Health Center, and Pasar Rebo Community Health Center. This research was conducted in the period 3-10 October 2019 in The Sunrise Project Program. Subjects were classified as diabetic, hypertensive and diabetic and hypertensive. Subjects were then examined for proteinuria using dipstick examination, and subjects with negative proteinuria using dipstick examination were examined for urine ACR. Data analysis was performed in this study with a univariate analysis to describe the characteristics of each variable. Inclusion criteria were patients aged ≥ 45 years who attended the Sunrise Project, and the exclusion criteria were subjects who were already enrolled in their respective community health center's Chronic Disease Management Program (Program Pengelolaan Penyakit Kronis), and have signs and symptoms of infection. The sampling method was consecutive sampling. The urinary ACR examination was done on patients with negative dipstick proteinuria. Due to the limitation of facilities, a maximum number of 20 patients from each district's community health centers were examined for urinary ACR.

RESULTS

Four hundred patients participated in this study. Over half of the subjects have hypertension (51%), subjects with diabetes mellitus (DM) were 68 patients (17%), and patients with both DM and hypertension were 104 patients (26%). A large proportion of patients was aged 51-69 years (40%). The majority of the subjects were female (76%). There were 117 diabetic patients with controlled diabetes (29.3%). Diabetic patients who had been diagnosed in less than 5 years before this study were 104 patients (26%). Other characteristic data can be seen in Table 1. In the group of diabetes mellitus patients with negative dipstick proteinuria, there is an ACR <30 mg/g in about 19 patients. Subjects with both DM and hypertension group, 12 patients are having ACR of 30-300 mg/g. In Table 3, the distribution of ACR in patients with diabetes, hypertension and both of them is 65 patients.

DISCUSSION

Over the past 6 years, data from the International Diabetes Federation shows an increasing number whereas in 2017 the figure reached 10.3 million patients.[11] In our study, 17% of patients were diabetic and 26% were diabetic concurrent with hypertension, which means 43% of the subjects have diabetes. In diabetic patients with negative dipstick proteinuria, albumin-creatinine ratio levels of 30-300 mg/g can be found in as many as 16.7% and one subject has ACR > 300 mg/. Albumin-creatinine ration level of 30-300mg/g can be found in 30.8% in both diabetes and hypertension' patients with negative dipstick proteinuria. Although dipstick proteinuria examination is the preferred method to screen proteinuria due to its sensitivity, specificity, and cost-effectiveness, clinicians must be aware of the possibility of false-negative results. Dipstick proteinuria examination can be affected by the urinary specific gravity, pH, hematuria, antiseptic use in obtaining urine samples, etc. Albumin-creatinine ratio ≥30 mg/g is more frequently used when proteinuria of 30–300 mg/g (i.e., microalbuminuria) is known to be related to risk factor for ESRD.[9] A study by Yamamoto et al found that 24% of patients with negative dipstick proteinuria has ACR of 30–300 mg/g.[10]

Poor glycemic control may lead to the production of reactive oxygen species (ROS) which will induce injury to endothelial cells, and increase the risk of cardiovascular diseases. This injury will also affect the glomerular endothelial cells and cause abruption in the normal glomerular filtration function, causing albuminuria. Persistent albuminuria can cause the tubular cells to produce proinflammatory cytokines, and further damage the endothelial cells and nephrons. Albuminuria is the first sign of renal damage in diabetic patients, rendering screening for albumin and albumin-to-creatinine ratio important in early detection of CKD in the population. Chronic hypertension will also induce proinflammatory cytokines production by endothelial cells, leading to cellular destruction and loss of nephrons. Poorly controlled hypertension will disrupt the regulatory system of the kidney which leads to albuminuria. The role of primary care health professionals in controlling diabetes and hypertension is therefore crucial in curbing the incidence of CKD in these populations.

Table 1. Subjects' baseline characteristics

CHARACTERISTICS	VALUES
DM (%)	68 (17%)
Hypertension (%)	204 (51%)
DM and Hypertension (%)	104 (26%)
Unknown (%)	24 (6%)
Age (%)	
<30 years	2 (0.5%)
30-40 years	16 (4%)
41-50 years	81 (20.3%)
51-60 years	160 (40%)
>60 years	141 (35.3%)
Gender:	
Female (%)	304 (76%)
Male (%)	96 (24%)
Glycaemic control of diabetic patients (n=163)	
Controlled	117 (29.3%)
Uncontrolled	28 (7%)
Unknown	18 (4.5%)
No Answer	237 (59.3%
Random blood glucose, median (min-max)	121 (67-508)
Duration of diabetes (n=167)	
<5 years	104 (26%)
5-10 years	34 (8.5%)
>10 years	29 (7.2%)
Systolic Blood Pressure, median (min-max)	140 (89-250)
Diastolic Blood Pressure, median (min-max)	80 (50-128)
Blood pressure control of hypertensive patients	
Controlled	217 (54.3%
Uncontrolled	46 (11.5%
Unknown	35 (8.8%)
No Answer	102 (25.5%)
Duration of Hypertension (n=298)	
0-5 years	195 (48.7%)
5-10 years	49 (12.3%
>10 years	54 (13.5%)
History of Kidney Disease (%)	
Yes	29 (7.2)
No	358 (96.8%)
No Answer	13 (3.3%)
Smoking (%)	
Yes	17(4.3%)
No	344 (86%)
Have quitted smoking	22 (5.5%)
No Answer	17 (4.3%)

Table 2. Subjects' characteristics based on proteinuria and urinary albumin-creatinine ratio.

	PROTEINURIA		URINARY ALBUMIN-CREATININE RATIO IN SUBJECTS WITH NEGATIVE DIPSTICK PROTEIN-URIA			
	Negative	Positive	<30	30-300	>300	Not examined
History of Kidney Disease						
Yes	15	14	3	4	0	22
No	208	150	45	11	1	301
No Answer	6	7		1	0	12
Smoking						
Yes	8	9	2	2	0	13
No	198	146	0	12	1	287
Have quitted smok-ing	11	11	0	0	0	22
No Answer	12	5	2	2	0	13
Education Level						
Elementary School	35	34	9	1	0	56
Middle School	38	27	9	3	0	53
High School	88	69	15	6	0	136
Undergraduate	51	28	11	1	1	66
Others	6	3	1	1	0	7
No Answer	11	10	3	1	0	17

Table 3. Distribution of Albumin-Creatinine Ratio in Patients with Diabetes, Hypertension and Both Diabetes and Hypertension with Negative Dipstick Proteinuria

Albumin-creatinine ratio (mg/g)	Diabetes mellitus (n=24)	Hypertension (n=2)	DM and Hypertension (n=39)
< 30	19 (79.2%)	2 (100%)	27 (69.2%)
30-300	4 (16.7%)	0	12 (30.8%)
> 300	1 (4.2%)	0	0

The ACR is an examination that costs more when compared to dipstick proteinuria, so the examination was limited. However, it can be seen in table 2, that 171 patients with positive dipstick proteinuria were those at risk for CKD, consistent with the results of several studies.[12,13] Therefore, the examination of ACR can be allocated to those with risk factors of CKD and negative dipstick proteinuria for cost efficiency.

This study has limitations such as not all patients with negative dipstick proteinuria have their urinary ACR examined due to limited resources. Another limitation is that this study is a cross-sectional study, therefore it cannot follow up on whether the patients have persistent microalbuminuria and whether they end up developing CKD in the long term. Future studies need to follow-up on patients and the development of CKD in all groups.

CONCLUSION

In our study, it was found that there were subjects with diabetes and/or hypertension with negative dipstick proteinuria, upon further examination showed increased ACR. This study should prompt further investigations in the prevalence of albuminuria and reduced glomerular filtration rate in patients with risks of CKD in primary health care settings. The risk for CKD in the diabetic and/or hypertensive population

in primary health care settings requires more attention, related to the prevention of progression and control of risk factors in primary health facilities because primary health care setting holds a big role in preventing and delaying the onset of CKD.

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DISCLOSURE

By the time of publication, D.L.G. worked at Fresenius Medical Care Indonesia. G.N., A.L., T.D.S., D.O., have nothing to declare.

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