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Age, Family History of Chronic Kidney Disease, Hypertension and diabetes mellitus as a Risk Factors of CKD in Acute Coronary Syndrome Subjects

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Abstract

Background: Chronic Kidney Disease (CKD) is defined as a abnormalities of kidney structure or function, present for a minimum of 3 months which has implications for health. The proportion of CKD patients is expected to increase, this is influenced by risk factors known as renal risk factors. Chronic kidney disease are also risk factors for Cardio-Vascular Disease (CVD) including Acute Coronary Syndrome (ACS), due to the presence of conditions known as uremic risk factors that accelerate the process of atherosclerosis.

Objective: This study aims to determine the prevalence of CKD in ACS populations and to assess risk factors of CKD in ACS populations.

Methods: This study was a cross-sectional study at Dr. Wahidin Sudirohusodo Hospital, Makassar. The research population is ACS patients who were admitted to the emergency unit from june 2022 until december 2023. Acute coronary syndrome diagnose based on anamnesis, abnormality of electrocardiography, and increase of cardiac biomarker titer. Chronic kidney disease is defined based on kidney disease improving global outcomes (KDIGO) 2024 as a abnormalities of kidney structure or function, present for a minimum of 3 months. We analyze risk factors of CKD namely age, gender, family history of CKD, hypertension, diabetes mellitus, dislipidemia, obesity, smoking. Statistical analysis is considered meaningful if $p < 0,05$.

Results: This study involved 472 subjects. The prevalence of CKD (GFR <60 ml/min/m2) is 99 subjects (21%). Age, family history, hypertension and diabetes mellitus (DM) with CKD are risk factors for CKD in ACS with OR of 2.9, 1.7, 1.9, and 1.5 respectively. In multivariate analysis it showed that from the 4 significant risk factors, Age is the major risk factor for CKD in ACS subjects (p=0,00).

Conclusion: Age, family history of CKD, hypertension and DM are risk factors for CKD in subjects with ACS. Age is the major risk factor for CKD in ACS subjects (p=0,00).

Keywords: Chronic Kidney Disease, Acute Coronary Syndrome, Renal Risk Factors, Uremik Related Risk Factors.

INTRODUCTION

Chronic Kidney Disease (CKD) is defined based on kidney disease improving global outcomes (KDIGO) 2024 as a abnormalities of kidney structure or function, present for a minimum of 3 months with implications for health.. Data shows that the prevalence of CKD is increasing, estimated at around 10-13% in the adult population aged > 18 years. The proportion

of CKD sufferers is expected to increase, this is influenced by risk factors known as renal risk factors.(1)

Acute coronary syndrome is a collection of clinical symptoms of myocardial ischemia that occurs suddenly due to lack of blood flow to the myocardium in the form of chest pain, ST segment changes on the Electrocardiogram (ECG), and changes in cardiac biomarkers, which is one of the causes of morbidity and mortality globally. In 2023 WHO reported that from total world population that reach 8 billion, 620 million people suffer from CVD.(2)

Chronic kidney disease is a risk factor for CVD. This condition is caused by traditional risk factors for CKD and CVD (hypertension, diabetes mellitus, obesity, dyslipidemia, smoking, aging). In addition, uremic related risk factors are also known, which are considered to play a role in increasing cardiovascular events in CKD subjects. Uremic related risk factors are: uremic toxins, increased oxidative stress and inflammation, anemia, left ventricular hypertrophy, endothelial dysfunction, and vascular calcification.(3)

In previous study, Go et all. Studied 1,120,195 CVD patients during the period 1996-2000 with an average observation period of 2.84 years. It found that the risk of CVD events increased by 1.4 times in GFR 45-59 ml/min/1.73m2, 2,0 times in GFR 30-44 ml/min/1.73m2, 2,8 times in GFR 15-29 ml/min/1.73m2 and 3,4 times in GFR <15 ml/min/1.73m2.(4)

METHODS

This study was a cross-sectional study at Dr. Wahidin Sudirohusodo Hospital, Makassar. The research population is ACS patients who were admitted to the emergency unit from june 2022 until december 2023. Acute coronary syndrome diagnose based on anamnesis, abnormality of electrocardiography, and increase of cardiac biomarker titer. Chronic kidney disease is defined based on kidney disease improving global outcomes (KDIGO) 2024 as a abnormalities of kidney structure or function, present for a minimum of 3 months. We analyze risk factors of CKD namely age, gender, family history of CKD, hypertension, diabetes mellitus, dislipidemia, obesity, smoking. Statistical analysis is considered meaningful if p <0,05.

RESULTS

The incidence of CKD (GFR < 60 ml/min/m2) was found in 99 subjects (21%) from a total of 472 subjects and not CKD (GFR ≥60 ml/min/m2) in 373 subjects (79%).

This study analyzed the relationship between renal risk factors which is age, family history of CKD and hypertension with incidence of CKD in ACS patients. The proportion of CKD was found to be higher in subjects aged ≥ 60 years (32%) compared to those aged < 60 years (12.4%), Higher in those with a family history (25.0%) compared to those without a family history (17.2%), Higher in subjects with DM (27.3%) compared to those without DM (17.9%), and higher in subjects with hypertension (26.4%) compared to those without

hypertension (13.8%). In this study, there was a significant association (p<0.05) between age, family history of CKD, hypertension, and DM.

In multivariate analysis, it was found that age is a most significant risk factor and increased risk of CKD in ACS subject (OR, 2.9; 95% CI, 1.82-4.74; p<0,01).

DISCUSSION

In this study, from 472 subjects that met the criteria, it was found that the incidence of CKD in ACS patients was 21%, this is in accordance with the research of Fox et al., and Wong et al., who reported that almost 40% of patients with NSTEMI, and 30% of those with STEMI had CKD.[5,6]

In this study, the incidence of CKD based on age in patients with ACS increased with age, with statistically significant results (p = 0.000). This study is in accordance with various studies summarized by the CDC in 2023, where the incidence of CKD was found to increase with age. In addition, the incidence of CKD was also higher in people aged 65 years or older (34%) compared to people aged 45–64 years (12%) or 18–44 years (6%).[7,8]

This study also found that there is a significant relationship between family history of CKD and the incidence of CKD in patients with ACS The proportion of CKD was found to be higher in those with a family history (25.0%) compared to those without a family history (17.2%). This is in line with the study of Kim et al. 37 who studied 881 thousand patients who were newly diagnosed with CKD and found that the presence of family members with CKD was associated with a significantly higher risk of CKD with adjusted OR (95% CI) of 1.42 (1.38–1.45), 1.50 (1.46–1.55), 1.70 (1.64–1.77), for individuals who had parents, offspring, and siblings affected, respectively.[9]

In this study, it was found that the proportion of CKD was found to be higher in hypertension (26.4%) compared to those without hypertension (13.8%). The results of statistical tests showed that the difference was significant (p <0.01). This study is in line with existing research, namely in a cohort by Haekyuk et al. 42 who conducted a study on 7,343 individuals with hypertension who did not receive antihypertensive drugs and were followed up for 10 years, it was found that the risk of developing CKD increased with increasing blood pressure. The risk of CKD increased successively by 1.39 times, 1.79 times, 3.22 times at systolic blood pressure (SBP) 130-139 mmHg, 140-159 mmHg, and >160 mmHg when compared to normal controls .[10]

This study also found a significant relationship was found between DM and the incidence of CKD in patients with ACS. The incidence of CKD in this study was quite high, namely 27.3% compared to those without DM, namely 17.9%. This study is in accordance with previous studies, a meta-analysis conducted by Shen et al. 31 involving 5 million people with DM found that the incidence of CKD in the DM population increased by 3.34 times in women and 2.84 times in men. The 10-year mortality rate in these patients also increased by 31%.[11]

Based on multivariate analysis in this study, the most significant is age (p<0.001) with an Odds Ratio value (OR=2.9). This shows that ACS subjects aged >=60 years have a 2.9 times greater risk of suffering from CKD than ACS subjects aged <60 years, assuming that

hypertension status and family history are the same. The incidence of CKD increases with age, according to the Third National Health and Nutrition Examination Survey (NHANES) study in the United States (US), which examined 13,000 patients who were followed from 1999 to 2004, the prevalence of CKD in those over 60 years of age was around 40%, this is quite high compared to the incidence of CKD in those under 60 years of age which is only around 20%.[12]

CONCLUSIONS

There is an association between age, family history of CKD, hypertensin and DM with incidence of CKD in ACS subjects. Age is the most significant risk factor for CKD with OR 2.9.

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ETHICS COMMITTEE APPROVAL

This research was approved by the Ethics Committee for Biomedical Research on Humans, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia. Based on recommendation letter Number: 222/UN4.6.4.5.31/PP36/2024, with protocol number: UH24030155

STATEMENT OF CONFLICT OF INTEREST

Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interests, patent/licensing arrangements, etc.) that might give rise to a conflict of interest with respect to the submitted article.

AUTHOR CONTRIBUTIONS

LA (Concept, Design, Sources, Materials, Data Collection and Processing, Analysis and Interpretation, Literature Search, Manuscript Writing). SRZ (Concept, Design, Supervision, Analysis and Interpretation, Literature Search). PT (Concept, Design, Supervision, Analysis and Interpretation, Literature Search). SB (Concept, Design, Supervision, Analysis and Interpretation, Literature Search). FS (Concept, Design, Supervision, Analysis and Interpretation, Literature Search). AS (Concept, Design, Analysis and Interpretation, Critical Review). All authors were involved in drafting the manuscript, revising it, and evaluating its content. They have all read and approved the manuscript, confirming the accuracy and integrity of the research details. All authors read and approve the final manuscript.

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TABLES

Table 1. Characteristics of research subject

Variabel	n	%

Gender	Male	382	80,9
	Female	90	19,1
Age	>=60 Years	206	43,6
	<60 Years	266	56,4
Obesity	Obesity	208	44,1
	Non-Obesity	264	55,9
Family history of CKD	Yes	228	48,3
	No	244	51,7
Smoking	Yes	279	59,1
	No	193	40,9
Hypertension	Yes	269	57,0
	No	203	43,0
DM	Yes	154	32,6
	No	318	67,4
Dyslipidemia	Yes	174	36,9
	No	298	63,1

Table 2. Prevalence of CKD in ACS subjects

Variabel		n	%
CKD by category	G1	214	45,3
	G2	159	33,7
	G3	68	14,4
	G4	23	4,9
	G5	8	1,7
CKD	Yes	99	21,0
	No	373	79,0

Table 3. Relationship between Age with CKD

	CKD			P Value	OR
Age	Yes	No	Total		

	>=60 Years	n	66	140	206	0,000	2,9
		%	32,0%	68,0%	100,0%		
	<60 Years	n	33	233	266		
		%	12,4%	87,6%	100,0%		
Total		n	99	373	472		
		%	21,0%	79,0%	100,0%		

Table 4. Relationship between Family History with CKD

Family History			CKD		Total	P Value	OR
			Yes	No			
	Yes	n	57	171	228	0,038	1,7
		%	25,0%	75,0%	100,0%		
	No	n	42	202	244		
		%	17,2%	82,8%	100,0%		
Total		n	99	373	472		
		%	21,0%	79,0%	100,0%		

Table 5. Relationship between hypertension with CKD

Hypertension			CKD		Total	P Value	OR
			Yes	No			
	Yes	n	71	198	269	0,001	1,9
		%	26,4%	73,6%	100,0%		
	No	n	28	175	203		
		%	13,8%	86,2%	100,0%		
Total		n	99	373	472		
		%	21,0%	79,0%	100,0%		

Table 6. Relationship between DM with CKD

DM			CKD		Total	P Value	OR
			Yes	No			
	Yes	n	42	112	154	0,082	1,5
		%	27,3%	72,7%	100,0%		
	No	n	57	261	318		
		%	17,9%	82,1%	100,0%		
Total		n	99	373	472		
		%	21,0%	79,0%	100,0%		

Table 7. Multivariate analysis

Step	Variabel	B	S.E.	Wald	p	OR	95% C.I.	
							Lower	Upper

Step 1	Age	1,060	0,245	18,809	0,000	2,9	1,79	4,66
	Family history	0,511	0,240	4,529	0,033	1,7	1,04	2,67
	Hypertension	0,658	0,259	6,463	0,011	1,9	1,16	3,21
	DM	0,424	0,244	3,030	0,082	1,5	0,95	2,46
Step 2	Age	1,079	0,244	19,624	0,000	2,9	1,82	4,74
	Family history	0,526	0,239	4,842	0,028	1,7	1,06	2,71
	Hypertension	0,691	0,258	7,196	0,007	2,0	1,20	3,31