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CORRELATION BETWEEN CARDIOVASCULAR RISK FACTORS WITH PERIPHERAL ARTERIAL DISEASE IN KIDNEY FAILURE PATIENTS UNDERGOING HEMODIALYSIS FOR MORE THAN THREE MONTHS IN HAJI ADAM MALIK GENERAL HOSPITAL MEDAN YEAR 2018

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Abstract

Peripheral Arterial Disease (PAD) is a common disease experienced by more than 202 million people worldwide, with an incidence that is directly proportional with age. PAD is a disorder of blood supply to the extremities mainly caused by obstruction, which can primarily be atherosclerosis, thrombosis, embolism, vasculitis, or fibro muscular dysplasia. Studies showed that a high number of patients with Chronic Kidney Disease also had PAD. CKD increases the risk cardiovascular diseases which can increase the risk of PAD. This is a cross sectional study analyzing patients with End Stage Renal Failure who underwent hemodialysis and fulfilled the inclusion and exclusion criteria. The patients diagnosed with CKD had several risk factors such as Diabetes Mellitus, Hypertension, Dyslipidemia, Obesity, and Smoking. These risk factors are similar to those of cardiovascular diseases. This study was conducted at the Hemodialysis Room of Haji Adam Malik General Hospital during the months of May to August 2018.There is a significance in every criterion between the risk of cardiovascular disease and PAD, with every risk factor having the p value of less than 0.05.This study showed a significant correlation between PAD in patients with CKD that had the cardiovascular of risk factors.

Introduction

Peripheral arterial disease (PAD) is a disruption of blood supply to the upper or lower extremities due to the obstruction of blood vessels. The majority of obstruction of blood supply in PAD is caused by atherosclerosis – but can also be caused by thrombosis, embolisms, vasculitis, or fibromuscular dysplasia.[1] 80-90% of the cases reported involve the femoral and popliteal arteries. Patients with PAD can be asymptomatic or present with symptoms such as claudication, pain at rest, ulceration, or gangrene.[2]

At present, it is estimated that more than 202 million people in the world suffer from peripheral arterial disease (PAD).[3] The prevalence of peripheral arterial disease (PAD) in individuals aged $\geq$ 40 years is 4.3%, whereas for individuals aged $\geq$ 70 years is 14.5%.[4] The prevalence of peripheral arterial disease (PAD) in Indonesia is 9.7%, as shown in A Global Atherothrombosis Assessment (AGATHA) study by the American Society of Cardiology in 2006, in which Indonesia was included as a research subject alongside 24 other countries. Other prevalence data on peripheral arterial disease (PAD) were obtained from a multi-national study by the Peripheral Arterial Disease - Screening and Evaluation of Diabetic Patients in Asian Regions Characterized by High Risk Factors (PAD-SEARCH), in which Indonesia was also the subject of research.

Chronic Kidney Disease (CKD) is a pathophysiological process with a variety of etiologies, resulting in a progressive decline in kidney function and generally ending in kidney failure. Kidney failure on the other hand, is a clinical condition characterized by a decline in irreversible kidney function at a time that requires kidney replacement therapy in the form of dialysis or kidney transplantation.[5]

Atherosclerosis Risk in Communities (ARIC) conducted a study on 14,280 adults with a glomerular filtration rate (GFR) of more than or equal to 90 ml/minute (normal), 60 – 89 ml/minute (mild), and 15 - 59 ml/minute (chronic) per 1.73 m^2, after being followed for 13.1 years. The results of the study showed that the incidence of PAD per 1000 people per year was 4.7, 4.9 and 8.6 respectively for normal kidney function, mildly decreased kidney function and stage 3 and 4 chronic kidney disease.[6]

INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

The prevalence of PAD varies greatly depending on which population is studied. In the United States, the prevalence of patients who have recently undergone hemodialysis ranges from 14-15%, while in patients undergoing chronic hemodialysis, the prevalence increases to 25% according to the HEMO study and USRDS data base.

This study was conducted to determine the correlation of cardiovascular risk factors with peripheral arterial disease in patients with renal failure undergoing regular hemodialysis.

Methodology

This study uses a cross sectional design, which is a research design by taking measurements or observations simultaneously at the same time. This study was carried out in the Hemodialysis Room at Haji Adam Malik General Hospital in Medan for the period May to August 2018.

The population in this study were patients withend stage renal failure who underwent hemodialysis in the Haji Adam Malik General Hospital in 2018, with a sample size of 100 people that was calculated using the population estimated sample formula.

The samples obtained were patients that had fulfilled the inclusion and exclusion criteria. Inclusion criteria were end stage renal failure patients who underwent hemodialysis, patients aged older than 18 years, patients willing to undergo training. Exclusion criteria were patients with Critical Limb Ischemic disorders, local infection in the skin area around the wrist or foot and patients using platelet aggression drugs.

Data Analysis

The data was first analyzed using the Kolmogrov – Smirnov Test, proceeded by the One – Way Anova Test and Pearson Correlation Test. The data was then interpreted by using SPSS Software Version 22.0. The results were considered significant if the p value < 0.05.

Results and conclusion

Table 1. Demographic of study participants

NO	VARIABLES	FREQUENCY	
		N	%
A	AGE		
	Range 20 – 69		
	MEAN 50,81 (SD 13,49)		
B	MARITAL STATUS		
	Single	1	1,0
	Married	95	95,0
	Divorce	4	4,0
	TOTAL	100	100,0
C	EDUCATION		
	Primary	22	22,0
	Elementary high school	8	8,0
	Senior high school	28	28,0
	Bachelor degree	41	41,0
	Master degree	1	1,0
	TOTAL	100	100,0
D	OCCUPATION		

INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

Government officers	16	16,0
Private company officers	47	47,0
Entrepreneur	31	31,0
Retired man	6	6,0
TOTAL	100	100,0

This study was done with 100 participants. The mean age of the participants were 50,81 years. The most common cardiovascular risk factor in this group of participants was hypertension (53%), followed by obesity, with more than a quarter of the sample size (33%), diabetes (25%), dyslipidemia (12%) and smoking (11%).

Table 2. Cardiovascular risk factors

NO	VARIABLE	FREQUENCY	
		N	%
A	Diabetes Mellitus		
	Yes	25	25,0
	No	75	75,0
	TOTAL	100	100,0
B	Hypertension		
	Yes	53	53,0
	No	47	47,0
	TOTAL	100	100,0
C	Dyslipidemia		
	Yes	12	12,0
	No	88	88,0
	TOTAL	100	100,0
D	Obesity		
	Yes	37	37,0
	No	63	63,0
	TOTAL	100	100
4	Smoking		
	Yes	11	11,0
	No	89	89,0
	TOTAL	100	100

Participants were also examined for their ankle brachial index. The results showed that most participants' ankle brachial index were moderate (42%). Other patients had normal (25%) and mild (22%) ankle brachial index. Only few participants had calcified arteries (7%) and severe (4%) ankle brachial index.

INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

Table 3. Ankle brachial index criteria

NO	VARIABLE	FREQUENCY (N=100)	%
1	Mild	22	22,0
2	Moderate	42	42,0
3	Severe	4	4,0
4	Normal	25	25,0
5	Artery Calcification(Suspect)	7	7,0

Peripheral arterial disease was significantly correlated with diabetes mellitus dyslipidemia, smoking, hypertension, obesity.

Table 4. Correlation between cardiovascular risk factors and peripheral artery disease

NO	RISK FACTORS	Peripheral Artery Disease	p
1	Diabetes Mellitus	0,337	0,001
2	Hypertension	0,048	0,033
3	Dyslipidemia	0,269	0,007
4	Obesity	0,027	0,009
5	Smoking	0,254	0,011

Based on the results obtained, all variables had a significant correlation and a coefficient correlation value with the incidence of peripheral arterial disease. The five variables were: diabetes mellitus, hypertension, dyslipidemia, obesity, and smoking. The results of the Spearmen Test showed that there was a significant relationship between diabetes and the incidence of peripheral arterial disease. This is indicated by the p-value of 0.001. In addition, the correlation coefficient (0.337) also shows a very strong correlation to.

Based on the values obtained, it can be concluded that diabetes mellitus should be seriously considered as a risk factor of PAD. The presence of diabetes status in hypertensive patients can increase the likelihood of peripheral arterial disease. A study by Ilminovia (2015) states that a person with one risk factor has a 1.5 times chance of suffering from PAD as compared to someone without any risk factor, and if there are two risk factors, the likelihood of peripheral arterial disease incidence increases by 3.7 times.[7] This study is also in line with the research conducted by Elizabeth Selvin, et al. (2014) where results showed that diabetes mellitus was positively associated with the incidence of PAD (OR = 2.71; 95% CI 1.03 - 7.12). Although in the study it was also found that smoking factors were the most influential risk factors for the incidence of PAD (OR = 4.46; 95% CI 2.25 - 8.84).[4]

A strong correlation between DM and the incidence of PAD in several studies has been found. Identification of PAD caused by DM is an important thing to do.[8] The presence of diabetes in hypertensive patients is estimated to increase the likelihood of PAD.(2) The Ilminovia study (2015) states that a person with one risk factor has a 1.5-fold chance of suffering from PAD. The results of the study found based on the Spearmen Test showed a significant association with dyslipidemia with PAD events. This was indicated by the p-value of 0.007. In addition, the correlation coefficient (0.269) also shows a very strong correlation.[8]

The correlation between dyslipidemia and PAD is in the occurrence of atherosclerosis.[9] In patients with dyslipidemia provide a risk factor for the onset of atherosclerosis. Dyslipidemia manifests with hyperglycemia, excess free fatty acids and insulin resistance which causes increased oxidative stress, decreased nitric oxide (NO), increased endhotelin-1, increased angiotensin II, platelet activation, and reduced fibrinolysis which all cause endothelium dysfunction.[10]

This endothelial dysfunction causes lipoproteins to infiltrate endothelium easily. The role of dyslipidemia is by increasing triglycerides, then modification of the LDL form to becomes small and dense, where this form will easily enter the endothelium so that the atherogenesis process occurs. HDL plays a role in supporting transport

INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

behind cholesterol and can prevent lipoprotein oxidation, become anti-inflammatory in vitro, and support cell proliferation. In addition, HDL encourages the formation of NO. Decreasing HDL causes reduced protection against atherosclerosis.[11] Several studies found that high total cholesterol levels and low HDL were independently associated with increased risk of PAD.[12] Therefore, patients with dyslipidemia have higher chance of PAD than people with only one risk factor.[13]

Aryani's (2016) study showed that correlation between dyslipidemia and the incidence of PAD was very strong with a value of p = 0.008.[8] This is in accordance with the explanation of F Brian Boudi, MD that the combination of low HDL and high triglycerides is often found in DM patients and is often referred to the incidence atherogenic dyslipidemia.[14]

Another study by Sarah et al (2012) which followed 20,000 research subjects showed a close association between LDL particles and the incidence of vascular disease in the subjects. The correlation between LDL and PAD was found in the atherosclerosis process. The atherosclerosis process begins with damage of the endothelial layer on the arterial wall. Possible causes of endothelial damage can be caused by increased levels of LDL.[15] If LDL levels are high, then cholesterol transported by LDL can settle in the subendothelial layer, therefore LDL is atherogenic. This sub-endothelial space has low antioxidant protection, so LDL easily enters this place. After LDL enters into endothelial cells, LDL is then oxidized.[16]

The latest evidence explains that oxidized LDL contributes to endothelial damage, migration of monocytes and lymphocytes to the intima tunic, converting monocytes to macrophages, and other events that occur in the progress of the atherosclerosis process. A study shows an increase in serum LDL in animals can cause atherosclerosis in the absence of other risk factors.[17]

The results of our study showed that there was a significant association of obesity with the incidence of PAD (p = 0.009, R= 0.027).Obesity increases the risk of a number of chronic diseases such as type 2 diabetes, hypertension, stroke, high cholesterol, heart failure, cancer, gout, gallbladder stones, and osteoarthritis.
Mudaliar's study (2016) found that about 60% of those who are obese suffer from type 2 diabetes mellitus and PAD. The greater the body mass index (BMI), the greater the risk of developing type 2 diabetes mellitus which is accompanied by an increased risk of PAD.[18]

The results of the study based on the Spearmen test showed that there was a significant correlation of smoking with the incidence of PAD. This is indicated by the value p = 0.011. In addition, the correlation coefficient also shows a very strong association which is equal to 0.254. Smoking is a major risk factor for PAD disease. Then nicotine contained in cigarette smoke will stimulate the adrenaline hormone which consequently will change fat metabolism where HDL levels will decrease. Adrenaline will also cause stimulation of the heart and constriction of blood vessels.[19] Besides that, adrenaline will cause platelet grouping. So that all the narrowing processes will occur. So the seemingly simple cigarette smoke can be a cause of coronary heart disease. Some studies have found that there are 4,000 types of chemicals in cigarettes, with 40 of which are carcinogenic (which can cause cancer), where these toxins are mostly found in side fumes, for example 5 times more carbon monoxide (CO) is found in side smoke than the main smoke, benzopyrene 3 times, and ammonia 50 times. These ingredients can last up to several hours in the room after the cigarette stops.[20]

The survey conducted by the Indonesian Ministry of Health (2010) shows that smoking risk factors work synergistically with other factors, such as hypertension, high levels of fat or blood sugar, against the onset of CHD. The results of our study showed that there was a significant correlation (p=0.033, R=0,048) between hypertension and the incidence of PAD. This is consistent with Indonesian ministry of health study. Hypertension is a major risk factor for PAD disease. Hypertension can accumulate plaques in the arteries that carry blood to the head, organs, and limbs. People who have PAD are at increased risk for heart disease, heart attacks, and strokes.[1]

INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

There are significant correlations between diabetes mellitus, hypertension, dyslipidemia, obesity, and smoking and the incidences of peripheral arterial disease in patients on hemodialysis in Haji Adam Malik General Hospital.

Acknowledgements

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INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

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