

## **Factors Influence Carotid Intima Thickening Media Thickness in Chronic Kidney Disease Patients**

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### **Abstract**

Chronic kidney disease (CKD) is associated with high mortality rates related to cardiovascular complications. Atherosclerosis, arteriosclerosis and vascular calcification conditions are often found in CKD patients. Carotid intima media thickness (cIMT) thickening is one of the parameters of vascular disorders. a cross sectional study was conducted on patients with chronic kidney disease in the Mohammad Hoesin hospital Palembang. Blood samples were examined in the hospital laboratory. CIMT thickening was examined using echocardiography. 55 patients with stage 3-5 of chronic kidney disease were examined. The median cIMT was 0.8 (0.6-1.45) mm. Spearman's correlation analysis showed a significant correlation between triglyceride levels and thickening of cIMT ( $r = 0.303$ ,  $p = 0.025$ ). A significant correlation was also shown between phosphate levels and cIMT thickening ( $r = 0.290$ ,  $p = 0.032$ ). There were significant correlations of triglyceride levels and phosphate levels on the thickening of cIMT in chronic kidney disease patients at Mohammad Hoesin Hospital Palembang

Keywords: carotid intima media thickness, chronic kidney disease, vascular calcification

### **Introduction**

Chronic kidney disease (CKD) is associated with high mortality rates mainly related to cardiovascular disease. Risk factors for cardiovascular disease due to chronic kidney disease even exceed type 2 diabetes mellitus in which mild to moderate chronic kidney disease increases cardiovascular disease by up to 87%. The cause of the increased risk of cardiovascular disease is related to mineral and bone disorders that occur in chronic kidney disease.<sup>1,2</sup> The term Chronic Kidney Disease-Mineral Bone Disease (CKD-MBD) was first cited in 2006 by the Kidney Disease Improving Global Outcomes (KDIGO) . CKD-MBD consists of changes in serum calcium, phosphate, parathyroidhormone (PTH), vitamin D, fibroblast growth factor 23 (FGF-23), as well as bone turnover, mineralization and calcification outside the bone, especially vascular calcification.<sup>3</sup> Vascular calcification in CKD is part of CKD-MBD. Observational studies report

vascular calcification occurring in up to 25% of patients with stage 3 CKD and more than 50% in patients with dialysis. Vascular calcification can be measured in various ways, one of which is by examination using echocardiography to measure carotid intima media thickness (cIMT). CIMT measurement using echocardiography provides the advantage of being easy to do, noninvasive and sensitive enough to know the condition of vascular calcification. Several studies have shown an increase in cIMT in populations such as diabetes mellitus and CKD patients with increasing age and CKD progression. 8-10. This study aims to determine the factors that influence thickening of cIMT in patients with chronic kidney disease in the hospital. Mohammad Hoesin Palembang.<sup>4,5</sup>

## **Methods**

The study was conducted by cross sectional method in 55 patients with stage 3-5 chronic kidney disease in both outpatient, inpatient and hospital hemodialysis units. Mohammad Hoesin Palembang. Blood samples were examined in the hospital laboratory. Examination of cIMT thickening is carried out using echocardiography which is done by a cardiovascular consultant. Data analysis using IBM SPSS Version 24 software, where each data is presented in the form of a frequency distribution table, then continued with bivariate analysis between variables.

## **Results**

A total of 55 samples of patients with chronic diseases were obtained in this study consisting of 30 patients with end stage renal disease with hemodialysis and 25 patients with stage 3-4 CKD. Demographic and clinical characteristics of the study subjects can be seen in Table 1. Median age of study subjects 56 years with a minimum age of 23 years and a maximum of 79 years. The study subjects consisted of 37 (67.3%) men and 18 (32.7%) women. The duration of chronic kidney disease suffered by subjects ranging from 1 year to 12 years. The mean body mass index (BMI) of the study sample is  $22.8 \pm 3.67$ . In this study the most common causes of CKD were hypertension 19 (34.5%) people, followed by diabetes mellitus 15 people (27.3%), glomerulonephritis 6 people (10.9%), obstructive uropathy 3 (5.5%), hypertension and diabetes mellitus 12 people (27.3%) 21.8%). In our study a median cIMT of 0.8 (0.6-1.45) mm was obtained.

**Table 1. Characteristics of patients with Chronic Kidney Disease**

Characteristics	n=55
Ages	56 (23-79)
Sex	
Man	37 (67.3%)
Woman	18 (32.7)
Duration of CKD (Year)	1 (1-12)
BMI	22.8 ± 3.67
Etiology of CKD	
Hipertension	19 (34.5%)
DM	15 (27.3%)
Uropati obstruktive	3 (5.5%)
Glomerulonephritis	6 (10.9%)
DM + Hipertension	12 (21.8%)
Ureum (mg/dl)	77.7 ± 36.5
Kreatinin(mg/dl)	3.93 (1.51-15.9)
LDL (mg/dl)	100 ± 41.1
Triglicerida(mg/dl)	140.1 ± 66.4
CRP (mg/dl)	10 (4-230)
Phospat(mg/dl)	3.7 (1.5-10.5)
Calsium(mg/dl)	9 (7-118)
Albumin(mg/dl)	3.8 (1.9-6,8)
PTH (pg/ml)	36.4 (6.8-1251.2)
Diameter cIMT (mm)	0.8 (0.6-1.45)

The results of Spearman's correlation analysis between risk factor variables and cIMT diameter in patients with chronic kidney disease are shown in table 2. Spearman analysis shows the relationship between cIMT diameter and triglyceride variables ( $p = 0.002$ ,  $r = 0.541$ ) and phosphate variables ( $p = 0.022$ ,  $r = 0.416$ ).

**Table 2. Spearman Correlation Analysis**

Risk Factor	cIMT	
	r	p
Ages	-0.149	0.278
Sex	-	0.977 <sup>a</sup>
Duration of CKD (Year)	0.250	0.066
BMI	0.104	0.450
DM	-	0.063 <sup>a</sup>
Hipertension	-	0.801 <sup>a</sup>
LDL (mg/dl)	-0.099	0.472
Triglicerida(mg/dl)	<b>0.303</b>	<b>0.025</b>
CRP (mg/dl)	-0.243	0.074
Phospat(mg/dl)	<b>0.290</b>	<b>0.032</b>
Calsium(mg/dl)	0.010	0.943
Albumin(mg/dl)	-0.065	0.638
PTH(pg/ml)	0.183	0.180

## Discussion

In this study, the etiology of hypertension was the most etiologic of chronic kidney disease patients in our study, 34.5% followed by diabetes mellitus 27.3%. Based on data from the Indonesia Renal Registry (IRR) 2017, the most common cause of CKD patients undergoing hemodialysis in Indonesia is hypertension, which reaches 51% followed by diabetes mellitus by 21%. In our sample of ESRD patients, some patients had experienced a significant increase in PTH and had a CKD-MBD condition where there was an increase in phosphate and PTH levels and vascular calcification.<sup>6</sup> In our study we had a median cIMT 0.8 (0.6-1.45) mm in patients with chronic kidney disease in Hospital Mohammad Hoesin Palembang. Reysginawati's study in Palembang in hemodialysis patients obtained a mean cIMT of  $0.810 \pm 0.190$  mm with a cIMT thickening of 44%, almost the same as our study. While Lahoti et al obtained an average diameter of cIMT in CKD patients  $0.80 \pm 0.28$  mm. Lahoti et al also analyzed the cIMT diameter in each CKD stage 1-5 and did not get any correlation of the CKD stage with the cIMT diameter ( $p = 0.146$ ,  $r = 0.119$ ).<sup>7,8</sup> Several studies have shown an association between male sex with thickening cIMT. Kuswardhani et al's study of a sample of hemodialysis patients in Indonesia found that cIMT thickness in men was higher than in women ( $0.7056$  vs  $0.6141$  mm;  $P = 0.003$ ). The study of Pourafkari et al in the Iranian population found that the average cIMT in men was higher than in women. In our study we did not get gender as a risk factor for cIMT thickening. This could be due to factors other than age more strongly affecting cIMT in our sample of CKD patients and these non-age factors were balanced in both sexes.<sup>9,10</sup> Our study did not show age as a cIMT thickening factor. Kuswardhani et al's research showed cIMT was correlated with age in hemodialysis samples in Indonesia ( $R = 0.607$ ;  $P < 0.001$ ). In our study, there was no age relationship with cIMT because in our sample some patients had chronic kidney disease since young. Some of our chronic kidney disease patients even come from pediatric patients. These patients although still relatively young age but obtained thick cIMT. These results cause the results of our analysis to show no relationship between age and cIMT as in other studies.<sup>9</sup> Our study shows a correlation between serum phosphate levels and cIMT thickness ( $r = 0.290$ ,  $p = 0.032$ ). In the study of Kuswardhani et al also found a correlation between phosphate and cIMT thickening ( $r = .20.294$ ,  $p = 0.015$ ). The Kuo et al study also found a correlation between serum phosphate levels and cIMT thickening ( $r = 0.604$ ,  $p < 0.01$ ).<sup>9,11</sup> In this study, the median calcium concentration of study subjects  $9 (7-18)$  mg / dl was almost the same as Kuswardhani research.  $9.0 \pm 0.66$ . These relatively normal levels of calcium indicate that some samples have not yet experienced advanced CKD-MBD problems.<sup>9</sup> At the beginning of the glomerular filtration rate, there is a decrease in serum calcium levels and an increase in the levels of parathyroid hormone

and phosphate. High serum phosphorus levels in patients with end-stage renal disease were found to be significant and are independent risk factors for all causes of cardiovascular death and vascular calcification. High serum phosphate levels are a significant and independent factor associated with advanced atherosclerosis in CKD patients with or without diabetes, other than old age. Calcium-phosphate was also associated with an increased risk of cardiovascular morbidity and mortality in patients with CKD.<sup>1,12,13</sup> In this study we found a correlation between triglycerides and carotid intima media thickness ( $r = 0.541$   $p = 0.002$ ). The pathophysiology underlying triglycerides as an important factor in the formation of atherosclerosis has been very strong. Rich lipoprotein triglycerides (TRLs) are produced from chylomicrons and VLDL cholesterol and are said to have a strong atherogenic effect. Compared to LDL, Triglycerides rich lipoprotein (TRLs) carry more cholesterol per particle because of their larger size. Each section of TRLs carries 40 times more cholesterol than LDL. And cholesterol from these TRLs does not need to be modified / oxidized to be atherogenic and delivered to macrophages five times faster than LDL so it is said to be strong atherogenic. Chhajed et al also obtained the same results where total cholesterol ( $r = 0.236$ ,  $p \leq 0.018$ ) and serum triglycerides ( $r = 0.387$ ,  $p \leq 0.001$ ) correlated with cIMT thickening in CKD patients.<sup>14-17</sup> In this study no correlation was found between hormones parathyroid with carotid intima media thickness (cIMT) thickening ( $p = 0.180$ ). Research Costa et al showed different results in which the correlation between parathyroid hormone and carotid intima medi thickening was obtained

## **Conclusion**

There is a significant correlation of triglyceride levels and phosphate levels to cIMT thickening in patients with chronic kidney disease

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