


## Relationship between Stage of Chronic Kidney Disease with Cardiomegaly Imaging in Posteroanterior Chest X-Ray at Haji Adam Malik Hospital Medan

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### ABSTRACT

**Introduction:** Chronic kidney disease (CKD) is one of the most serious health problems still faced globally. Cardiovascular complications are a major cause of morbidity and mortality in patients with chronic kidney disease. In general, cardiomegaly is found in patients with uremia which causes dysregulation of calcium and phosphate levels and increases the development of cardiovascular disease in hemodialysis patients. The aim of this study was to analyze the relationship between stages of chronic kidney disease with cardiomegaly imaging in posteroanterior chest x-ray at H. Adam Malik Hospital Medan.

**Method:** This study was an observational analytic study with a cross-sectional design on 78 CKD patients who underwent posteroanterior chest x-ray at H. Adam Malik Medan General Hospital from January to December 2022.

**Results:** Of the 78 patients studied, the subjects were female (56.4%) with a mean age of  $50.94 \pm 12.80$  years. The mean weight and BMI of the subjects were  $70.49 \pm 9.01$  and  $24.80 \pm 2.82 \text{ kg/m}^2$ , respectively. The mean creatinine and GFR were  $7.91 \pm 4.22 \text{ mg/dl}$  and  $16.08 \pm 15.22 \text{ mL/min/1.73m}^2$ , respectively. The majority of subjects had creatinine  $>2.5 \text{ mg/dl}$  in as many as 72 subjects (92.3%) and GFR  $<60 \text{ mL/min/1.73m}^2$  as many as 62 subjects (79.4%). Most of the subjects were in CKD stage 5, as many as 59 people (75.6%). There was a positive and significant correlation between the stages of chronic kidney disease and cardiomegaly imaging in posteroanterior chest x ray with p-value  $<0.001$ . Subjects with GFR  $<60 \text{ mL/min/1.73m}^2$  and overweight BMI status (25.0 - 29.9  $\text{kg/m}^2$ ) had a greater risk factor for cardiomegaly.

**Conclusion:** There is a positive and significant correlation between the stages of chronic kidney disease with cardiomegaly imaging in posteroanterior chest x-ray at H. Adam Malik General Hospital Medan with p value  $<0.001$ .

Chronic kidney disease, Cardiomegaly, Chest X-ray

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### INTRODUCTION

Chronic kidney disease (CKD) is one of the most serious health problems still faced globally.[1] Chronic kidney disease is a condition characterized by damage, dysfunction, or structural abnormalities of the kidneys, either with or without a decrease in the glomerular filtration rate.[2] The National Kidney Foundation estimates that chronic kidney disease affects about 10% of the world's population and millions of people die from inadequate treatment each year. Initially, patients with chronic kidney disease do not experience any symptoms or are asymptomatic, but serum creatinine and urea concentrations begin to increase. Patients with chronic kidney disease begin to experience symptoms when they are in stages 3 and 4 or when the glomerular filtration rate is less than 30%.[3]

Hemodialysis is the most common treatment for patients with chronic kidney disease. Hemodialysis aims to reduce symptoms due to decreased renal function so it is expected to improve the prognosis and quality of life of patients.[2] However, prolonged hemodialysis can lead to complications. Hemodialysis can lead to complications that include dysfunction of the cardiovascular system and noncardiovascular, or respiratory systems. Cardiovascular complications are the main cause of morbidity and mortality in patients with chronic kidney disease.[1] Cardiovascular complications are also the most common cause of death in patients who undergo hemodialysis regularly. The prevalence of cardiomegaly is found to increase with the progression of chronic kidney disease. About 70-90% of chronic kidney disease patients show a picture of cardiomegaly with different levels of severity in stage five chronic kidney disease.[1] These results are also in agreement with other studies by Liou et al. in 2016 which reported that most patients with chronic kidney disease receiving hemodialysis had imaging chest x-ray results showing the presence of cardiomegaly with a total of 61.4% of 622 patients.[4]

This study aims to analyze the risk factors associated with the relationship of chronic kidney disease stages with cardiomegaly imaging in posteroanterior chest x-rays at the Adam Malik Medan General Hospital. H. Adam Malik Medan.

## **METHOD**

This research is an observational analytic study with a cross-sectional design in patients who perform posteroanterior chest x-ray at H. Adam Malik Medan General Hospital period January to December 2022 with a total of 78 patients. Excluded patients were patients with congenital heart conditions, difficulty determining the heart contour, scoliosis vertebral, abnormalities of one of the chest walls, and posteroanterior chest x-ray with insufficient inspiration.

The basic data on subjects age, gender, body mass index (BMI), blood pressure, serum creatinine, and estimated glomerular filtration rate (eGFR) using the CKD-Epi creatinine formula. Chest x-ray was used to assess cardiomegaly imaging, assessed by a radiology resident and radiologist.

Data will be analyzed descriptively to determine the frequency distribution of each variable demographic characteristics and risk factors. The data to be analyzed will be tested for inter-rater agreement between two readers of chest X-ray images using the Kappa test. Then continued with inferential analysis to analyze the relationship between stages of chronic kidney disease with cardiomegaly imaging in posteroanterior chest x-ray using the chi-square test. The results of the study were declared meaningful with a p-value <0.05. Variables with a p-value < 0.25 will be further analyzed using multivariate analysis in the form of logistic regression.

## **RESULT**

### **General Characteristics of the Subjects**

The characteristics of all the study subjects (n=78) are provided in Table 1. Majority of the subjects are female, it was 44 subjects (56.4%). The average age of the subjects was  $50.94 \pm 12.80$  years, while the average body weight and BMI of the subjects are  $70.49 \pm 9.01$  kg and  $24.80 \pm 2.82$  kg/m<sup>2</sup>. The majority of the subjects are overweight, with 53 subjects (67.9%). Meanwhile, the average creatinine and GFR are  $7.91 \pm 4.22$  mg/dL and  $16.08 \pm 15.22$  mL/min/1.73m<sup>2</sup>. The majority of the subjects have creatinine levels >2.5 mg/dL in 72 subjects (92.3%), and GFR <60 mL/min/1.73m<sup>2</sup> was 62 subjects (79.4%). Most subjects are in stage CKD 5, with 59 subjects (75.6%). The majority of the subjects have prehypertension and stage 1 hypertension 27 subjects (34.6%) and 24 subjects (30.8%), respectively. In the hemoglobin examination, 75 subjects (96.2%) are found to have anemia. The researcher and comparator measurements reveal that most subjects have cardiomegaly, with 59 subjects (75.6%) and 61 subjects (78.2%).

Table 1. Characteristics of the subjects

Characteristics	N (%) or Mean $\pm$ SD
Gender	
Male	34 (43,6%)
Female	44 (56,4%)
Age	50,94 $\pm$ 12,80 tahun
Body Weight	70,49 $\pm$ 9,01 kg
BMI	24,80 $\pm$ 2,82 kg/m <sup>2</sup>
Underweight (<18,5 kg/m <sup>2</sup> )	6 (7,7%)
Normal weight (18,5 – 24,9 kg/m <sup>2</sup> )	19 (24,4%)
Overweight (25,0 – 29,9 kg/m <sup>2</sup> )	53 (67,9%)
Obesity I (30,0-34,9 kg/m <sup>2</sup> )	0 (0,0%)
Obesity II (35,0-39,9 kg/m <sup>2</sup> )	0 (0,0%)
Obesity III (>40 kg/m <sup>2</sup> )	0 (0,0%)
Creatinin	7,91 $\pm$ 4,22 mg/dl
0,8-1,0 mg/dl	0 (0,0%)
1,1-1,6 mg/dl	5 (6,4%)
1,7-2,5 mg/dl	1 (1,2%)
>2,5 mg/dl	72 (92,3%)
GFR	16,08 $\pm$ 15,22 mL/min/1,73m <sup>2</sup>
>60 ml/min/1,73m <sup>2</sup>	6 (7,6%)
<60 ml/min/1,73m <sup>2</sup>	62 (79,4%)
Stage of CKD	
Stage 2	6 (7,7%)
Stage 3a	0 (0,0%)
Stage 3b	6 (7,7%)
Stage 4	7 (9,0%)
Stage 5	59 (75,6%)
Blood Pressure	
Normal	17 (21,8%)
Prehypertension	27 (34,6%)
Hypertension stage I	24 (30,8%)
Hypertension stage II	10 (12,8%)
Anemia	
Yes	
No	75 (96,2%)
Yes	3 (3,8%)
Cardiomegaly ( by the researcher)	
Yes	59 (75,6%)
No	19 (24,4%)
Cardiomegaly (by the comparator)	
Yes	61 (78,2%)
No	17 (21,8%)

### Data Uniformity Test

The data uniformity test between the two readers of chest x-ray in this study was assessed using the Kappa test. The results of the Kappa test indicate a 92% agreement between the two readers, which is statistically significant ( $p < 0.05$ ) with a  $p$ -value  $< 0.001$ . The analysis suggests that both the measurements by the researcher and the comparator regarding the interpretation of chest x-ray images for cardiomegaly are generally consistent, and inferential analysis can be performed using a single dataset.

### Bivariate Analysis

Bivariate analysis was performed to evaluate the relationship between independent and confounding variables on cardiomegaly. Table 2 shows the Chi-Square comparative test showed that there was a significant relationship ( $p < 0.05$ ) between the stage of CKD, GFR, BMI, age, gender, creatinine, blood pressure, and

anemia with the incidence of cardiomegaly. The stage of CKD as an independent variable was significantly associated with the incidence of cardiomegaly ( $p < 0.001$ ) and the majority of patients with cardiomegaly had CKD stage 5, as many as 51 subjects (86.4%). Meanwhile, other confounding variables were significantly associated with cardiomegaly, such as age ( $p = 0.034$ ), gender ( $p = 0.045$ ), BMI ( $p = 0.005$ ), GFR ( $p = 0.002$ ), creatinine ( $p = 0.032$ ), anemia ( $p = 0.013$ ), and blood pressure ( $p = 0.045$ ). All variables were candidates for multivariate analysis because they had  $p$  values  $< 0.25$ .

Table 2. Chi square comparative with cardiomegaly

Subject characteristics	Cardiomegaly		P value	Multivariate Candidates
	Yes	No		
Age				
>51 years	38 (84,4%)	7 (15,6%)	0,034*	Candidate**
≤51 years	21 (63,6%)	12 (36,4%)		
Jenis Kelamin				
Female	36 (81,8%)	8 (18,1%)	0,045*	Candidate**
Male	23 (67,6%)	11 (32,3%)		
BMI				
<18,5 kg/m <sup>2</sup>	2 (33,3%)	4 (66,7%)	0,005*	Candidate **
18,5 – 24,9 kg/m <sup>2</sup>	8 (42,1%)	11 (57,9%)		
25,0 – 29,9 kg/m <sup>2</sup>	49 (92,5%)	4 (7,5%)		
GFR				
<60 ml/min/1,73m <sup>2</sup>	58 (80,5%)	14 (19,4%)	0,002*	Candidate **
>60 ml/min/1,73m <sup>2</sup>	2 (33,3%)	4 (66,6%)		
Creatinin				
1,1 – 1,6 mg/dl	2 (40,0%)	3 (60,0%)	0,032*	Candidate **
1,7-2,5 mg/dl	1 (50,0%)	1 (50,0%)		
>2,5 mg/dl	56 (78,9%)	15 (21,1%)		
Anemia				
Yes	59 (78,7%)	16 (21,3%)	0,013*	Candidate **
No	0 (0,0%)	3 (100,0%)		
Blood pressure				
Normal	10 (58,8%)	7 (41,2%)	0,045*	Candidate **
Prehypertension	19 (70,3%)	8 (29,6%)		
Hypertension stage 1	23 (95,8%)	1 (4,1%)		
Hypertension stage 2	7 (70,0%)	3 (30,0%)		
Stage of CKD				
Stage 2	2 (33,3%)	4 (66,7%)	<0,001*	Candidate **
Stage 3b	3 (50,0%)	3 (50,0%)		
Stage 4	3 (42,9%)	4 (57,1%)		
Stage 5	51 (86,4%)	8 (13,6%)		

\* significant ( $p < 0,05$ ); \*\* multivariate candidate ( $p < 0,25$ )

### Multivariate Analysis

Multivariate analysis was performed to evaluate the relationship between the independent variables and the dependent variable after confounding variables were controlled. CKD stages 3 and 4 with stage 2 as reference were not significantly associated with cardiomegaly with  $p > 0.05$ . Meanwhile, CKD stage 5 was significantly associated with cardiomegaly with  $p = 0.001$  and OR (95%CI) = 21.857 (3.669-130.217). Multivariate analysis showed that overweight BMI had the greatest influence on cardiomegaly statistically as it had a  $p$ -value = 0.002 (significant) with OR (95%CI) = 56.729 (4.146-776.203). This indicates that subjects with overweight conditions have a 56.729 times greater risk of cardiomegaly than subjects with underweight. Then, the multivariate analysis also showed that GFR  $< 60$  ml/min/1.73m<sup>2</sup> had a statistically significant effect on cardiomegaly because it had a  $p$ -value = 0.005 (significant) with OR (95%CI) = 31.027 (2.835-339.611). This indicates that patients with GFR  $< 60$  ml/min/1.73m<sup>2</sup> have a 31.027 times greater risk of cardiomegaly than patients with  $> 60$  ml/min/1.73m<sup>2</sup>. The results of the multivariate analysis are presented in Table 3.

Tabel 3. Multivariate Analysis

Subject characteristics	Cardiomegaly	
	P value	OR (95%CI) Lower-Upper
Age		
>51 year	0,015*	5,620 (1,398 – 22,588)
≤51 year		
Gender		
Female	0,021*	5,150 (1,282 – 20,687)
Male		
BMI		ref
<18,5 kg/m <sup>2</sup>	0,510	2,164 (0,218-21,447)
18,5 – 24,9 kg/m <sup>2</sup>	0,002*	56,729 (4,146-776,203)
25,0 – 29,9 kg/m <sup>2</sup>		
GFR	0,005*	31,027 (2,835-339,611)
<60 ml/minutes/1,73m <sup>2</sup>	-	ref
>60 ml/minutes/1,73m <sup>2</sup>		
Kreatinin		
1,1 – 1,6 mg/dl	0,475	16,168 (0,008-33447,081)
1,7-2,5 mg/dl	0,422	7,359 (0,056-964,493)
>2,5 mg/dl	0,869	1,513 (0,011-208,892)
Anemia		
Yes	0,999	-
No		
Blood pressure		
Normal	-	ref
Prehypertension	0,551	1,716 (0,290 – 10,143)
Hypertension stage 1	0,205	5,049 (0,412 – 61,913)
Hypertension stage 2	0,111	4,620 (0,703 – 30,340)
Stage of CKD		
Stage 2	-	ref
Stage 3b	0,219	4,500 (0,408-49,627)
Stage 4	0,468	2,250 (0,251-20,131)
Stage 5	0,001*	21,857 (3,669-130,217)

\*significant (p<0,05); OR = odds ratio; CI = confidence interval; ref = reference

## DISCUSSION

Based on this study, In this study, most of the subjects were female, 56.4%. This finding is in agreement with a previous observational study by Amadita P, Priatna, and Priyadi H who evaluated the picture of cardiomegaly on posteroanterior x-ray findings of 30 CKD patients in Indonesia, reporting that most CKD patients were female, as many as 18 subjects (60.0%).[1] Lewandowski MJ et al in Austria reported a significantly higher proportion of female patients than male patients in several countries including Asia. This finding may be because the majority of advanced CKD patients who are women have a higher survival rate than men. Kidney function generally declines with age more rapidly in men than in women.[5] However, another observational study by Duan J, Wang Cn et al involving 119 subjects in the Nephrology Ward, Allied Hospital, Faisalabad reported that most of the end-stage renal disease patients were male, with 131 subjects (64.5%).[6]

In this study, the average age of patients was 51 years. This finding is in agreement with previous research conducted by Singh P et al reporting that the largest age group in patients is the age 46-60 years, with as many as 62 subjects (52.1%).[6] Anand S et al in an observational study in Bangladesh involving 402 CKD patients aged >30 years also reported a similar average age of 49.5 ± 12.7 years.[7] A cohort study conducted by Tuttle KR et al involving 600,064 CKD patients through the Center for Kidney Disease Research, Education, and Hope (CURE-CKD) also reported that the largest age group of patients was in the 50-69 year group, which amounted to 43.7%, including in the group of CKD patients with heart disease such as hypertension, at 29.3%. [8] These findings suggest that increasing age is associated with a significant increase

in CKD progressivity. In another study by Chen SC et al involving 568 CKD patients in Taiwan, the average age of CKD patients with CTR  $\leq 50\%$  and  $>50\%$  was  $62.1 \pm 13.6$  (172 patients) and  $65.2 \pm 12.8$  (109 patients) years.[9]

In this study, the subjects average body weight and BMI were 70.5 kg and 24.8. This finding is similar to a previous cross-sectional study by Ji AI with 38,038 participants aged 60-109 years in Qingdao, China, which reported an increase in body weight in the population group with CKD, which was characterized by high BMI characteristics, where BMI  $>24$  in most participants (71.3%).[10] High body mass index is one of the strongest risk factors for new-onset CKD. This is due to the compensatory hyperfiltration process that occurs to meet the increased metabolic demands of increased body weight. Increased intraglomerular pressure can also damage the kidneys and increase the risk of CKD events in the long term.[11] However, in patients with CKD who have stage progression, low BMI generally reflects malnutrition and chronic inflammatory processes, causing endothelial dysfunction in pre-dialysis and dialysis patients. Decreased muscle mass along with inflammation may also be associated with increased patient mortality.[11]

In this study, the average GFR of patients was found to be  $16 \text{ mL/min/1.73 m}^2$  with an average creatinine of  $7.9 \text{ mg/dL}$ . This finding is in agreement with previous research by Chen SC et al, who reported that the average eGFR of 118 CKD patients with high left ventricular mass index (LVMI) was  $20.7 \pm 12.0 \text{ mL/min/1.73 m}^2$ . In addition, in the same study, most patients were at stage 4-5 (48.3%).[7,8] Another study by Huang JC et al involving 3,320 patients (1,938 men and 1,382 women) in southern Taiwan with stage 3-5 with a BMI of  $15.0\text{-}35.0 \text{ kg/m}^2$  also reported that the mean eGFR of patients was  $29.2 \pm 16.2 \text{ mL/min/1.73 m}^2$  with most patients at stage 5 (53.6%).[12] Another cross-sectional study by Babua C et al in Uganda that evaluated the risk of cardiovascular disorders in 217 CKD patients with an average age of 43 years reported that most patients were at stage 5, as many as 111 patients (51.15%).[13] Another cohort study by Kim H et al involving 2,238 participants using data from the Korean Cohort Study for Outcomes in Patients with Chronic Kidney Disease (KNOW-CKD) reported that most patients were at stages 4 and 5 with 522 (23.3%) and 145 (6.5%) patients, and an average creatinine level of  $1.8 \pm 1.1 \text{ mg/dL}$ . [14]

The subjects were in an advanced stage, indicating that there is an increased risk of cardiovascular events, especially cardiomegaly. The findings of this study regarding the majority of patients diagnosed with cardiomegaly are in agreement with previous research by Amadita P and Priatna, Priyadi H who reported that most CKD patients were diagnosed with cardiomegaly, as many as 59 (75.6%) subjects.[1] The majority of subjects were also reported to have prehypertension and grade I hypertension. Hypertension is both a cause and a consequence of CKD. An increase in the prevalence of CKD is in line with an increase in the prevalence of hypertension and is reversed. Based on epidemiological data from the National Health and Nutrition Examination Survey (NHANES) II study involving 15,600 patients, 40% of patients with GFR  $60\text{-}90 \text{ mL/min/1.73 m}^2$  had blood pressure (BP)  $>140/90 \text{ mmHg}$ . Furthermore, a decrease in GFR is also proportional to an increase in the prevalence of hypertension. The multicenter NHANES III study also reported that about 75% of patients with GFR  $<30 \text{ mL/min/1.73 m}^2$  had hypertension. Hypertensive conditions are associated with decreased glomerular filtration rate (GFR), including extracellular fluid (ECF) volume expansion; activation of the sympathetic and/or renin-angiotensin-aldosterone systems; vascular wall changes with or without calcification; large or small vessel renovascular disease; hyperparathyroidism; and changes in other endogenous substances, such as uric acid, homocysteine, prostaglandins and/or endothelin.[15,16]

In hemoglobin examination, almost all subjects had anemia. This finding is in agreement with a national study in the US by Sofue T et al which reported that the incidence of anemia was twice as common in people with CKD (15.4%) than in the general population (7.6%). The prevalence of anemia also increased with the CKD stage, from 8.4% in stage 1 to 53.4% in stage 5. 22.8% of CKD patients with anemia reported being treated for anemia in the previous 3 months-14.6% of patients in stage 1-2 CKD and 26.4% of patients in stage 3-4.[17] In addition, an Asian study by Babitt JL and Lin HY also reported that the mean (standard deviation) hemoglobin level was  $11.4 (2.1) \text{ g/dL}$  in patients with stage 4 CKD and  $11.2 (1.8) \text{ g/dL}$  in patients with stage 5 CKD. The prevalence of anemia was reported as 40.1% in patients with stage 4 CKD and 60.3% in patients

with stage 5 CKD.[18] In CKD patients (particularly in end-stage renal disease patients undergoing hemodialysis), hepcidin levels are found to be very high, due to reduced renal clearance and induction by inflammation, leading to iron-restricted erythropoiesis. In addition, CKD also inhibits the production of EPO by the kidneys, and can also lead to uremic-induced inhibitors of erythropoiesis in the circulation, shortening the lifespan of red blood cells, and increasing blood loss.[19]

This study shows that there is a significant relationship between CKD stages and cardiomegaly imaging in posteroanterior chest x-rays. Similar results were also found in a previous study by Amadita P, Priatna, and Priyadi H, where CKD was significantly correlated with the incidence of cardiomegaly which was mostly characterized by enlargement of the left ventricle.[1] In this study, the majority of subjects were patients with stage 5 CKD, this is because chronic kidney disease initially has asymptomatic, but serum creatinine and urea concentrations begin to increase. Patients with chronic kidney disease begin to experience symptoms when they are in stages 3 and 4 or when the glomerular filtration rate is less than 30%.[3] Due to the asymptomatic characteristics of chronic kidney disease, the majority of patients only begin treatment after complications occur.[2]

In this study, stage 5 CKD had the most cardiomegaly. This may be due to left ventricular hypertrophy in >70% of patients with end-stage renal disease accompanied by other manifestations of heart muscle disease such as focal scarring and diffuse interstitial fibrosis associated with uremic cardiomyopathy. Increased left ventricular mass in ESRD is generally due to myocyte hypertrophy and interstitial space dilatation.[20,21] Increased left ventricular mass and hypertrophy are common manifestations of CKD-related cardiomyopathy. Left ventricular hypertrophy is found in 48-84% of patients with predialysis CKD and up to 90% of patients undergoing hemodialysis.[22]

The pathophysiologic process underlying cardiomyopathy in CKD is myocardial fibrosis.[22] The development of cardiomyopathy resulting in cardiomegaly in CHD tends to be multifactorial. Hemodynamic factors include increased afterload due to hypertension and calcification of the arterial vessel wall, and increased preload generally caused by anemia and increased sodium levels in the blood. Humoral and local factors may also be involved, such as activation of the renin-angiotensin-aldosterone system, hyperuricemia, accumulation of uraemic toxins, hyperphosphatemia, abnormal bone mineral metabolism, increased levels of phosphate-regulating hormones (parathyroid hormone and fibroblast growth factor-23 (FGF-23)), oxidative stress and chronic inflammation have all been reported to be involved in the development of hypertrophy, myocardial fibrosis, and increased mortality from cardiovascular disorders.[20]

Abnormalities of all coronary vessels are seen in CKD cases accompanied by uremia with atherosclerosis and medial thickening and calcification of epicardial vessels, and medial hypertrophy and reduction of pre-arterial cross-sectional surface area. As a result of the failure to regulate myocardial blood flow homeostasis with circulatory demand due to myopathy, widespread ischemia, diffuse interstitial fibrosis, ventricular remodeling, and systolic-diastolic dysfunction with manifestations of cardiomegaly may occur.[23]

In this study, several variables, such as age, gender, body weight, GFR, creatinine, anemia, and blood pressure were also found to have a significant association with cardiomegaly. This is also in agreement with previous studies that other risk factors, such as obesity, hypertension, hyperglycemia, and renal dysfunction in CKD patients have been associated with the development of cardiomyopathy through inflammatory mechanisms and oxidative stress. The condition may be exacerbated by the presence of hypertension, increased arterial stiffness, and humoral factors such as FGF-23 and aldosterone in CKD patients leading to the clinical syndrome of uremic cardiomyopathy.[23] In addition, in another study by Segall L and Nistor I, Covic A also mentioned that one-third to two-thirds of patients with severe anemia were found to have cardiomegaly on chest x-ray.[24]

Based on multivariate analysis, patients with stage 5 CKD and GFR <60 ml/min/1.73m<sup>2</sup> were found to have a 21.857- and 31.027-times greater risk of cardiomegaly. CKD patients are characterized by decreased GFR. CKD patients with low GFR were reported to have a 2.57 times higher risk of cardiomegaly.[1] CKD was also mentioned as a strong and independent risk factor for cardiovascular disease where heart failure is

highly prevalent in patients with CKD and end-stage renal disease and is strongly associated with mortality in these patients.<sup>87</sup> Another study by Takagi A et al also reported that lower eGFR at baseline can be an independent predictor for mortality of acute heart failure patients.[25]

In this study, the multivariate analysis also showed that overweight patients had a 56.729 times greater risk of cardiomegaly compared to underweight patients. These results are in agreement with a previous study by Stack AG et al who reported that multivariate analysis in ESRD patients showed results that extreme BMI (OR = 1.24 for BMI <21.1 and OR = 1.10 for BMI >30.0), age (OR = 1, 30 per 10 years older), black race (OR= 1.33), diabetes (OR= 1.26), hypertension (OR= 1.28), tobacco use (OR= 1.17), and serum albumin (OR= 1.36 per 1 g/dL lower) were significantly correlated with cardiomegaly.[26]

The relationship between increased BMI and cardiomegaly can be a direct relationship or an indirect relationship in the sense that excessive BMI first causes various risk factors for the occurrence of cardiovascular diseases such as hypertension and coronary heart disease. From these various processes, various pathophysiological processes will occur, including changes in hemodynamics, ventricular remodeling, production of inflammatory mediators, and the occurrence of hepatotoxicity in the heart.[26]

However, in this study, blood pressure and anemia were not found to be independent factors that significantly affected the incidence of cardiomegaly. This result may be because hypertension and anemia can cause cardiomegaly multifactorial along with other conditions of the patient. This result may also be because only one-third to two-thirds of patients with severe anemia were found to have cardiomegaly on chest radiographs, and the cardiac silhouette was reported to return to normal within a few weeks after the anemia was corrected.[19]

A patient with CKD is reported to have a significantly greater probability of cardiovascular death than progressing to end-stage renal disease.[27] Cardiomegaly is an important clinical outcome in the majority of patients.[28] Cardiomegaly is reported to be one of the conditions associated with heart failure.[29] Heart failure is a complex clinical syndrome that can be caused by structural and functional abnormalities of the heart. As many as >40% of heart failure patients develop CKD and the close association between CKD and heart failure worsens the prognosis of patients. Therefore, renal function should be evaluated using estimated glomerular filtration rate in heart failure patients to provide appropriate interventions and improve patient prognosis.[27]

## **CONCLUSION**

There is a positive and significant correlation between the stages of chronic kidney disease with cardiomegaly imaging in posteroanterior chest x-ray at H.Adam Malik General Hospital Medan with p value <0.001.

## **DECLARATIONS**

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

## **CONSENT FOR PUBLICATION**

The Authors agree to publication in Journal of Society Medicine.

## **FUNDING**

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## **COMPETING INTERESTS**

The authors declare that there is no conflict of interest.



## AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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