

# Prevalence of Mitral Annular Calcification in Nepalese Chronic Kidney Disease Patients Under Hemodialysis in A Tertiary Care Centre of Western Nepal

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## Abstract

**Background and aims:** Mitral annular calcification (MAC) is a chronic process. Elderly patients have a higher prevalence of MAC. Chronic kidney disease (CKD) patients and cases with multiple cardiovascular risk factors have a higher chance of having MAC. MAC is associated with higher chances of having major adverse cardiovascular events (MACE). MAC is more common in CKD patients, probably because of abnormal calcium and phosphorus metabolism. The main aim of our study is to find out the prevalence of mitral annular calcification in chronic kidney disease patients under hemodialysis.

**Methods:** It was a prospective, observational, and single-centered study conducted in the department of internal medicine, Pokhara Academy of Health Sciences (POAHS), Nepal. This study was conducted over a period of a year between 9<sup>th</sup> November 2022 and 8<sup>th</sup> November 2023. Patients with CKD under maintenance hemodialysis (MHD) were enrolled. Data (Age, Sex, HD duration and frequency, presence of other risk factors like Hypertension, DM, smoking, history of coronary angiography and revascularization, electrocardiography for MAC, left ventricular systolic and diastolic functions (LVEF and LVDD), left ventricular hypertrophy) were collected after complete history taking followed physical examination, relevant laboratory investigations, and transthoracic echocardiography (TTE). Statistical analysis (descriptive analysis for proportion and percentage, and 2x2 contingency table for odds ratio and binary logistic) was performed using the latest version of SPSS.

**Results:** The total number of patients enrolled was 121. The mean age of the cases enrolled was 54.26 years (SD=15.25). The majority were male patients (67%). 111 (91.74%) were hypertensives, and 40 (33%) were diabetics. MAC was found in 36 (29.75%) of patients enrolled. 6.6% patients had coronary artery disease (CAD) and 1.65% underwent coronary revascularization in past. Higher odds of having MAC were observed in CKD patients with smoking (OR=10.13), HD duration >12 months (OR=4.24), DM (OR=2.86), and HTN (OR=1.77). However, in binary regression analysis after adjusting for confounders, the AORs for age, HD duration, and DM were 9.8, 13.3, and 3.3, respectively.

**Conclusion:** There is a high prevalence of MAC in CKD patients under maintenance HD. Advanced age, CAD, longer duration of HD, DM, HTN, and smoking are important factors associated with MAC. TTE is an important tool to detect MAC in CKD patients.

**Keywords:** Coronary artery disease, Chronic kidney disease, Hemodialysis, Mitral annular calcification.

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## Introduction

Mitral annular calcification (MAC) is basically a process of chronic degeneration with involvement of mitral valve's fibrous base<sup>1-3</sup>. Posterior mitral annulus is the area to be commonly involved<sup>4,5</sup>.

Overall prevalence is about 10% as per various autopsy studies<sup>6,7</sup>, but prevalence ranges between 8-15% and goes up significantly in elderly population and CKD patients<sup>6,8-11</sup>.

It is linked with heightened risk of CVD and mortality and it increases the incidence of arrhythmia and mitral valve disease<sup>2,12,13</sup>. Transthoracic echocardiography (TTE) is a simple tool to identify MAC. MAC is demonstrated by TTE as an echo dense structure at an angle between left ventricular posterior free wall and posterior aspect of mitral leaflet. It has an irregular and lumpy appearance and has posterior acoustic shadowing. It is seen both in systole and diastole. TTE in SAX view at the level of mitral annulus can also help stratify the severity of MAC. It is mild when it is focal, moderate when 1/3<sup>rd</sup> to 1/2 of the total circumference is involved, and severe when more than 1/2 of the total circumference is involved<sup>14</sup>.

Its prevalence is as high as 42% in elderly patients with cardiovascular diseases<sup>15</sup>. CKD cases have higher rates of aortic and mitral valvular calcifications which are said to independently predict cardiovascular events and overall mortality<sup>16-21</sup>. Calcification involving valves and coronary arteries have similar pathological features and hence share common risk factors<sup>22-24</sup>.

Studies have revealed that patients with age less than 65 years who have MAC have higher prevalence of CAD<sup>25</sup>.

Cardiovascular events are the main causes of mortality in CKD patients. ESRD patients under HD have higher risk of cardiovascular events and the prevalence of MAC is also quite high among them<sup>16,19,26</sup>.

Younger patients with low risks for CV events, when not accompanied by typical symptoms of CAD are not advised to undergo robust CV screening such as coronary angiography (CAG) to rule out significant CAD before renal transplantation but these patients if have MAC may be benefited or not by CV screening before renal transplantation is not clear.<sup>27-29</sup>

To the best of our knowledge, there are no studies on prevalence of mitral annular calcification in CKD patients on hemodialysis in our country till date, so our objective in this study is to determine prevalence of MAC in CKD patients under MHD along with their clinical profile.

## Methods

It was a prospective, observational study conducted in a single centre between 9<sup>th</sup> november 2022 to 8<sup>th</sup> november 2023 in Pokhara academy of health sciences (POAHS), a government tertiary health care centre in western Nepal.

**Inclusion criteria:** All consecutive CKD stage V cases under MHD (maintenance hemodialysis for  $\geq 3$  months), with age between 16 to 85 years, in the department of internal medicine of POAHS were enrolled.

**Exclusion criteria:** Patients without consent, patients with severe medical illnesses like acute infections and active malignancies, were excluded.

All cases underwent TTE to identify and stratify MAC. MAC was stratified as mild, moderate and severe. Study variables were: Age, Sex, HD duration and frequency per week, presence of other risk factors like HTN, DM, smoking, history of coronary angiography and revascularization, electrocardiography, left ventricular systolic and diastolic functions (LVEF and LVDD), left ventricular hypertrophy. Data collection from patients were done using questionnaires, clinical examination, laboratory investigations, echocardiography. Data entry in an excel sheet was done and then subsequent analysis (descriptive analysis for proportion and percentage, 2x2 contingency table for odds ratio, binary logistic regression analysis) using SPSS latest version was performed.

## Results

Total number of patients enrolled was 121. The mean age was  $54.26 \pm 15.25$  years. Of total patients 81 (67%) were males and 40 (33%) were females. Mean HD duration was  $32.45 \pm 27.21$  months. All patients had a dialysis frequency of twice a week. 111 (91.74%) were hypertensives and 40 (33%) were diabetics. 8 (6.6%) were patients with CAD and 2 (1.65%) gave history of coronary revascularization in the past. 16 (13.22%) were smokers.

MAC in this study was found in 36 (29.75%) of patients enrolled.

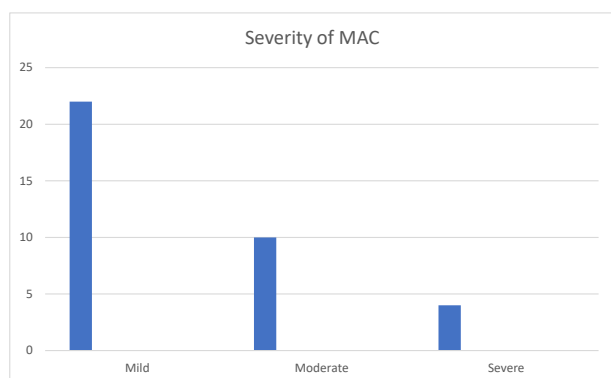
LVH (left ventricular hypertrophy) was observed in 77 (63.64%). Grade I and II left ventricular diastolic dysfunction (LVDD) were found in 80 (66.12%) and 19 (15.7%) cases respectively. Eight (6.61%) patients had left ventricular systolic dysfunction (LVSD).

**Table 1:** Patient characteristics at baseline

Baseline characteristics	
Characteristics	Total (n=121) (%)
Number of patients	121 (100%)
Mean age (years $\pm$ SD)	$54.26 \pm 15.25$
Male	81 (67%)
Female	40 (33%)
HD duration	
(months $\pm$ SD)	$32.45 \pm 27.21$
HD frequency	Twice a week
HTN	111 (91.74%)
DM	40 (33%)
History of CAD	8 (6.6%)
History of coronary revascularization	2 (1.65%)
MAC	36 (29.75%)
Smoking	16 (13.22%)
LVH	77 (63.64%)
LVDD1	80 (66.12%)
LVDD2	19 (15.7%)
LVSD	8 (6.61%)

As in figure 1, of total cases with MAC, 22 (61.11%) cases had mild MAC, 10 (27.78%) cases had moderate MAC and four (11.12%)

cases had severe MAC.



**Figure 1:** Prevalence of different grades of MAC by TTE

**Table 2:** Association of MAC with different risk factors (n=121)

Chi-square test was used to find the association between MAC and different risk factors taking p-value less than 0.05 as statistically significant.

Variables	Categories	MAC		p-value
		Present (%)	Absent (%)	
Age (years)	≤60	8 (22.2)	63 (74.1)	<0.001
	>60	28 (77.8)	22 (25.9)	
HD duration (in months)	≤12	6 (16.7)	39 (45.9)	0.002
	>12	30 (83.3)	46 (54.1)	
Smoking	Present	12 (33.3)	4 (4.7)	<0.001
	Absent	24 (66.7)	81 (95.3)	
Hypertension	Present	34 (94.4)	77 (90.6)	0.721
	Absent	2 (5.6)	8 (9.4)	
Diabetes	Present	18 (50.0)	22 (25.9)	0.010
	Absent	18 (50.0)	63 (74.1)	

**Table 3:** Unadjusted odds (OR) ratio for MAC and risk factors

First univariate analysis was done to find out the unadjusted odds ratio.

Risk factors	MAC	No MAC	95 % CI	Unadjusted OR
HTN	34	77	(0.36,8.76)	1.77
No HTN	2	8		
DM	18	22	(1.27,6.46)	2.86
No DM	18	63		
Smoking	12	4	(2.99,34.29)	10.13
No smoking	24	81		
HD duration (>12 months)	30	46	(1.6,11.24)	4.24
HD duration (≤12 months)	6	39		

MAC was present in six (16.67%) females and 30(83.33%) males. 34 (94.44%) hypertensive patients with CKD had MAC, (OR=1.77,CI=95%,0.36-8.76). 18 (50%) diabetic patients with CKD had MAC,(OR=2.86,CI=95%,1.27-6.46). Eight (22.22%) CAD patients with CKD had MAC. Six (16.66%) patients with LVSD with CKD had MAC. 12 (33.3%) smokers with CKD had MAC,(OR=10.13,CI=95%,2.99-34.29). Two (5.56%) male patients with CKD and age <45 years had MAC whereas none of the female CKD patients with age <55 years had MAC. The average duration of MHD in CKD patients with MAC was 43.56 months. 76 (62.8%) cases had the duration of HD >12 months,of which 30 (83.33% of total MAC patients) had MAC. For duration of HD>12 months,the odds of having MAC was 4.24 ,(OR=4.24,CI=95%,1.6-11.24).

**Table 4:** Binary logistic regression analysis to find out adjusted odds ratio (AOR)

Then to further explore the associations, binary logistic regression was applied using all risk factors found to have statistically significant association with MAC to find out the adjusted odds ratio (AOR) at p-value of less than 0.05 and 95% confidence interval. Smoking was not taken into consideration in the analysis as it had very wide CI because of small sample size.

Variables	Categories	β-coefficient	AOR	p-value	95% CI	
					Lower	Upper
Age (years)	≤60			Ref.		
	>60	2.290	9.87	<0.001	2.837	34.392
HD duration (months)	≤12			Ref.		
	>12	2.592	13.351	0.003	2.486	71.705
Diabetes	Absent			Ref.		
	Present	1.205	3.336	0.063	0.936	11.885

## Discussion

As in many other studies in the past ,our study has found a higher prevalence (29.75%) of MAC in CKD patients who are under HD <sup>16,27</sup>. Likewise patients with longer duration of HD had a higher chance of having MAC in our study,similar to some previous studies<sup>16,28</sup>. To the surprise,all of our CKD patients with the history of CAD had MAC ,thus supporting significant association between MAC and CAD just as in past literatures.<sup>28</sup>

This study revealed a higher probability of getting MAC in CKD patients with smoking (OR=10.13), HD duration>12 months (OR=4.24), DM (OR=2.86), HTN(OR=1.77) in that descending order. However in binary regression analysis after adjusting for confounders, the AOR for age, HD duration and DM were 9.8, 13.3 and 3.3 respectively.These findings support the fact that one with multiple comorbidities has a higher chance of having MAC.<sup>27</sup>

The other important factor worth mentioning here is older age which is more associated with MAC probably because of age related valvular degeneration. 77.8% of patients with MAC had age of more than 60 years (p< 0.001).Our bulk of patients with MAC belonged to an advanced age group (the average age of MAC positive patients=63.91 years).<sup>15</sup>

Another important issue is with the younger CKD patients with MAC who are planned for renal transplantation. According to Scientific Statement From the AHA and the ACC Foundation, cardiovascular screening is indicated in high risk CKD patients, however the high risk features do not include MAC.When young CKD patients with

MAC (male <45 years and females <55 years) and without other high risk features like DM, history of CAD, abnormal ECG, left ventricular dysfunction, smoking and HD duration <2 years are planned for renal transplantation whether to subject them to cardiovascular screening (such as coronary angiography to rule out CAD) is not clear and as we know many studies in the past had demonstrated MAC as an independent predictor of CAD. This needs to be addressed in the future by guidelines<sup>29</sup>.

MAC may signal towards a systemic vascular disease, so clinicians should focus on holistic cardiovascular care rather than focusing on management of MAC only.

## Conclusion

This study shows a high prevalence of MAC in CKD patients under maintenance HD. It also highlights the association with certain cardiovascular risk factors. Advanced age, CAD, longer duration of HD, DM, HTN, and smoking are important factors associated with MAC. TTE is an important modality to detect MAC in such patients. Our findings also suggest that identifying and monitoring MAC in this population may lead to improved cardiovascular outcomes through timely interventions. Further studies are warranted to explore causal mechanisms and to validate these findings across diverse patient cohorts.

## Limitations

- Small sample size and the short time period are important limitations of this study. So other well designed studies in future with large sample sizes are needed to establish strong association between risk factors and MAC.
- Intact parathyroid hormone, phosphorus and calcium were also not analysed which is one of the major limitations of this study.

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