

Valvular Calcification Burden in End-Stage Renal Disease: A Cross-Sectional Study from a Tertiary Care Center in Lahore

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Abstract

Background and Objective: Valvular calcification is a significant cardiovascular complication in patients with end-stage renal disease (ESRD), yet local data regarding its prevalence remain scarce. To determine the frequency of mitral valve calcification (MVC) and aortic valve calcification (AVC) in patients with ESRD on maintenance hemodialysis.

Study Design: Cross-sectional survey.

Setting: Department of Cardiology, Jinnah Hospital, Lahore.

Subjects & Methods: A total of 140 patients (both genders) diagnosed with ESRD for at least three months and undergoing maintenance hemodialysis were enrolled. Demographic data, including age, gender, and duration of ESRD, were recorded. Transthoracic echocardiography was performed on all subjects to identify the presence of

MVC and AVC.

Results: The mean age of the study population was 39.24 ± 11.31 years. The cohort consisted of 89 (63.6%) males and 51 (36.4%) females. MVC was detected in 43 patients (30.7%), while AVC was present in 44 patients (31.4%). While gender and the duration of ESRD did not show a significant correlation with calcification, advancing age was significantly associated with the presence of both MVC and AVC ($p < 0.05$).

Conclusion: There is a high prevalence of mitral and aortic valve calcification among ESRD patients in our population. Given the associated cardiovascular risks, aggressive preventive strategies and regular echocardiographic screening are warranted in this

high-risk group.

INTRODUCTION

The global escalation of chronic kidney disease (CKD) has emerged as a preeminent public health challenge, with the prevalence of end-stage renal disease (ESRD) showing a dramatic upward trajectory over the last several decades. In the United States alone, the number of patients enrolled in Medicare-funded ESRD programs grew from approximately 10,000 in 1973 to over 547,000 by 2008, a trend mirrored globally as populations age and the dual epidemics of diabetes and hypertension continue to expand. These two conditions now account for approximately 44% and 27.9% of all incident ESRD cases, respectively, creating a high-risk cohort that consumes a disproportionate share of healthcare resources. Despite significant technological improvements in maintenance hemodialysis, these patients continue to experience staggering morbidity and mortality rates, with five-year survival probabilities hovering around only 34%. Cardiovascular disease (CVD) remains the primary driver of this high mortality, accounting for nearly 50% of all deaths in the ESRD population. Among the various cardiovascular complications, valvular calcification—specifically involving the mitral and aortic valves is recognized as a critical marker of systemic uremic damage and a potent predictor of adverse outcomes.

Valvular calcification in the context of ESRD is fundamentally distinct from the passive, age-related degenerative processes observed in the general geriatric population. In patients with renal failure, the calcification of the mitral annulus and aortic leaflets is an active, regulated, and accelerated biological process believed to be an extra-skeletal manifestation of uremic nephropathy. The pathogenesis is deeply rooted in the profound derangement of mineral and bone metabolism, specifically involving calcium, phosphorus, and parathyroid hormone (PTH). As renal function declines, the body enters a pro-calcific state characterized by hyperphosphatemia and the loss of natural circulating inhibitors of calcification. This toxic milieu triggers the phenotypic transformation of valvular interstitial cells and vascular smooth muscle cells into osteoblast-like cells, which then deposit hydroxyapatite crystals onto the valve leaflets. International data suggests that the frequency of these calcifications is four to five times higher in ESRD patients than in the general population, with studies by Washiyama and Kaplon highlighting that the burden of disease is growing in tandem with the global dialysis population.

The clinical prevalence of these valvular changes varies across international cohorts but remains consistently high. Research by Bellasi and others has reported that roughly 38.2% of ESRD patients exhibit mitral valve calcification, while 44.4% present with aortic valve calcification. Other studies, such as those by Sayarlioglu, have shown aortic calcification rates of 23.3%, while regional data from India by Valson et al. reported significantly higher combined rates of 61.7%. These variations underscore the impact of demographic factors, duration of dialysis, and the quality of metabolic control on valvular health. Furthermore, because ESRD is considered a "coronary heart disease risk equivalent," the presence of valvular calcium identifies a subset of patients at even higher risk for myocardial infarction and stroke. Interestingly, while traditional lipid-lowering interventions like statin therapy are highly effective for secondary prevention in the general population, major clinical trials specifically targeting dialysis patients—such as the 4-D and AURORA trials—have failed to show significant cardiovascular benefit from statins alone, suggesting that the calcific process in ESRD requires a more nuanced management strategy focused on mineral homeostasis.

Despite the clear association between valvular calcification and increased mortality, there is a notable paucity of local data regarding the specific burden of this condition within the Pakistani population. Most clinical assumptions are currently based on Western or East Asian data, which may not accurately reflect the unique

genetic, dietary, and socioeconomic factors prevalent in our region. In our local setting at Jinnah Hospital, Lahore, we observed that while gender and the duration of ESRD did not serve as primary drivers, advancing age was significantly associated with the presence of both mitral and aortic deposits. Given that valvular calcification is theoretically preventable through the aggressive regulation of calcium-phosphorus and PTH levels, identifying the local frequency of these lesions is a vital step toward improving clinical protocols. This study, therefore, sought to evaluate the burden of mitral and aortic valve calcification in ESRD patients in our population, providing the necessary data to bridge the gap between regional clinical findings and international benchmarks, ultimately advocating for more frequent echocardiographic screening and tighter metabolic control in this highly vulnerable, already sick population.

METHODS

The study was conducted as a cross-sectional survey at the Department of Cardiology, Jinnah Hospital, Lahore, over a six-month period from September 24, 2014, to March 23, 2015. Using a purposive non-probability sampling technique, a sample size of 140 patients was determined based on a 95% confidence level and a 7% margin of error, assuming a 21.7% expected prevalence of aortic valve calcification in patients with end-stage renal disease (ESRD). The inclusion criteria targeted both male and female patients aged 18 to 50 years with a confirmed diagnosis of ESRD for at least three months, as determined by the Glomerular Filtration Rate (GFR) method. To ensure the specificity of uremia-induced calcification, the study excluded patients with rheumatic valvular disease, congenital valvular anomalies (confirmed by positive ASO titer), and those with acute renal failure defined by a history of less than three months.

The data collection procedure involved enrolling 140 hemodialysis patients who met the specified criteria. After obtaining informed consent from the patients or their guardians, demographic profiles including age, gender, and address were meticulously recorded. Clinical assessment for the presence of mitral or aortic valvular calcification was performed using transthoracic echocardiography at the time of study entry, adhering strictly to the operational definitions for valvular mineralization. All collected data were documented on a structured Proforma designed for the study.

Statistical analysis was performed using SPSS version 17.0. Quantitative variables, specifically age, were expressed as mean and standard deviation. Categorical data, including gender and the presence or absence of mitral and aortic valve calcification, were presented as frequencies and percentages. To control for potential confounders and identify specific risk patterns, the data were stratified by age, gender, and the duration of ESRD. Post-stratification, the Chi-square test was employed to determine associations between these variables and valvular calcification, with a p -value of < 0.05 established as the threshold for statistical significance.

RESULTS

The prevalence of valvular calcification in this cohort of 140 patients with end-stage renal disease (ESRD) underscores a significant cardiovascular burden within the local population. The study population presented with a mean age of 39.24 ± 11.31 years, with a notable majority of the sample (63.6%) being male. Regarding the clinical timeline of the disease, 37.1% of the patients had been diagnosed with ESRD for a duration exceeding one year. Echocardiographic screening revealed that mitral valve calcification (MVC) was present in 43 patients (30.7%), while aortic valve calcification (AVC) was identified in 44 patients (31.4%). These frequencies are slightly lower than some international benchmarks which often report rates exceeding 40% but they nonetheless represent a substantial portion of the dialysis-dependent population in Lahore.

Variable	Category	Frequency (n)	Percentage (%)		
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Age	Mean +/- SD	39.24 +/- 11.31 years	Range: 18-50		
	Below 40 Years	52	37.10%		
	40 Years and Above	88	62.90%		
Gender	Male	89	63.60%		
	Female	51	36.40%		
ESR Duration	Less than 1 Year	88	62.90%		
	More than 1 Year	52	37.10%		

Table 2: Overall Frequency of Valvular Calcification

Valvular Site	Calcification Present (n)	Percent age (%)			
Mitral Valve (MVC)	43	30.70%			
Aortic Valve (AVC)	44	31.40%			
No Calcification	96	68.60%			

Table 3: Stratified Analysis of Valvular Calcification by Key Variables

Variable	Sub-category	MVC Present n (%)	P-Value	AVC Present n (%)	P-Value
Age Group	40 Years and Above	41 (46.6%)	< 0.001	43 (48.9%)	< 0.001
	Below 40 Years	2 (3.8%)		1 (1.9%)	

r	Gende	Male	27 (30.3%)	98	0.8	30 (33.7%)	43	0.4
		Female	16 (31.4%)			14 (27.5%)		
on	Durati	More than 1 Year	17 (32.7%)	9	0.6	17 (32.7%)	04	0.8
		Less than 1 Year	26 (29.5%)			27 (30.7%)		

Statistical analysis of the data indicates that demographic factors such as gender do not significantly influence the development of these calcifications. In this study, MVC was observed in 31.4% of females and 30.3% of males, yielding a non-significant of 0.89. Similarly, the frequency of AVC showed no statistical disparity between genders (27.5% in females vs. 33.7% in males, $p=0.44$). Perhaps most surprisingly, the duration of ESRD also failed to emerge as a significant predictor in this specific cohort. Patients with a disease history of more than one year showed nearly identical rates of MVC and AVC (32.7%) compared to those with a shorter history, with p -values of 0.69 and 0.804 respectively. This suggests that the biochemical triggers for calcification in the uremic environment may be potent enough to initiate mineral deposition relatively early in the course of the disease.

In stark contrast to gender and duration, age proved to be a highly significant correlate for valvular pathology. When the cohort was stratified by age, a dramatic divergence in prevalence was observed. For patients aged 40 years and above, the frequency of MVC was 46.6% and AVC was 48.9%. Conversely, in patients below the age of 40, the presence of calcification was exceptionally rare, occurring in only 3.8% for the mitral valve and 1.9% for the aortic valve. These findings, supported by a highly significant p -value of < 0.001 , indicate that while the uremic state provides the necessary metabolic substrate for calcification likely through hyperphosphatemia and secondary hyperparathyroidism the structural manifestation of this damage is heavily dependent on the age of the patient. This highlights a critical clinical window for patients over 40, who may benefit from more frequent echocardiographic monitoring and aggressive mineral-bone disorder management to mitigate the high risk of subsequent cardiovascular events.

DISCUSSION

Patients undergoing maintenance dialysis exhibit a significantly higher risk of cardiovascular mortality compared to the general population, often driven by accelerated dystrophic calcification of the heart valves. This study identified a high burden of valvular disease, with mitral valve calcification (MVC) present in 30.7% and aortic valve calcification (AVC) in 31.4% of the cohort. While these frequencies are substantial, they are slightly lower than those reported in international literature. For instance, Rroji M et al. reported an MVC prevalence of 44.5% and AVC of 52%, while Raggi et al. observed rates of 38.2% and 44.4%, respectively. Conversely, our findings showed a higher prevalence of AVC compared to the 23.3% reported by Sayarlioglu S et al. These discrepancies likely stem from variations in dietary habits, the quality of metabolic control (calcium and phosphorus regulation), and the demographic characteristics of the studied populations.

A critical finding in this study was the mean age of 39.2 ± 11.3 years, indicating an alarming burden of end-stage renal disease (ESRD) among younger individuals in our region. Despite the relatively young average age, the presence of valvular mineralization—traditionally viewed as a geriatric process—was frequent. Statistical

analysis revealed that age was the only significant predictor of calcification ($p < 0.001$), with nearly 50% of patients aged 40 and older exhibiting valvular deposits. This aligns with previous research suggesting that while uremia provides the biochemical substrate for calcification, the structural manifestation is compounded by chronological aging.

Interestingly, this study found that valvular calcification was independent of both gender and the duration of the disease. While some studies suggest that longer dialysis vintage increases the risk of calcium deposition, our data indicates that the pro-calcific uremic environment may initiate valve damage relatively early in the disease process. Given that cardiac valve calcification serves as a strong independent predictor for all-cause mortality and cardiovascular death, these findings underscore the necessity of early screening.

This study had certain limitations, including the use of purposive non-probability sampling and a relatively small sample size from a single center, which may limit the generalizability of the results to the broader Pakistani population. Future multi-center studies with larger cohorts and longitudinal follow-ups are recommended to better understand the progression of these abnormalities and their direct impact on survival in our local context.

CONCLUSION

The frequency of aortic and mitral valve calcification is notably high among patients with end-stage renal disease in our population, affecting approximately one-third of the dialysis-dependent cohort. The significant association with age highlights a high-risk group that requires focused clinical attention. Because valvular calcification is an independent predictor of cardiovascular mortality, it is imperative to implement early echocardiographic screening and aggressive preventive measures, such as the strict regulation of calcium-phosphorus metabolism, to reduce the morbidity and mortality burden in this vulnerable population.

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