Original article

Association between Uric Acid Changes during Hemodialysis and Severity of Left Ventricular Diastolic Dysfunction in ESRD Patients

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ABSTRAC

Background: Hyperuricemia has been implicated in cardiovascular disease, the leading cause of mortality in dialysis patients. Elevated SUA can contribute to left ventricular hypertrophy and diastolic dysfunction through pro-inflammatory mechanisms and by impacting metabolic pathways. The role of serum uric acid (SUA) in left ventricular diastolic dysfunction (LVDD), however, remains unclear in patients with end-stage renal disease (ESRD) undergoing hemodialysis. This study is aimed to determine the association of hyperuricemia with left ventricular diastolic dysfunction in end stage renal disease patient on maintenance hemodialysis.

Methods: A prospective study was carried on 129 patients with end stage renal disease of either gender of aged between 18 to 70 years who initiated maintenance hemodialysis at our hospital. Before and after hemodialysis, SUA levels were measured via standard enzymatic assay, and LVDD through echocardiographic evaluation followed ASE guidelines.

Results: The mean age of the eligible participants was 42.80 ±10.86 years. 65 (50.3%) of the patients were male and 64 (49.6%) were female. Most of the patients had dialysis twice a week 91 (70.5%). The pre-dialysis, uric acid was 6.89 $\pm$ 1.23 and post-dialysis it reduced to 4.78 $\pm$ 1.13, significant difference was as p-value was <0.05. Similarly, frequency of hyperuricemia was also compared which shows also a significant difference. Further, a moderately strong positive correlation was found between post-dialysis uric acid levels and LVDD grading (Spearman's r = 0.518), suggesting a direct association between residual hyperuricemia and cardiac dysfunction severity.

Conclusion: Haemodialysis alone has a moderate effect on uric acid clearance, even though it is the primary option for renal replacement therapy in low-income countries for patients with ESRD. These findings underscore the potential role of serum uric acid as a modifiable cardiovascular risk factor in dialysis-dependent patients.

Keywords:
Chronic Kidney disease, Diastolic Dysfunction, End Stage Renal disease, Hemodialysis, Uric acid

INTRODUCTION

Chronic kidney disease (CKD) is one of the main causes of early mortality and a high burden of morbidities. Nearly 700 million people worldwide are estimated to have it, with a prevalence rate of roughly 9.1%[1]. Numerous epidemiological factors contribute to Pakistan's higher incidence of chronic kidney disease (CKD); according to several studies conducted there, the prevalence of CKD can range from 12.5% to 29.9%[2].

ARTICLE INFO

Article History
Received: 08.11.2024 | Accepted: 27.06.2025
Conflict of Interest: The authors declare no conflict of interest exist.
Funding: None.

Citation: Zohrah KT, Mal P, Lal SI, Fatima A, Ali S, Memon A, Kumar M. Association between uric acid changes during hemodialysis and severity of left ventricular diastolic dysfunction in ESRD patients. J Fatima Jinnah Med Univ. 2025; 19(2): 105-109.

DOI: https://doi.org/10.37018/YKJE6274

In addition to the high burden of traditional CVD risk factors, patients with chronic kidney disease (CKD) also have CKD-related risk factors, including inflammation, elevated calcium and phosphorus product levels, uremic toxins, anaemia, and fluid overload.[2] Renal dysfunction can exacerbate renal function by contributing to structural and functional abnormalities in the heart, which is why the cardiovascular system and renal function are tightly associated[3]. Left ventricular hypertrophy (LVH) and left ventricular diastolic dysfunction (LVDD) are prevalent cardiac issues in people with chronic kidney disease (CKD) and are strongly linked to a higher risk of CVD death in these patients[2,4]. Therefore, in order to stratify individuals with CKD for CVD risk, it is crucial to validate predictors of LVH and LVDD.

A metabolic byproduct of purine breakdown by xanthine oxidase (XO) is serum uric acid (SUA). Uric acid, the final byproduct of purine metabolism, is eliminated via the kidneys (60–70%) and the intestines (30–40%). Consequently, rising serum uric acid levels are associated with declining renal function, and hyperuricemia affects 40–80% of patients with end-stage renal disease (ESRD)[5,6]. In hemodialysis patients, SUA is efficiently eliminated from blood because to its sieving coefficient (1.01) and

clearance +7/pattern; consequently, 1 g of uric acid is usually eliminated following one hemodialysis session[7]. Recent findings indicate a strong correlation between SUA and cardiovascular events and risk, including heart failure, coronary artery disease, and hypertension[8]. Moreover, LVH and LVDD have been connected to elevated SUA levels[9,10]. However, there hasn't been much research done on the connection between SUA levels and LVH/LVDD in the CKD population.

Given the thought to the high prevalence of Chronic Kidney Disease and cardiovascular disease, therefore, this study was designed to determine the association of hyperuricemia with left ventricular diastolic dysfunction in End stage renal disease patient on maintenance hemodialysis.

METHODOLOGY

This prospective study was carried from October 2023 to April 2024 in the department of Department of Nephrology, Liaquat University Hospital, Hyderabad. Approval from the ethical review committee of the hospital [LUMHS/REC/115] was sought prior conducting the study. After taking written informed consent, a total of 129 patients with end stage renal disease of either gender of aged between 18 to 70 years who initiated maintenance hemodialysis at our hospital were included in the study via non-probability sampling technique. Patients with atrial fibrillation, mitral stenosis, left bundle branch block, mitral annular calcification, and lost to follow-up were excluded. Patients with tumor lysis syndrome or on chemotherapy, pregnancy, and patients with thyroid diseases, were also excluded. OPEN EPI calculator was used to calculate the sample size by taking the prevalence of CKD i.e. 29.9%%, margin of error = 8%, confidence interval = 95%, then calculated sample was 129. Demographic data and clinical characteristics, including age, sex, body mass index (BMI), blood pressure, co-morbidities, medications, and reasons for dialysis initiation were recorded at dialysis initiation. Blood samples taken just before to the start of hemodialysis were used to measure the following laboratory parameters: uric acid before and after hemodialysis (six months after dialysis), hemoglobin, phosphorus, and albumin. When uric acid levels in male patients were greater than 7 mg/dL, hyperuricemia was classified as positive; in female patients, the threshold value was greater than 6 mg/dL. Before beginning hemodialysis, a consultant cardiologist performed an echocardiogram to check for the presence of left ventricular dysfunction.LV diastolic dysfunction was considered depressed when left ventricular ejection fraction (LVEF) is found less than 45%.

The data was stored and analyzed in SPSS version 17.0. Mean and standard deviation (SD) was calculated for numeric variables like age, BMI, hemoglobin, phosphorus, albumin, pre and post dialysis uric acid and post dialysis grading of diastolic dysfunction. Frequencies and percentages were computed for categorical variables like gender, frequency of HD per week, causes of CKD and hyperuricemia. Pre and post uric acid dialysis was compared using paired t-test. Mc-nemers test was applied to compare the frequency of pre and post dialysis hyperuricemia. Spearman's correlation was applied to see the Correlation between Post-Dialysis Uric Acid and Left Ventricular Diastolic Dysfunction Grading. P-value < 0.05 was considered as significant.

RESULTS

The mean age of the eligible participants was 42.80 ±10.86 years, mean BMI was 29.64 $\pm$ 2.93 kg/m^2 and mean duration of disease was 3 $\pm$ 0.36 hours. 65 (50.3%) of the patients were male and 64 (49.6%) were female. Most of the patients had dialysis twice a week 91 (70.5%). The Most common cause of CKD was hypertension 60 (38%) then diabetes 39 (30.2%), glomerulonephritis 4 (3%) and urolithiasis 3 (2.3%). The mean hemoglobin was 7.736 $\pm$ 1.51 mg/dL, mean phosphorus was 6.23 $\pm$ 2.63 mg/dL and mean albumin was 3.02 $\pm$ 0.63 g/dL, as shown in Table 1.

The pre-dialysis, uric acid was 6.89 $\pm$ 1.23 and post-dialysis it reduced to 4.78 $\pm$ 1.13, significant difference was as p-value was 0.00. Similarly, frequency of hyperuricemia was also compared which shows also significant difference, as shown in Table 2 and 3.

A moderately strong positive correlation was found between post-dialysis uric acid levels and LVDD grading (Spearman's r = 0.518), suggesting a direct association between residual hyperuricemia and cardiac dysfunction severity, as shown in Table 4.

DISCUSSION

Uric acid (UA), a terminal product of purine metabolism via xanthine oxidase, serves as a plasma antioxidant. However, elevated serum UA levels have been associated with the onset of oxidative stress-related disorders. Consequently, it has been shown that elevated serum UA is associated with a higher risk of coronary heart disease, cardiovascular disease, stroke, hypertension, diabetes mellitus, and all-cause and CV mortality in the general population[11,12].

The precise role of UA in the development of CKD is still uncertain, despite the fact that higher blood UA levels were associated with higher all-cause and CV mortality in CKD patients[13-15]. UA levels are usually elevated in CKD patients. The impact of the UA level on the morbidity and mortality of haemodialysis (HD) patients is still unclear and up for debate. Serum UA levels vary significantly among HD patients.

Table 1: Demographic and clinical data of the Patients

Baseline Data	Mean ± SD/n (%)
Age	42.80 ±10.86 years
Duration of Dialysis	3 ± 0.36 hours
BMI	29.64 ± 2.93 kg/m^2
Frequency of dialysis per week	
• Once	08 (6.2%)
• Twice	91 (70.5%)
• Thrice	30 (23.25%)
Gender	
• Male	65 (50.3%)
• Female	64 (49.6%)
Cause of CKD	
• Hypertension	60 (38%)
• Diabetes	39 (30.2%)
• Glomerulonephritis	4 (3%)
• Urolithiasis	3 (2.3%)
Laboratory Parameters	
• Hemoglobin	7.736 ± 1.51 mg/dL
• Phosphorus mg/dL	6.23 ± 2.63 mg/dL
• Albumin g/dL	3.02 ± 0.63 g/dL

Table 2: Comparison of pre- and post-dialysis Uric Acid among hemodialysis dependent patients

Characteristics	Pre-dialysis	Post-dialysis	p-value
Uric acid (mg/dL)	6.89 ± 1.23	4.78 ± 1.13	0.000

Table 3: Comparison of frequency of pre and post dialysis hyperuricemia

Hyperuricemia	Yes n (%)	No n (%)	p-value
Pre-dialysis	107 (82.9%)	22 (17.1%)	0.000
Post-dialysis	32 (24%)	97 (75.1%)	

Table 4: Correlation between Post-dialysis Uric Acid and Left Ventricular Diastolic Dysfunction Grading

Parameters	Mean ± SD	r-coefficient
Post-dialysis serum uric acid	4.78 ± 1.31	
Post-dialysis Left Ventricular Diastolic Dysfunction Grading	2.53 ± 0.63	0.518

Research indicates that 40–80% of HD patients had serum UA levels below 7 mg/dL[16,17]. The results of our study also support the findings that that post-dialysis around 24% of the patients hadhyperurecemia.

The objective of our study was to assess the differences in uric acid levels between pre- and post-dialysis and to see the correlation between post dialysis uric acid with left ventricular diastolic dysfunction in End stage renal disease patient on maintenance hemodialysis. According to the current study's findings, serum levels of uric acid were significantly different before and after hemo-dialysis (p 0.001). After hemodialysis, the mean ± SD serum levels of uric acid, of the patients who were being investigated dramatically decreased. (6.89 ± 1.23 and 4.78 ± 1.13 mg/dl, respectively).

Due to decreased clearance, uric acid levels are higher in patients with renal failure. Dialysis can be used to partially eliminate uric acid from blood[18]. Research has shown that haemodialysis patients who have higher uric acid levels also have higher mortality rates[19]. Up to 50% of patients with end-stage renal illness have been found to have hyperuricemia, which is likely caused by a lack of UA excretion. In agreement with our results, it was reported that mean pre-dialysis serum uric acid was 6.89 ± 1.23 mg/dl while the post dialysis serum uric acid was mean 4.78 ± 1.13 mg/dl[20]. There was a significant reduction around 50% in serum uric acid after hemodialysis. This outcome is comparable to that of Alaraj et al. in Saudi Arabia[21], who discovered that dialysis reduced the risk by 66.14% (±18.8). It is different, nevertheless, from findings of Soriano et al. in Spain, who discovered that a greater percentage of patients (56.7%) had a reduction of more than 80%[22]. This difference could be explained by the fact that Soriano et al. worked on a population who had been on maintenance HD for a long time, which was not the case in our study.

The current investigation's findings indicate a positive association (0.518) between uric acid and left ventricular diastolic dysfunction; a study by Ibrahim ME et al.[23] also revealed a similar relationship. Additionally, it was shown that elevated uric acid was linked to high LVMI, and that LVMI decreased with effective dialysis

sessions and decreased volume overload, which is consistent with our findings[24].

Our findings were supported by a team of researchers who found a direct correlation (p = 0.03) between the ejection fraction and blood uric acid levels, meaning that patients with higher uric acid levels were more likely to have a lower ejection percentage. Additionally, it was determined that there is a substantial correlation between the severity of congestive heart failure and the left ventricular ejection fraction and greater serum uric acid levels[25].

Despite the significance of our findings, the following limitations should be taken into account when interpreting them: (1) the small sample size that could be improved in a multicenter study; (2) the lack of a strong criterion for evaluating diet, which is a major source of purines and thus affects SUA levels; (3) Hemodialysis was not standardized across all participants; the majority received dialysis twice weekly rather than the recommended thrice-weekly schedule. This inconsistency may influence solute clearance, including uric acid, and impact cardiac outcomes; (4) Post-dialysis uric acid was measured only after six months, without serial measurements or long-term cardiac follow-up. SUA levels may fluctuate over time and further echocardiographic assessments would improve understanding of sustained cardiovascular effects; (5) The mean hemoglobin was notably low (7.74 ± 1.51 g/dL), which itself can contribute to LVDD due to impaired oxygen delivery and increased cardiac workload. This confounding factor should be considered when interpreting the relationship between SUA and LVDD.

CONCLUSION

Haemodialysis alone has a moderate effect on uric acid clearance, even though it is the primary option for renal replacement therapy in low-income countries for patients with ESRD. These findings underscore the potential role of serum uric acid as a modifiable cardiovascular risk factor in dialysis-dependent patients. However, given the limitations of sample size, dialysis frequency variability, and confounding clinical factors, further multicenter investigations with larger cohorts and long-term follow-up are warranted to establish robust clinical recommendations.

Author Contributions

- Dr. Khadija tuz Zohrah, Conception and design, analysis and interpretation of data, drafting the article, critical revision for important intellectual content, final approval.
- Dr. Pooran Mal: Conception and design, analysis and interpretation of data.
- Dr. Sunil Ishwer Lal: Analysis and interpretation of data, drafting the article.
- Dr. Aqsa Fatima: Acquisition of data, conception and design, analysis and interpretation.
- Dr. Salam Ali: Analysis and interpretation of data, proofreading.
- Dr. Asfa Memon: Conception and design, analysis and interpretation of data.
- Mukesh Kumar: Conception and design, analysis and interpretation of data.

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