

Prevalence of Hyperuricemia in Thrice Weekly Maintenance Hemodialysis Patients

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Abstract

Background: Hyperuricemia is a well-established prognostic marker for chronic kidney disease (CKD) patients. Therefore, in this study, our aim was to determine the prevalence of hyperuricemia in thrice-weekly HD patients at a tertiary care hospital in Karachi, Pakistan.

Methods: This was a descriptive cross-sectional study that included consecutive patients diagnosed with end-stage renal disease (ESRD) on maintenance thrice-weekly HD (HD). Based on serum urate concentrations, hyperuricemia was labeled in male patients with > 7 mg/dL, and in female patients, the threshold value was >6 mg/dL.

Results: The study included a total of 73 thrice-weekly HD patients out of which 64.4% (47) were male and mean age of the study sample was 50.3 ± 12.1 years. Hyperuricemia was observed in 76.7% (56) of the patients. Female gender, diabetes mellitus and glomerulonephritis were relatively more common among patients with hyperuricemia. Similarly, cardiac abnormalities including severe left ventricular dysfunction, severe mitral regurgitation and severe tricuspid regurgitation were also common among patients with hyperuricemia.

Conclusion: Hyperuricemia was prevalent in more than $3/4^{\text{th}}$ of the thrice-weekly HD patients. Females, diabetics, glomerulonephritis, and cardiac abnormalities were relatively more common among hyperuricemic HD patients.

Keywords: End-stage renal disease, HD, hyperuricemia, thrice-weekly, diabetes mellitus, Pakistan.

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DOI: 10.53778/pjkd63205

Received: 2 July, 2022 and accepted 10 September, 2022

PJKD 2022;6(3):10-14

Introduction

Chronic kidney disease (CKD) is one of the leading causes of premature deaths and an increased burden of morbidities. In the year 2017, it was estimated to affect nearly 700 million individuals globally with a prevalence rate of approximately 9.1%.¹ Pakistan has an increased incidence of CKD due to multiple epidemiological factors, the prevalence of CKD is reported to be as high as 12.5% to 29.9% in various studies from Pakistan.²⁻⁴ Significant variations in the patterns of CKD and its etiology have been reported between urban and rural dwellers of the country. Kidney stones disease and glomerulonephritis are more commonly observed etiologies in rural populations while CKD of hypertensive and diabetic origin was more common among the urban population.^{3,4}

Kidney is a vital organ responsible for removing extra fluid and wastes from the human body, impaired functioning of this vital organ leads to multiple complications including hyperuricemia. Its prevalence is reported to be as high as 60% among patients with advanced kidney disease.⁵ Only 30% of the urate is removed by the gastrointestinal tract and its bacteria while the remaining 70% of it is eliminated by the kidney, which is why nearly 50% of the patients with CDK develop hyperuricemia even before the initiation of hemodialysis (HD).^{6,7}

Hyperuricemia & Hemodialysis

In recent years there has been growing evidence that hyperuricemia is not merely a marker of renal dysfunction but is believed to play important role in the progression and pathogenesis of the disease itself, however, several unanswered questions revolve around whether the association between hyperuricemia and CKD is a coincidental, compensatory, or casual phenomenon.⁸ Nonetheless, the prognostic significance of hyperuricemia in patients with CKD is well established. Elevated uric acid levels are reported to be associated with an increased risk of cardiovascular or all-cause mortality among patients with stage III/IV CKD or on HD.⁹⁻¹²

Considering the prognostic significance of hyperuricemia in CKD patients, its true prevalence in our HD population may help in better clinical decision-making identify associated complications. Therefore, in this study, our aim was to determine the prevalence of hyperuricemia in thrice-weekly HD patients at a tertiary care hospital in Karachi, Pakistan.

Methods

This was a descriptive cross-sectional study conducted between June 2021 and May 2022 at a tertiary care hospital namely, the Karachi Institute of Kidney Disease (KIKD), Karachi, Pakistan. In accordance with the Declaration of Helsinki, the study was approved by the institutional ethical review committee (KIKD/KMC-57/20) and verbal consent for participation was obtained from all the patients included in this study.

Study inclusion criteria were either gender patients with more than or equal to 18 years of age diagnosed with end-stage renal disease (ESRD) on maintenance thrice-weekly HD. Patients with differed consent, recent ESRD (on maintenance HD for less than one month), or weekly HD frequency of less than three were not included in this study.

A detailed history of the patients was obtained using a structured predefined proforma including history regarding risk factors, frequency and duration of HD sessions, duration of disease, and residual urine status. Additionally pre- and post-dialysis laboratory investigations were also obtained which included hemoglobin (Hb), calcium (Ca), phosphorus (PO₄), albumin, urea, and uric acid levels. Based on pre-dialysis serum urate concentrations, hyperuricemia was labeled in male patients with >7 mg/dL, and in female patients, the threshold value was >6 mg/dL. Echocardiographic findings regarding structural and functional abnormalities were also recorded which included, left ventricular hypertrophy (LVH), left ventricular (LV) systolic and diastolic dysfunction, tricuspid regurgitation (TR) and mitral regurgitation (MR) grading.

Collected data were managed and analyzed on IBM SPSS version 21. Variables were summarized as either frequency (%) or mean $\pm$ standard deviation (SD), appropriately. Pre- and post-dialysis uric acid concentration along with other laboratory parameters were assessed with the help of paired sample t-test. The statistical association between hyperuricemia and patients or the diseases related characteristics was established with the help of the Chi-square test/independent sample t-test, appropriately, with a 5% level of significance.

Results

The study included a total of 73 thrice-weekly HD patients out of which 64.4% (47) were male and mean age of the study sample was 50.3 ± 12.1 years. Hyperuricemia was observed in 76.7% (56) of the patients. Females (41.1% vs. 17.6%), Diabetes Mellitus (46.4% vs. 23.5%), and glomerulonephritis (5.4% vs. 0%) were relatively more common among patients with hyperuricemia than non- hyperuricemia patients, respectively (Table 1). Similarly, severe LV dysfunction (75% vs. 35.3%), severe mitral regurgitation (14.3% vs. 5.9%), and severe tricuspid regurgitation (12.5% vs. 5.9%) were relatively more common among patients with hyperuricemia than non- hyperuricemia patients, respectively, Table 1.

A comparison of pre- and post-dialysis laboratory parameters is presented in Table 2. A significant post-dialysis reduction in uric acid level has been observed, from 8.1 ± 1.7 to 7.3 ± 1.4 mg/dL. Similarly, a significant post-dialysis reduction has been observed in hemoglobin, calcium, phosphorus, albumin, and urea level.

Hyperuricemia & Hemodialysis

Table 1: Demographic and clinical characteristics of 73 maintenance hemodialysis patients stratified by hyperuricemia.

	Total	Hyperuricemia		P-value
		No	Yes	
Total	73	23.3% (17)	76.7% (56)	-
Gender				
Male	64.4% (47)	82.4% (14)	58.9% (33)	0.77
Female	35.6% (26)	17.6% (3)	41.1% (23)	
Age (years)	50.3 ± 12.1	52.5 ± 12.8	49.6 ± 11.9	0.36
Body mass index (kg/m²)	20.9 ± 2.6	20.7 ± 2.2	20.9 ± 2.7	0.74
Etiology of Kidney Disease				
Hypertension	52.1% (38)	70.6% (12)	46.4% (26)	0.18
Diabetes	41.1% (30)	23.5% (4)	46.4% (26)	
Glomerulonephritis	4.1% (3)	0% (0)	5.4% (3)	
urolithiasis	2.7% (2)	5.9% (1)	1.8% (1)	
Duration of kidney disease	2.8 ± 1.8	3.1 ± 2.1	2.8 ± 1.7	0.57
Duration of each session				
Three hours	1.4% (1)	5.9% (1)	0% (0)	0.07
Four hours	98.6% (72)	94.1% (16)	100% (56)	
Residual urine				
Less than 100 ml / 24 hours	97.3% (71)	100% (17)	96.4% (54)	0.43
More than 100 ml / 24 hours	2.7% (2)	0% (0)	3.6% (2)	
Systolic blood pressure (mmHg)	140.4 ± 19.3	143.9 ± 19.4	139.4 ± 19.3	0.40
Diastolic blood pressure (mmHg)	85.9 ± 8.8	88.3 ± 10.3	85.2 ± 8.3	0.21
Left ventricular dysfunction				
None	6.8% (5)	17.6% (3)	3.6% (2)	0.02
Mild	5.5% (4)	11.8% (2)	3.6% (2)	
Moderate	21.9% (16)	35.3% (6)	17.9% (10)	
Severe	65.8% (48)	35.3% (6)	75% (42)	
Left ventricular hypertrophy	15.1% (11)	29.4% (5)	10.7% (6)	0.06
Diastolic dysfunction	17.8% (13)	11.8% (2)	19.6% (11)	0.46
Mitral regurgitation				
None	24.7% (18)	47.1% (8)	17.9% (10)	0.10
Mild	42.5% (31)	29.4% (5)	46.4% (26)	
Moderate	20.5% (15)	17.6% (3)	21.4% (12)	
Severe	12.3% (9)	5.9% (1)	14.3% (8)	
Tricuspid regurgitation				
None	57.5% (42)	70.6% (12)	53.6% (30)	0.295
Mild	11% (8)	0% (0)	14.3% (8)	
Moderate	20.5% (15)	23.5% (4)	19.6% (11)	
Severe	11% (8)	5.9% (1)	12.5% (7)	

Table 2: Comparison of pre- and post-dialysis laboratory parameters among 73 maintenance hemodialysis patients undergoing thrice per week hemodialysis.

	Pre-dialysis	Post-dialysis	P-value
Hemoglobin (mg/dL)	10.2 ± 1.6	9.8 ± 1.3	<0.001
Calcium (mg/dL)	7.8 ± 0.8	7.3 ± 0.7	<0.001
Phosphorus (mg/dL)	5.4 ± 1.5	4.8 ± 1.3	<0.001
Albumin (g/dL)	3.4 ± 0.5	3 ± 0.4	<0.001
Urea (mg/dL)	117.2 ± 37.2	61.6 ± 40.2	<0.001
Uric acid (mg/dL)	8.1 ± 1.7	7.3 ± 1.4	<0.001

Discussion

Hyperuricemia is a common complication of CKD which is associated with adverse clinical outcomes in these patients. Therefore, in this study, we have evaluated the prevalence of hyperuricemia in thrice-weekly HD patients. The prevalence of hyperuricemia was found in more than 3/4th (76.7%) of the thrice-weekly HD patients. Females, diabetics, glomerulonephritis, severe LV dysfunction with mitral regurgitation, and tricuspid regurgitation were relatively more common among hyperuricemic patients. All patients with elevated uric acid may not exhibit symptoms, as there are several studies suggesting lowering uric acid can slow down the rate of deterioration of renal function in the early stages of CKD.¹³ Lifestyle changes and simple pharmacological management of hyperuricemia needs special consideration to slow down the deterioration of renal function.

Studies have reported varying rates of hyperuricemia in CKD patients depending on the extent and severity of the disease and the population under study. Petreski et al. reported 28.3% hyperuricemic patients in a study of 120 CKD patients who were primarily not on HD.¹⁴ The study further reported a strong association between hyperuricemia and the risk of long-term mortality. Costa et al. conducted a retrospective study of not on HD 922 ≥ 3 stage CKD patients of Caucasian origin and reported the rate of hyperuricemia as 62.4% and the presence of hyperuricemia was found to be an independent predictor of secondary hyperparathyroidism.¹⁵ In a study of Japanese CKD patients not on HD, the prevalence of hyperuricemia was reported to be 70.4% and 50.4% in patients with CKD stage G5 and G4, respectively.¹⁶ Abderraman et al. reported 15.2% prevalence of hyperuricemia in a study of 712 hospitalized CKD patients in N' Djamena (Chad).¹⁷ Petreski et al. reported 24.1% in a study of 120 patients with CKD who eventually transitioned to HD.¹⁸

Data from Pakistan also suggests a higher prevalence of hyperuricemia. A population-based study by Qudwai et al. included 2,727 individuals without CKD from across Pakistan and reported hyperuricemia in 39%. A higher percentage of females were hyperuricemic in their study, 27.9% among males and 49.3% among females. Most of the hyperuricemic individuals, 90.8% were symptomatic.¹⁹ Another study of 375 individuals from various outpatient clinics by Raja et al.^[20] reported hyperuricemia in 30.1% of the individuals and 33.3% in yet another study by Shaikh et. al.^[21] In pre-dialysis CKD patients hyperuricemia was reported to be 62.5%.²² In a prospective study of 394 individual, the presence of CKD correlated with the presence of hyperuricemia.²³ No study from Pakistan exists that addresses hyperuricemia among hemodialysis population.

The prognostic significance of hyperuricemia in CKD is well established,⁹⁻¹² however, the role of hyperuricemia in the progression of CKD is not very clear. There is insufficient evidence to support hyperuricemia management at an early stage due to the lack of benefit in asymptomatic hyperuricemic CKD patients.²⁴ In the absence of sufficient evidence to validate the causative role of hyperuricemia in CKD progression, its pharmacological treatment is questionable even in HD patients. However, lifestyle modifications and targeted pharmacological urate-lowering therapy can be beneficial in certain sub-groups of patients and systematic identification of such patients is another big challenge for the clinicians.²⁵

Limitations of our study was being a single-center study and having a small sample size and limits the generalizability of study findings.

Conclusion

Hyperuricemia was prevalent in more than 3/4th of the thrice-weekly HD patients. Females, diabetes, glomerulonephritis, severe LV dysfunction with severe mitral regurgitation, and severe tricuspid regurgitation were relatively more common among hyperuricemic patients. Further studies with strategies to lower hyperuricemia at the pre-CKD and initiation of HD with long follow-up may help in clarifying the role of hyperuricemia in the morbidity and mortality of CKD- 5 HD patients.

Source of Funding: None to declare.

Conflict of interest: None to declare

Disclosure: None to declare

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