Original paper

Prevalence of Hyperuricemia in Adult Renal Transplant Patients at The Kenyatta National Hospital, Nairobi, Kenya

Kapule I, Kayima J, Mcligeyo SO, Amayo EO, Oyoo GO

Department of Clinical Medicine and Therapeutics, School of Medicine, Faculty of Health Sciences, University of Nairobi, P. O. Box 19676-00202, Nairobi, Kenya

Address for Correspondence: Dr. Ijaa Kapule. Email: ijaaak@gmail.com

Abstract

Background: Hyperuricemia is prevalent in renal transplant recipients and has been shown to be a cause of adverse graft outcome through its direct effects on the kidney and indirectly through its cardiovascular effects that can result in impaired graft function. Hyperuricemia is modifiable in renal transplant recipients.

Objective: To determine the burden of hyperuricemia and clinical features associated with it among patients attending the renal transplant clinic at a tertiary hospital in Nairobi, Kenya.

Design: Cross sectional study.

Setting: Renal transplant clinic at the Kenyatta National hospital

Methods: A total of 96 patients were included in the study. Clinical characteristics, blood uric acid and creatinine levels for the purpose of estimating the glomerular filtration rate were determined from renal transplant recipients greater than 6 months post-transplant. Hyperuricemia was defined as serum uric acid of greater than 360 umol/l in females and greater 420 umol/l in males

Results: The mean age of the patients was 46.4 (SD 14.3) years, mean post-transplant time was 5.9 (SD 5.3) years, mean creatinine was 135.5 (SD 117.6) umol/l. The prevalence of hyperuricemia was 40.6% (n=96). The patients were predominantly male at 65.6%. The most common cause of End Stage Renal Disease (ESRD) was hypertension at 32%. Hyperuricemic patients had worse graft function (mean eGFR 59.4 vs. 74.5 mL/min/1.73 m^2; p=0.005), higher creatinine levels (116.0 vs. 98.0 umol/l; p=0.014), less likely to be diabetic patients (12.8% vs. 33.3%, p=0.023), or be on insulin (7.7% vs. 29.8%; p=0.009).

Conclusion: Prevalence of post-transplant hyperuricemia is high, particularly in those with higher creatinine and estimated Glomerular Filtration Rate (eGFR) and lower in diabetics and those who use insulin.

Recommendation: Screening for hyperuricemia should be done regularly for renal transplant recipients at the Kenyatta National Hospital transplant clinic due to its high prevalence

Key words: Uric acid, Hyperuricemia, renal transplant recipients, Kenyatta National Hospital, Prevalence

Introduction

Hyperuricemia is common among patients who have received renal transplants with incidence varying from 25% to 80% in those on cyclosporine (1) especially those on cyclosporine. It also varies depending on the population studied (2,3). It has been associated with poor graft outcome (chronic allograft nephropathy), hypertension and cardiovascular disease that can result in impaired graft function indirectly (4). Research has shown that progressive deterioration of renal graft function and eventual renal graft loss is associated with hyperuricemia (5). This can be as a consequence of the toxic effects of uric acid on the graft or possible cardiovascular effects. Hyperuricemia is potentially modifiable with drug switches, urate lowering drugs and lifestyle modification (6).

This study sought to determine the burden of hyperuricemia in renal transplant recipients attending the transplant clinic at Kenyatta National Hospital and to determine factors associated with hyperuricemia. There is currently no published data on the prevalence of hyperuricemia and associated risk factors among renal transplant patients, at the Kenyatta National Hospital. Associations of hyperuricemia in renal transplant recipients include older age, dialysis vintage, male gender, diabetes mellitus, reduced glomerular filtration rate, obesity and drugs such as cyclosporine and diuretics (7). Diet has also been implicated in playing a role in worsening already preexisting hyperuricemia especially diets that are rich in purines such as fructose containing foods, sea food and high alcoholic intake (8).

Materials and methods

The study objective was to determine the prevalence of hyperuricemia in renal transplant recipients attending the Kenyatta National Hospital renal unit. The study design was a cross sectional descriptive study conducted among consenting adult renal transplant recipients at the renal transplant clinic at the Kenyatta National Hospital, a tax funded tertiary hospital in Nairobi, Kenya. It is the largest hospital in East and Central Africa. Approximately 150 patients actively attend the renal transplant clinic. The clinic runs every Tuesday except for public holidays. The clinic attends to approximately 15 renal transplant recipients on clinic days and a smaller number of renal allograft donors. Patients are seen by the nephrologists, nephrology fellows and post graduate student doctors.

The study population were stable ambulatory renal transplant recipients aged above 18 years attending the renal transplant clinic who consented to participate in the study. Patients who were more than 6 months post renal transplant were enrolled to the study. Sample size was calculated using Fischer formula, correcting for finite population. N was determined to be 96.

Hyperuricemia is defined as serum uric acid of

- ≥ 420 micromol/L in men, and
- ≥ 360 micromol/L in women

The instrument for collecting data was a clinician administered questionnaire. Information obtained included: age, sex, Body Mass Index (BMI), drugs patients were on, immunosuppressive drug regimen, whether they were on diuretics or not, cause of the end Stage Renal Disease and smoking status. Patients were recruited as they attended the renal transplant clinic at the Kenyatta National Hospital. Five milliliters of venous blood were collected from each participant for the purpose of measuring serum uric acid and serum creatinine levels.

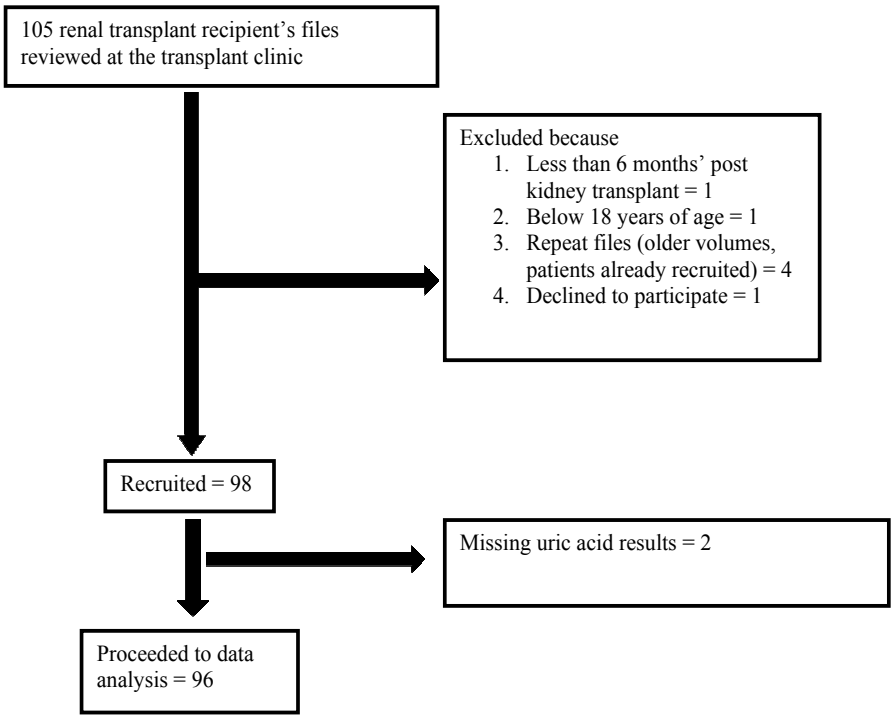
Statistical analysis was carried out by SPSS. Analysis for variables which were categorical such as smoking status or sex were analyzed using the chi square test. Means or medians were used to analyze continuous variables such as length of time on dialysis or age. Standard deviations, or inter quartile ranges were then computed where necessary. For comparison of clinical characteristics of different sub levels of uric acid, for example hyperuricemia versus normouricemia, univariate analyses techniques were used. Factors associated with hyperuricemia were assessed using multivariate logistic regression methods. Prevalence of hyperuricemia was calculated by dividing the total number of patients who are hyperuricemic by the total number of patients and was reported as a percentage. Glomerular Filtration Rate (GFR) was calculated using the CKD-EPI formula.

Results

Screening and enrolment to study

The study took place during the months of December 2022 and March 2023. A total of 105 patient files were reviewed for eligibility at the transplant clinic of which 96 were enrolled as shown in Figure 1.

Figure 1: Enrolment schema



Baseline characteristics

The mean age of the patients was 46.4 (SD 14.3) years, with an age range of 18 to 72 years. The median age was 47.5 (IR 35.5 – 58.0) years. The mean creatinine was 135.5 (SD 117.6) umol/l, with a range of 52.0 umol/l to 1,017.0 umol/l. The median creatinine was 102.0 (IR 86.0 – 139.5) umol/l. The mean post-transplant time was 5.9 (SD 5.3) years, where the minimum was 0.5 years, and maximum was 29.0 years. The median time was 5.0 (2.0 – 9.0) years. The patients were predominantly male at 65.6%. The most common cause of End Stage Renal Disease (ESRD) was hypertension at 32%, chronic glomerulonephritis 26% and diabetes mellitus 25%. The most common immunosuppressive regimen was tacrolimus and mycophenolate at 66.7%. Ninety one percent of patients were on steroids. The findings are summarized in Tables 1 to 4.

Table 1: Demographic characteristics of the patients

	Frequency (n=96) Mean ±SD (%)
Age (years)	46.4 ±14.3
≤30	17(17.7)
31-40	19(19.8)
41-50	19(19.8)
51-60	23(24)
>60	18(18.8)
Sex	
Male	63(65.6)
Female	33(34.4)
Donor	
Child	6(6.3)
Spouse	4(4.2)
Sibling	39(40.6)
Parent	4(4.2)
Other relative	43(44.8)
Transplantation site	
AKUH	5(5.2)
KNH	74(77.1)
India	12(12.5)
Mediheal (Eldoret)	1(1)
MP Shah	1(1)
MTRH	1(1)
TNH	1(1)

Table 2: Baseline characteristics -BMI, eGFR, post-transplant time and dialysis vintage

	Frequency (n=96)/ Mean ± SD (%)
BMI	
<18.5	7 (7.3)
18.5 – 24.9	44 (45.8)
25.0 – 29.9	35 (36.5)
≥30.0	10 (10.4)
eGFR	
Stage 1 (90+)	19 (19.8)
Stage 2 (60 – 89)	45 (46.9)
Stage 3 (30 – 59)	23 (24)
Stage 4 (15 – 29)	4 (4.2)
Stage 5 (<15)	5 (5.2)

	Frequency (n=96)/ Mean ± SD (%)
Creatinine	135.5 ± 117.6
Post-transplant time (years)	
< 1.0	12 (12.5)
1.0 – 5.0	43 (44.8)
5.1 – 10.0	29 (30.2)
>10.0	12 (12.5)
Dialysis vintage	
≤1.0	39 (40.6)
1.1 – 2.0	25 (26)
2.1 – 3.0	10 (10.4)
>3.0	12 (12.5)
Unknown	7 (7.3)
Pre-emptive transplant	3 (3.1)

Table 3: Baseline characteristics- cause of end stage renal disease

	Frequency (n=96)/ Mean ± SD (%)
Cause of ESRD	
Alportsyndrome	1 (1)
CGN (unclassified)	25 (26)
Diabetes	24 (25)
FSGN	5 (5.2)
HIVAN	1 (1)
Hypertension	31 (32.3)
Obstructive uropathy (PUV)	1 (1)
Polycystic kidney disease	5 (5.2)
RPGN	1 (1)
Unknown	2 (2.1)
Immunosuppressive drug	
Azathioprine	19 (19.8)
Cyclosporine	8 (8.3)
Everolimus	3 (3.1)
Mycophenolate	74 (77.1)
Tacrolimus	83 (86.5)

Table 4: Baseline characteristics- medication use among renal transplant recipients

	Frequency (n=96)/ Mean ± SD
Immunosuppressive regimen	
Azathioprine	3 (3.1)
Cyclosporine, Azathioprine	1 (1)
Mycophenolate, Azathioprine	1 (1)
Mycophenolate, Cyclosporine	7 (7.3)
Mycophenolate, Everolimus	1 (1)
Mycophenolate, Tacrolimus	64 (66.7)
Mycophenolate, Tacrolimus, Azathioprine	1 (1)
Tacrolimus	3 (3.1)
Tacrolimus, Azathioprine	13 (13.5)
Tacrolimus, Everolimus	2 (2.1)

	Frequency (n=96)/ Mean ± SD
Antihypertensive drugs	
B-Blockers	56 (53.8)
Calciumchannelblockers	71 (74)
Renin,angiotensinblockers	24 (25)
Vasodilators	28 (29.2)
Central acting hypertensive	14 (14.6)
Insulin	20 (20.8)
Statins	37 (38.5)
Steroids	88 (91.7)
Diuretics	12 (12.5)
Smoking	0
Alcohol	0

The prevalence of hyperuricemia was 40.6% (95% CI, 31.4% - 50.6%) as shown in Table 5.

Table 5: Prevalence of hyperuricemia

Hyperuricemia	Frequency (n=96)	Percent	95% CI
Yes	39 (M=25)	40.6	31.4% – 50.6%
No	57 (M=38)	59.4	

Clinical characteristics of hyperuricemic renal transplant recipients: Table 6 summaries the clinical characteristics of the hyperuricemic renal transplant recipients. The mean age of the hyperuricemic patients was 44.6 years. The mean creatinine was 116 umol/l, the mean eGFR was 59.4 ml/min. The median post-transplant time was 5 years and the median time on dialysis was 2 years. The patients were predominantly male at 64.1%. The most common cause of ESRD was hypertension at 35.9% followed by chronic glomerulonephritis 33.3% and diabetes mellitus at 12.8%.

Clinical characteristics of normouricemic renal transplant recipients: The mean age of the normouricemic patients was 47.6 years. The mean creatinine was 98 umol/l, the mean eGFR was 74.5 ml/min. The median post-transplant time was 5 years, and the median time on dialysis was 1 year. The patients were predominantly male at 66.7%. The most common cause of ESRD was diabetes mellitus at 33.3 %, followed by hypertension 29.8% and chronic glomerulonephritis at 21.1%. The clinical characteristics of the normouricemic renal transplant recipients are summarized in results (Table 6).

Comparison of clinical characteristics of hyperuricemic and normouricemic renal transplant recipients: Of the 96 patients, 57 (59.4%) had normal uricemia and 39 (40.6%) had hyperuricemia. Their clinical characteristics and comparison between them is shown on Table 6. Hyperuricemic patients had worse graft function (mean eGFR 59.4 vs. 74.5 mL/min/1.73 m2; p=0.005), higher creatinine levels (116.0 vs. 98.0 umol/l; p=0.014), fewer diabetic patients (12.8% vs. 33.3%, p=0.023), and fewer patients on insulin (7.7% vs. 29.8%; p=0.009). There was no statistical difference between normal uricemia and hyperuricemia with regards to other parameters measured. Established risk factors for hyperuricemia such as high BMI and cyclosporine use were not associated with hyperuricemia. Table 6 summarizes comparison of clinical characteristics of hyperuricemic and normouricemic renal transplant recipients.

Table 6: Comparison of clinical characteristics

	Hyperuricemic (n=39)	Normouricemic (n=57)	P-value
Age, *Mean±SD*	44.6±*12.9*	47.6±15.1	0.325
Sex, n(%)			
Male	25 (64.1)	38 (66.7)	0.795
Female	14 (35.9)	19 (33.3)	
BMI, Mean±SD	24.7±4.5	24.4±21.7	0.669
eGFR, Mean±SD	59.4±29.4	74.5±21.7	0.005
Creatinine, Median (IQR)	116(92.0–180.5)	98.0(82.0–112.0)	0.014
Post-transplant time (years), Median (IQR)	5.0 (2.0–9.0)	5.0 (2.0–8.0)	0.783
Dialysis vintage, Median (IQR)	2.0 (1.0–3.0)	1.0 (1.0–2.0)	0.240
Cause of ESRD, n (%)			
CGN	13 (33.3)	12 (211)	0.178
Diabetes	5 (12.8)	19 (33.3)	0.023
Hypertension	14 (35.9)	17 (29.8)	0.532
Immunosuppressive drug, n (%)	Hyperuricemic, (n=39)	Normouricemic, (n=57)	P-value
Azathioprine	9 (23.1)	10 (17.5)	0.504
Cyclosporine	3 (7.7)	5 (8.8)	0.851
Everolimus	2 (5.1)	1 (1.8)	0.351
Mycophenolate	29 (74.4)	45 (78.9)	0.599
Tacrolimus	35 (89.7)	48 (84.2)	0.436
Insulin, n (%)	3 (7.7)	17 (29.8)	0.009
Statins, n (%)	12 (30.8)	25 (43.9)	0.196
Steroids, n (%)	37 (94.9)	51 (89.5)	0.347
Diuretics, n (%)	8 (20.5)	4 (7.0)	0.060

Discussion

Hyperuricemia was found to have a 40.6 % prevalence among the renal transplant recipients at the Kenyatta National Hospital renal unit. This was largely in keeping with findings from studies from different parts of the world on renal transplant recipients, Turkey 39.9% (9), South Korea 40.8% (10) and Portugal 42.1% (11) . The sample size in this populations ranged from 133 to 693. The populations were predominantly white for study in Portugal and Turkey and predominantly Asian for the study in South Korea.

Renal transplant patients in our study had higher rates of hyperuricemia than the general population. In Kenya the prevalence of hyperuricemia in the general population is unknown however it was found to be 25% in black Africans in a study by Moulin *et al* (12) in Angola. Compared to other disease populations for example among ambulatory patients with Type 2 diabetes at the Kenyatta National Hospital diabetes outpatient clinic prevalence was found to be 19% by Muffadal *et al* in 2018 (13). Among hypertensive patients at Moi Teaching and Referral Hospital, Eldoret hospital prevalence was found to be at 44% by Sylvia *et al* (14). However, the definition of hyperuricemia used by Sylvia *et al* (14) was lower than our study, greater than 320umol/l for females and greater than 420umol for males compared to our definition of greater than 360umol/l in females and greater than 420umol/l in males. Hence the slightly higher prevalence.

In our study, serum uric acid levels correlated with mean eGFR and creatinine levels. Higher creatinine levels and lower eGFR being associated with higher uric acid levels. Since uric acid excretion is highly dependent on the eGFR (15) it comes to no surprise that our study found that low eGFR (mean eGFR 59.4 vs. 74.5 mL/min/1.73 m2; p=0.005), and high creatinine (116.0 vs. 98.0 umol/l; p=0.014) were positively correlated with high uric acid levels.

Being diabetic has been considered as a risk of hyperuricemia, in our study the opposite was found to be true (12.8% vs. 33.3%, p=0.023). In addition, patients on insulin were less likely to have hyperuricemia (7.7% vs. 29.8%; p=0.009). A possible theory to explain this could be that the diabetics in the clinic undergo very intense nutritional counselling in addition to the nutrition counselling they get at diabetic clinics. A nutritionist is available daily at the transplant clinic. Consumption of sugar sweetened drinks has been shown to be a risk factor for hyperuricemia (16) and in the diabetics the consumption of these drinks is restricted.

None of the participants' smokes cigarettes or consumes alcohol. Unfortunately, detailed nutrition history information was not collected in this study. This could be an area to be looked into in follow up studies.

Unlike other studies (11) that showed cyclosporine use to be associated with hyperuricemia, our results did not show any association between cyclosporine use and increased uric acid levels. This could be due to the study not being powered enough to demonstrate this association. Only 8 (8.3%) patients were on cyclosporine. Tacrolimus was the more popular calcinuerin inhibitor with 83 (86%) of the patients using it.

Diuretic use was also associated with hyperuricemia with half of the patients on diuretics being hyperuricemic though this result was not statistically significant (P value 0.060). Diuretics lessen uric acid excretion directly and indirectly via increasing urate reabsorption as well as reducing urate secretion mainly in the proximal tubules of the kidneys (17). Only two patients were on thiazide diuretics. No other drug use was found to have correlation with uric acid levels other than insulin use.

Being on dialysis for a longer period of time pre renal transplant has been associated with higher levels of uric acid post-transplant (18) the mechanisms are not clear but may be associated with hyperparathyroidism, oxidative stress exposure and hypoxia effects during the haemodialysis period that persisted long after transplantation. Though our population who were hyperuricemic had higher periods of time on dialysis compared to normuricemic patients (2 years' vs 1 year) results were not statistically significant (p value 0.24).

Increased BMI has been associated with hyperuricemia (19). In our study the mean BMI for hyperuricemic patients was found to be slightly higher 24.7 compared to 24.4 in the normuricemic population. However, these results were not statistically significant P value 0.669. Mean age, male sex and hypertension were not found to be associated with hyperuricemia unlike in another similar study by Malheiro *et al* (11).

Hyperuricemia has been associated with higher rates of graft loss compared to those who are not hyperuricemic (4,20). It has also been shown that lowering uric acid can prolong graft survival and lessen the risk of cardiovascular deaths (21,22). The most common cause of death in renal transplant recipients is cardiovascular events as found in a study by Wang *et al* (23). This study shows that more than a third of renal transplant recipients have hyperuricemia. This study can serve as the basis of forming guidelines and protocols for addressing hyperuricemia. which can potentially prolong renal graft survival. It can also be used as a baseline for future research on hyperuricemia in renal transplant population or even for follow up studies to assess the long term outcomes of hyperuricemia.

Conclusion

The prevalence of hyperuricemia is high (40.6%) among renal transplant recipients at the Kenyatta National Hospital renal unit.

There was significant positive association between high creatinine levels and low eGFR and hyperuricemia.

Being diabetic and on insulin use can put you at a lower risk of hyperuricemia.

Study limitations

The limitation of this study was it was a descriptive study design and not an analytical study. It had a relatively small sample size sot the study was not powered to make some conclusions, it was purely descriptive. It was also a cross sectional study and not follow up study. Some of the participants may not have had persistent hyperuricemia. No dietary history was taken in this study. Diet is a major risk factor for hyperuricemia.

Recommendations

From the study it has been shown that the prevalence of hyperuricemia is high among the renal transplant patients. Hyperuricemia is an established cardiovascular risk factor so regular screening of uric acid is recommended. Formulation of guidelines and protocols to assist management of hyperuricemia can be made available. Since the numbers of renal transplant patients are limited and are relatively few and prevalence of hyperuricemia in renal transplant recipients is now known to be 40.6%, a case control design may help answer questions on what other differences are there between the two populations. A follow up study on this population is recommended.

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