Elderly Renal Transplant Recipients and Renal Dysfunction: A Risk Factor for Hyperuricemia

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Abstract

Objectives: **To date, limited data are currently available on posttransplant hyperuricemia in elderly renal transplant patients.**

Materials and Methods: **We conducted a retrospective study on 120 renal transplant patients aged ≥ 60 years old who received a kidney with at least a minimum time of 1 year after transplant between 2008 and 2011 in Iran. Hyperuricemia was defined if serum uric acid was ≥ 416.36 μmol/L in men (7.0 mg/dL), and ≥ 356.88 μmol/L in women (6 mg/dL) that persisted for at least 2 consecutive tests. Moderate-to-severe hyperuricemia also was defined as a serum uric acid of ≥ 475.84 μmol/L (8.0 mg/dL) in both sexes.**

Results: **The majority of cases were men (66%) and only 9% received their grafts from deceased donors. The rate of deceased kidney transplant was higher in normouricemic patients. The prevalence of late posttransplant hyperuricemia was 37.5% of patients (n=45). Moderate-to-severe hyperuricemia was seen in 21 patients (17.5%). Although hyperuricemia was commonly observed in women than in men (43% in women vs 32% in men; *P* = .02), the rate of moderate-to-severe hyperuricemia was similar among both sexes (4.5% vs 4.3%; *P* = .9). Hyperuricemia frequently occurred in patients receiving kidney from a female donor (50% vs 29%; *P* = .005). In univariate analysis, a significant correlation was seen between serum uric acid and serum creatinine (r=0.5, *P* = .000). On multivariate regression, high serum creatinine was only a risk factor for posttransplant hyperuricemia in elderly kidney transplants (*P* = .000).**

Conclusions: **Posttransplant hyperuricemia was a quite common among elderly aged kidney recipients. It was correlated with renal allograft impairment.**

Key words: *Renal transplant, Renal failure, Uric acid, Elderly, Recipients*

Introduction

Hyperuricemia is a frequent problem in the general population that may be present in up to 10% of adults at least once in their lifetime.[1] It also is quite a common metabolic complication after renal transplant, accounting for 30% to 84% of transplant patients receiving cyclosporine.[2-5] The rising prevalence of posttransplant hyperuricemia may be attributed to growing of the organ transplant population. Other factors that might be involved include the Westernization of diets, diminished renal function, and the widespread use of cyclosporine and diuretics.[6-7] Although the mechanism of cyclosporine-induced hyperuricemia is still not fully understood, several mechanisms suggest including increased renal tubular reabsorption of urate, decreased glomerular filtration rate, and chronic nephrotoxicity of a drug (such as calcineurin inhibitors).[2, 8, 9] Serum uric acid levels also may increase with aging and obesity[10]; hence, advanced age may play a role in increasing serum uric acid concentrations.[6-7]

To date, limited data are available on posttransplant hyperuricemia in elderly renal transplant patients. We, therefore, made a plan to detect the prevalence and its risk factors of hyperuricemia among elderly kidney transplant recipients.

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Materials and Methods

Study population

We conducted a retrospective study on 120 renal transplant patients aged ≥ 60 years old who received a kidney for the first time with at least a minimum time of 1 year after transplant (5.7 ± 3.9 years) to detect the prevalence of hyperuricemia and its risk factors in a 3-year period between 2008 and 2011, living in Tehran, Iran. Living and deceased renal transplants were both enrolled. Patients were excluded if they were recently on diuretic therapy or used allopurinol. The present study was approved by the local Ethics Committee of Baqiyatallah University of Medical Sciences and the protocol conforms with the ethical guidelines of the 1975 Helsinki Declaration. Written, informed consent was obtained from all of the subjects.

Data collection

The clinical and biochemical data recorded for all patients were age and sex of recipients and donors, donor source (living or deceased), plasma creatinine level, fasting blood sugar, cyclosporine blood levels, hemoglobin concentration and lipid profile (triglyceride), cholesterol, and HDL-cholesterol and LDL-cholesterol.

Definition of hyperuricemia after kidney transplant

Hyperuricemia was defined if serum uric acid concentration was ≥ 416.36 μmol/L (7.0 mg/dL) in men and ≥ 356.88 μmol/L (6 mg/dL) in women that persisted for at least 2 consecutive tests. Moderate-to-severe hyperuricemia was also defined as a serum uric acid of ≥ 475.84 μmol/L (8.0 mg/dL) in both sexes.

Immunosuppressive agents

All patients received cyclosporine (targeting a trough level of 200 to 300 ng/mL for first 3 months, 100 to 250 ng/mL for the fourth to the 12th month, and 100 to 150 ng/mL thereafter; while using target of 2-hour postdose level was 800 to 1000 ng/mL for first 3 months and 400 to 600 ng/mL for subsequent months) plus mycophenolate mofetil, or azathioprine and prednisolone.

Statistical Analyses

Statistical analyses were performed with SPSS software for Windows (Statistical Product and Service Solutions, version 17.0, SSPS Inc, Chicago, IL, USA). Quantitative variables are expressed as means ± SD, while qualitative variables are shown by number and percentage. The Kolmogorov-Smirnov test showed that uric acid levels were not distributed normally ($P = .03$); hence, nonparametric tests such as Spearman's rank correlation coefficient and the Mann-Whitney U tests were used. Comparisons of qualitative data were performed by the chi-square test. Multivariate logistic regression analyses were used to examine the influence of factors predisposing hyperuricemia. All tests were 2-tailed, and P values of less than .05 were considered statistically significant.

Results

Demographic setting

The population characteristics of all patients are shown in (Table 1). The majority of cases were men (66%), while women were more likely to be hyperuricemic than men ($P = .02$). No significant differences were seen in the age of the recipient and the donor between both groups (Table 1). The majority of grafts came from living donors, especially in hyperuricemic group (Table 1). The rate of deceased kidney transplant was higher in normouricemic patients when compared to individuals with hyperuricemia.

Prevalence

The prevalence of late posttransplant hyperuricemia was 37.5% of patients (n=45). The moderate-to-severe hyperuricemia was seen in 21 of the all patients (17.5%). Although hyperuricemia was commonly observed in women (43% in women vs 32% in men; $P = .02$), the rate of moderate-to-severe hyperuricemia was similar in both sexes (4.5% vs 4.3%; $P = .9$). Hyperuricemia frequently occurred in patients receiving kidneys from female donors (50% vs 29%; $P = .005$).

Univariate analysis

A significant correlation was seen between serum uric acid and serum creatinine concentration (r=0.5; $P = .000$, Table 2). The concentration of triglyceride in hyperuricemic recipients also was significantly higher than those that had normal levels of serum uric acid (Table 1). There was no significant association between serum uric acid and other parameters (Tables 1 and 2).

Table 1. Definitions of terms used in the current study.

Variables	All patients (n=120)	Normouricemic patient (n=75)	Hyperuricemic patient (n=45)	*P* value
Sex of recipient, M/F, n, %	79/41 (66/34)	51/24 (68/32)	28/17 (61/39)	.02
Sex of donor, M/F, %	85/15	84/16	85/15	.005
Donor source, % LRD/LURD/Deceased	6/85/9	8.1/82.4/9.5	3/94/3	.08
Age of recipient, y, Mean ± SD	68 ± 8 (60-84)	67 ± 7	69 ± 8	.1
Age of donor, y, mean ± SD	28 ± 5 (19-47)	28 ± 4	28 ± 6	.2
Uric acid, μmol/L (mg/dL), mean ± SD	362.82 ± 113.01 (6.1 ± 1.9)	303.34 ± 65.42 (5.1 ± 1.1)	481.78 ± 83.27 (8.1 ± 1.4)	-
Last serum creatinine, μmol/L (mg/dL), mean ± SD	132.67 ± 68.95 (1.58 ± 0.78)	121.1 ± 41.54 (1.37 ± 0.47)	174.14 ± 91.05 (1.97 ± 1.03)	.000
Through level of cyclosporine, ng/mL, mean ± SD	140 ± 77	140 ± 78	140 ± 73	.8
2-Hour postdose level of cyclosporine, ng/mL, mean ± SD	513 ± 176	508 ± 180	527 ± 167	.2
Hb, g/L (g/dl), mean ± SD	128 ± 19 (12.8 ± 1.9)	129 ± 17 (12.9 ± 1.7)	127 ± 22 (12.7 ± 2.2)	.3
FBS, mmol/L (mg/dL), mean ± SD	5.99 ± 2.5 (108 ± 46)	6.16 ± 2.7 (111 ± 50)	5.71 ± 2.05 (103 ± 37)	.4
LDL-Cholesterol, mmol/L (mg/dL), mean ± SD	2.46 ± 0.8 (95 ± 31)	2.46 ± 0.69 (95 ± 27)	2.51 ± 0.93 (97 ± 36)	.8
HDL-Cholesterol, mmol/L (mg/dL), mean ± SD	1.26 ± 0.36 (49 ± 14)	1.26 ± 0.28 (49 ± 11)	1.29 ± 0.46 (50 ± 18)	.8
TG, mmol/L (mg/dL), mean ± SD	1.78 ± 0.91 (158 ± 81)	1.69 ± 0.83 (150 ± 73)	1.93 ± 1.05 (171 ± 93)	.02
Cholesterol, mmol/L (mg/dL), mean ± SD	4.61 ± 1.52 (178 ± 59)	4.58 ± 1.29 (177 ± 50)	4.66 ± 1.19 (180 ± 46)	.7
Transplantation duration	5.7 ± 3.9	5.8 ± 3.9	5.5 ± 3.7	.4

Abbreviations: F, female; FBS, fasting blood sugar; Hb, hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; M, male; SD, standard deviation; TG, triglyceride; Y, year

Table 2. Univariate correlation between serum uric acid and other parameters.

Variables	*P* value (r)*
Serum creatinine	.000 (0.54)
Trough level of cyclosporine	.5 (0.02)
2-h Postdose level of cyclosporine	.6 (0.03)
Age of recipient	.2 (0.05)
Hemoglobin	.7 (0.02)
FBS	.6 (-0.02)
Cholesterol	.4 (-0.04)
Triglyceride	.01 (0.12)
LDL-Cholesterol	.6 (0.03)
HDL-Cholesterol	.08 (-0.11)

*Correlation coefficient

Abbreviations: FBS, fasting blood sugar

Multivariate regression analysis

At multivariate logistic regression after adjustment for other factors, we found the increased concentration of serum creatinine was the only risk factor for posttransplant hyperuricemia in elderly kidney transplants (P = .000). On the other hand, female sex, cyclosporine blood levels, and dyslipidemia were not associated with higher probability of hyperuricemia after kidney transplant.

Discussion

The present study highlights a high prevalence of hyperuricemia among elderly aged kidney recipients in the late period after transplant; it accounted for 37.5% of all patients. It was allied to prolonged cyclosporine use rather than to blood levels, which matches other reports.[11] Min and associates also have shown that the prevalence of hyperuricemia was 21% of all recipients at 6 months' posttransplant, but this increased to 41% at 4 years after kidney transplant.[12] The occurrence of posttransplant hyperuricemia is obviously related to cyclosporine therapy[2, 5, 9, 13-14] and resolves upon withdrawal of the drug.[2]

In a series of 218 kidney transplants, advanced age was not associated with the rate of posttransplant

hyperuricemia.[12] In addition, a subanalysis of the Symphony study on 1645 recipients reported a lack of any significant association between serum uric acid levels and recipient age in the first month after renal transplant.[15] In another study on 589 cases of renal recipients, serum uric acid did not correlate with increasing age.[14]

This study shows an association between renal allograft dysfunction posttransplant hyperuricemia, which is consistent with the findings of other studies.[9, 16-18] One small study demonstrated that 5-year graft survival in hyperuricemic recipients was lower than those who had a normal level of serum uric acid (17). In contrast, Meier-Kriesche and associates showed that no association was seen between serum uric acid concentration and deterioration of renal allograft function in the first 3 posttransplant years.[15] Two small and short-term follow-up studies also have shown findings different from our results, suggesting that hyperuricemia had no adverse effect on the graft survival.[3, 19] Moreover, advanced age is a risk factor for chronic allograft nephropathy; hence, further studies are required to confirm the correlation of hyperuricemia with progression of renal allograft dysfunction in elderly kidney transplants.

The current study reveals a predominant chance of posttransplant hyperuricemia in females, which is opposite of findings of other reports that reported that male sex was an independent factor at multivariate analysis.[12, 14]

The association between hyperuricemia and serum lipids is also controversial,[1] no correlation was seen between dyslipidemia and hyperuricemia in the present study.

Although our study was clearly limited by the relatively small number of elderly recipients and lack of long-term follow-up, limited data are currently available in the literature. Thus, this study can be encouraging to investigators to report their experience on posttransplant hyperuricemia among advanced age patients. In addition, we recommend that close follow-up is necessary in case serum uric acid levels rise further.

Conclusions

Posttransplant hyperuricemia was a quite common among elderly kidney recipients. It is correlated with renal allograft impairment.

Because a great deal of hyperuricemic patients after kidney transplant are cyclosporine induced, it is reasonable that screening tests for hyperuricemia after transplant to be considered seriously just immediately after transplant. Even we recommend patients with an established history of hyperuricemia or gout before transplant should be on treatment for hyperuricemia before cyclosporine is started. Also, interaction between azathioprine and allopurinol must be seriously considered.

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