ORIGINAL ARTICLE

Correlation between Hyperuricemia and Rapidly Decline Kidney Functions

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ABSTRACT

Background: The patients of chronic kidney disease (CKD) are recurrently come across with Hyperuricemia. We weathered the assumption that influence of uric acid on glomerular filtration rate (GFR) and is linked with decline in kidney function in aged Pakistani patients.
Methods: About 200 aged subjects' ranges 60-70 years were registered for their routine follow up medical health check. Estimated GFR (eGFR) was calculated by means of the amendment of Diet in kidney Disease Study equation. eGFR < 60 ml/min/1.73m2 was used to examine the occurrence and frequency of (CKD). The kidney function was significantly decline defined as reduction in eGFR in ≥ 2.9 ml/min/1.73m2 per yearly.
Results: The pervasiveness of CKD was 19.0% in the aged patients. The calculated Mean serum uric acid level was 7.5 mg/dl in males and 6.0 mg/dl in females, and eGFR was 70.5 ml/min/1.73m2. The levels of Uric acid were linked autonomously and pessimistically with eGFR after correction for predictable features of decline in kidney function. Out of two hundred fifty eight subjects 29% have observed significantly reduction in kidney function. The eGFR and uric acid levels linked each other as uric acid raised 1mg/dl, where as eGFR reduction raised by 1.207
Conclusion: The association of uric acid levels and eGFR leads to turn down the kidney function in aged Pakistani individuals. In future the hypo-uricemic treatment might slow down the succession of kidney function needs additional researches.
Keywords: Hyperuricemia, Estimated GFR, Chronic kidney disease.

INTRODUCTION

Gout, is the clinical expression of Uric acid deposition (crystalline monosodium urate (MSU), and in adults the most frequent inflammatory arthritis, particularly in men's, with worldwide increase in prevalence rate, which ranges from 0.2 to 10.1% and probably to be 3.8% in United States only. Serum uric acid ≥6.7 mg/dl defined as Hyperuricemia, which is the limit of urate solubility biochemically. By means of inhabitants, the intensity in gender related SUA division for defining hyperuricemia. Different studies showed that occurrence of 22.0% among male subjects SUA >7.2 mg/dl and 22.6% among females SUA >5.6 mg/dl. Through kidneys the urate excretion accounts two-thirds of total excretion and remaining one third thru gastrointestinal tract, so hyperuricemia is correlated with decrease in kidney function that suggested that hyperuricemia may potential risk factor and will be connected with the advancement and development of hypertension (HTN) and CKD. In spite of which is the causative factor or complication the correlation of CKD with hyperuricemia and gout is familiar. Approximately 22% of adult subjects having gout with (CKD Stage III ≥3) in comparison with 6% of subjects devoid of gout; were as 16% of adult subjects with hyperuricemia having (CKD stage III ≥3) in comparison with 4% of subjects devoid of hyperuricemia. The age related frequency of gout plus hyperuricemia raise as kidney functions turn down, with 23% of subjects with eGFR <60 ml/min contain gout in comparison with 2.8% of subjects with eGFR ≥ 90 ml/min. Hyperuricemia without symptoms is exceedingly prevailing in diagnosed subjects of (CKD). It might replicate decrease renal excretion of uric acid, and also accelerate as pathologically towards CKD. Endothelial dysfunction is contributed factor in renal function decline, proliferation of vascular smooth cell, insulin resistance, stimulated production of monocyte chemo attractant protein-1 (MCP-1), and impairment in production of vascular nitric oxide. In recent times, researchers recommend that there is a dominant cross-sectional relationship among baseline levels of uric acid and estimated glomerular filtration rate (eGFR), so an elevated level of uric acid (> 5.8 mg/dl) enhances the threat of a decrease in eGFR of > 2.9mL/min/1.73m2 annually and accomplished the results with the aim of levels of uric acid is an self-sufficient hazardous feature for occurrence renal disorder in the broad-spectrum residents. In addition to these research findings, gathering a data of proteinuria which is useful and influential interpreter for progression of kidney disorder. In the current study, we explore the prospective and cross-sectional alliance between levels of uric acid and functions of kidney in a general population.

MATERIAL AND METHODS

The current health assessment group was approaching the population support a group of research, which register aged subjects (60-70 years old) were routinely received an fitness workup during two years. A sum of 200 contributors, were registered in health assessment. Two hundred subjects were voluntarily participating in this current study

after taking informed and written approval from all contributors. Subject's individual characters are scheduled in Table 1. The period of 24 months was mean follow up health checkup duration. Measurements of Serum creatinine, uric acid, BUN, Fasting glucose, were done through chemical analyzer selectra pro S, Under the supervision of Pathologist, individual physical condition along with past and present history of multiple diseases like Hypertension (HTN), which was distinct as, systolic blood pressure more than 130mmHg and diastolic blood pressure more than 90mmHg; or diabetes mellitus (DM), which was labeled as, fasting blood glucose level more than 125mg/dl) along with using insulin, and oral hypoglycemic agents (OHA), with standard of living and activities e.g., Obesity, smoker, and using alcohol. The existence of protein in urine was distinct as micro-albuminuria e.g., 30–300 mg/dl and more than this will be highly sensitive and appeared in quantitative urine strips. For all contributor height, weight, and waist were measured by using a standardize scales, and body mass index (BMI) was also calculate. Kidney damage indicators and probable risk factors will be recognized in the inhabitants.

Statistical analysis: In this cross-sectional study, we used the chi-square (χ^2) test for definite variables and, for permanent variables analysis of variance (ANOVA) is used to estimate the relationship between baseline distinctiveness and risk factors through serum uric acid quintiles. For unremitting variables the data are obtainable as the mean standard deviation SD and as proportions for nominal variables. The linear deterioration was used to examine the cross-sectional relationship of uric acid with eGFR. Permanent variables considerably connected with eGFR. Longitudinal analysis is used to examine the connection of alteration in eGFR of ≥ 3 ml/min/1.73m2. Occurrence of CKD with baseline levels of serum uric acid logistic regression was being used for analyzing the results which shows dichotomy. Some variables which were significant with χ2 and ANOVA test and their association analysis were measured to be probable stagger the uric acid in multivariate models, even though that the new eGFR formula incorporated with some of these variables, like age, sex and serum creatinine levels. The ultimate model was accustomed for age, sex, BMI, proteinuria, smoking, serum (BUN) and sCr level, DM and HTN status. Statistical analysis was performing by using SPSS Version 24. A p value < 0.05 was measured significant statistically, and expresses confidence intervals (CI) about 95%.

RESULTS

Total contributor (n=200) and according to research mostly male participants (77%), with commonly age of 65.2 years. Mean serum uric acid level in males was 6.7mg/dl and in contrast female subjects has 5.5mg/dl. The whole study group the mean eGFR level were 72.8mL/min/1.73m2.One sixty two subjects (81%) with diagnosis of HTN and, ninety eight (49%) with DM. According to serum uric acid level quintiles the first, second, third, fourth, and fifth quintile was: ≤5.1mg/dl; 5.2–5.6mg/dl; 5.7–6.4mg/dl; 6.5–7.3mg/dl; >7.4 mg/dl) respectively. Raised levels of SCr, BUN, BMI and waist circumference expressed in a group of the highest quintiles also observing lesser eGFR levels (Table 1). The group showing raised serum uric acid levels had higher percentage of proteinuria which leads to CKD. The sum of 49(24.5) subjects out of 200 were make a diagnosis with CKD in this study group. At the same time the raised levels of uric acid , leads to elevate the percentage of CKD from 11.3% in the lowest quintile to 61.1% in the highest quintile (χ2=39.08; p<0.001). In association analysis, factors associated with lower eGFR were age, BMI, FBS, increased BUN, SCr, and elevated levels of serum uric acid these factors were labeled as significant interpreter of eGFR. It is stated that Each 1 mg/dl raised level of serum uric acid was connected considerably with a decline in level of eGFR [–1.656 (95% CI: –2.221 to –1.094) ml/min/ 1.73m2] and predictable SCr Clearance (Cockcroft- Gault equation) [–0.859 (95% CI: –1.258 to –0.458) ml/min].

Table 1: Quintiles of uric acid

Characteristics	Total (n=200)	≤ 5.1 (n=53)	5.2-5.6 (n=62)	5.7-6.4 (n=41)	6.5-7.3 (n=18)	≥7.4	P value
Age (yr)	65.2 ± 3.2	63.7 ± 2.7	64.7 ± 2.7	66.1 ± 3.1	65.4 ± 3.7	65.3 ± 3.1	0.252
Male	154 (77)	38 (71.6)	16 (61.5)	53 (85.4)	32 (78.0)	15 (83.3)	< 0.001
HTN	162 (81)	40 (75.4)	20 (76.9)	55 (88.7)	34 (82.9)	13 (72.2)	0.067
DM	98 (49)	25 (47.1)	14 (53.8)	35 (56.4)	12 (29.2)	12 (66.6)	0.065
BMI (kg/m2)	24.2 ± 3.1	23.1±2.5	24.4±3.2	23.4±3.2	24.3±3.4	24.5± 3.5	0.001
Waist circumference (cm)	85±10	84±9	84±8	85±9	85±10	85±10	< 0.001
Fasting glucose levels (mg/dL)	108±18	106±20	108±23	109±24	109±20	110±24	0.166
Serum BUN level (mg/dL)	18±6	17±5	18±5	16±7	20±8	21±9	< 0.001
Serum Cr level (mg/dL)	1.0±0.3	0.6±0.4	0.9±0.4	1.0±0.5	0.9±0.2	1.0±0.4	< 0.001
Serum uric acid level (mg/dL)	6.3±1.4	4.2±0.5	5.5±0.3	6.7±0.2	7.5±0.4	8.6±0.4	< 0.001
eGFR (mL/min)	70.6±14.6	74.5±16.3	72.4±13.6	73.6±12.2	68.9±14.3	64.3±16.4	< 0.001
Proteinuria	49(24.5)	4 (7.5)	5 (19.2)	13 (20.9)	15 (36.5)	12 (66.6)	< 0.001
CKD	49 (24.5)	6(11.3)	8 (30.7)	10 (16.1)	14 (34.1)	11 (61.1)	< 0.001

DISCUSSION

In this cross-sectional study, we established that the incidence of CKD was 24.5% in the elderly subjects, which was elevated than the prevalence 21.2% in the common population of Pakistan. The fifth or highest quintile of serum uric acid level was linked with the highest incidence (61.1%) of CKD. With the help of baseline proteinuria the level of serum uric acid was significantly related with eGFR. In this study, with each 1 mg/dl raise in the level of uric acid increases the risk up to 20.8% of a significantly decline in (eGFR). A number of outlines of confirmation might clarify that how increased levels of uric acid are associated with

eGFR and decline in renal functions. First, verified that inflammatory pathway commencement and vascular smooth muscle propagation is induced by soluble uric acid, crystal of uric acid can induce monocyte chemo-attractant protein 1(MCP-1) secretions in the cultured renal tubular cells. These cellular alterations may leads to development of progressive interstitial fibrosis and glomerulosclerosis. Secondly, current studies also expressed that oxonic acid inhibits the oxidation of uric acid to its relevant metabolite, allantoins, and resulting formation of hyperuricemia which in future induces moderate to severe hyperuricemia and leads to HTN and primary renal arteriopathy, and provocation of cyclosporine stimulate nephropathy. All of these studies support the concept that uric acid has a straight pathogenically responsible in rising renal damage. As a final point, in different epidemiological researches, that there has been an apparent alliance among hyperuricemia, hypertension and vascular diseases. Increased level of uric acid has been revealed to expect the development of innovative commencement of hypertension HTN, heart failure CCF and cerebral vascular accidents CVA, in competition of conservative cardiovascular risk factors, for example DM, obesity and hyperlipidemia. Seeing that to renal diseases, hyperuricemia has been confirmed to foresee conclusion of an immunoglobulin A (IgA) nephropathy, and the risk of leading early kidney failure and (ESRD) end stage renal disease. A further future studies commence to optimize the definite GFR in the elderly inhabitants, we exclude the subjects in this study who receive hypouricemic medication allopurinol because, it is probable that if uric acid were toxic to the kidneys, then this drug allopurinol will not affect the results extensively. Here we call our subjects for followed-up for two years, which might have covered the effect of uric acid on occurrence CKD in relative short study duration. Finally, the effect of insistent hypouricemic therapy for preservation of kidney function was not concentrate on in this study period and requires additional research.

CONCLUSION

The current study shows that uric acid has an autonomous cross-sectional connection with baseline GFR. Uric acid is also an autonomous interpreter of development of renal dysfunction, by means of alterations in eGFR as the measurement. These outcomes is suggestive that hyperuricemia may include some pathogenic function in renal disease development. Upcoming studies must examine the special effects to modify uric acid levels on definite renal results.

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