Original article

Role of Age and Uric Acid Levels on Dialysis Efficacy Among End Stage Renal Disease Patients in Saudi Arabia

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ABSTRACT

Background: Patients with end stage kidney dysfunction is increasing dramatically in Saudi Arabia; especially in the age group of more than 65 years, which constitutes 21% of all chronic kidney disease (CKD) patients. In recent years, more attention is paid to uric acid (UA) as a risk factor in kidney impairment patients.

Objectives: To assess the relationship between serum uric acid levels and hemodialysis efficiency among end stage renal disease patients in Hail, Saudi Arabia.

Methods: A total of 255 hemodialysis patients (102 males and 153 females) were enrolled in this retrospective study. The range was 25 to 83 years with median age of 51 years. Blood samples drawn from patients before and after the hemodialysis session were analyzed for urea, creatinine, and uric acid.

Results: The proportion of female patinets with CKD was significantly higher (60%,($p<0.05$), than the males in the patient group examined. Among hemodialysis patients, the incidence of hypertension was 86 % ($p<0.05$). There was a negative association between UA and hemodialysis efficiency in patients aged less than 50 years. In addition, a significant correlation was observed between levels of UA and urea ($r=0.579$ $p<0.001$) and creatinine ($r=0.736$ $p<0.001$).

Conclusion: Taken together, the results of this study indicate that the hemodialysis efficiency in HD subjects, particularly in the < 50 years of age may be improved by decreasing the serum uric levels.

Key words: Hail, Saudi Arabia, Kidney failure, Uric Acid, Hemodialysis, Chronic kidney disease (CKD)

INTRODUCTION

Chronic kidney disease (CKD) is a serious medical and social issue as its incidence is rising at an alarming rate globally [1]. The increase in prevalence of cardiovascular disorders (CVD), diabetes, hypertension and obesity are highly consistent with morbidity and mortality of chronic kidney disease (CKD) patients including end-stage renal disease (ESRD) and specifically hemodialysis (HD) patients [2] . Annually, mortality rate is about 40% for dialysis patients with CVD worldwide [2]. In a report of WHO in 2008, chronic disorders are responsible for 35% of mortality rate in the Saudi population per year [3]. At the beginning of 1980s, the prevalence of CKD patients receiving dialysis treatment in KSA was surprisingly higher in young ages of 26-45 years [4]. Nowadays, there is a shift in the age demographic for CKD incidence toward older age [5]. The number of HD patients in KSA is increasing significantly in the category of more than 65 years which constitutes 21% of all CKD patients in the kingdom [6].

In recent years, more attention is paid for UA as a risk factor for kidney impairment patients. UA is associated with hypertension, coronary heart disease and chronic kidney disease [7]. Uric acid is the end product of metabolic breakdown of purine nucleotides, high blood levels of UA cause gout. In addition, high UA also could independently predict CV events and mortality for patients with chronic diseases including CKD [8]. Although hyperuricemia is common in patients with chronic kidney disease, the impact of uric acid on mortality and CV events remains unclear. There are experimental and epidemiological data indicating that hyperuricemia may play a role in the pathogenesis of renal and CV diseases [9].

There is a lack of information on prevalence and severity of CKD in the province of Hail, KSA. This prompted us to conduct a cross-sectional study to evaluate levels of UA in HD patients. Our aim was to investigate the association of UA levels with other CKD parameters namely, creatinine and urea. In addition, we also explored the putative role of uric acid in renal pathogenesis in HD patients of different age groups in Hail region of Saudi Arabia.

MATERIALS AND METHODS

Sample collection

Samples were collected by medical care professionals at the King Khaled Hospital at Hail, KSA following a standard protocol.

Sample pre-treatment blood

This study was conducted on the outcome of dialysis study, which is a retrospective study as 255 blood samples were obtained from Saudi individuals in region of Hail with a history of chronic kidney failure. Informed consent was obtained from all patients prior to inclusion in this study. The samples were analyzed for kidney function test and uric acid. The protocol was approved by the Ethics committee of University of Hail.

Data collection

Demographic and clinical data including age, gender, socioeconomic status (income, education level, living condition, etc), primary renal disease, the presence of cardiovascular disease (CVD) and diabetes mellitus (DM) were collected at baseline. Blood pressure was measured according to the guidelines presented in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood pressure [10]. Biochemistry data including kidney function test of creatinine and urea beside the UA were examined using an automatic Hitachi chemistry analyzer.

Statistical Analysis

Data were expressed as M ± SD. The SPSS program version 15 was used in analysis. One way analysis of variance (ANOVA) followed by Duncan post hoc test and/or t-test were used in analysis. Pearson correlation coefficient was used to study correlations. P-values less than 0.05 were significant.

RESULTS

The present study was performed on a total of 255 HD patients who were recruited from the King Khaled Hospital hemodialysis Unit, Hail, KSA. There were 102 males and 153 females of age range between 25 and 83 years, median of 51 years. The population included 129 diabetic and 126 non-diabetic patients. The number of hypertensive patients were 219 and non-hypertensive patients were 36 (Table 1).

Table 1: Demographic Characteristics of Patients

	No.	Percent
Age (M ± SD)	50.09 ± 18.07	
Range	25 - 83	
Median	51	
Number	255	100
M/F	102/153	40/60*
Diabetic/Non	129/126	51/49
Diabetic (type I/ type II)	105/24	41/9
Hypertensive/Non	219/36	86/14*

* Significant

Table 2: Kidney function parameters- Comparison of pre- and post-dialysis blood concentrations

	Pre-dialysis	Post-dialysis	% reduction
Creatinine	795.7 ± 255.7*	338.7 ±148.9	57.62 ± 9.85
Uric acid	6.22 ± 1.50*	2.22 ±1.17	64.14 ± 18.8
Urea	22.84 ± 8.85*	7.53 ±3.98	67.03 ± 11.4

* Significant

Kidney function blood tests demonstrated significant decrease in creatinine, uric acid and urea levels in post-dialysis samples in comparison with pre-dialysis samples ($p < 0.001$) with a percent reduction of 57.62 ± 9.85, 64.14 ± 18.8 and 67.03 ± 11.4, respectively (Table 2).

Table 3 summarizes the comparison between pre- and post-dialysis samples of both males and females for the kidney function tests. The creatinine, uric acid and urea levels were higher in pre-dialysis samples of females than in males. There was more pronounced reduction in the above parameters in females than in males.

It was also found that creatinine, uric acid and urea blood levels were significantly lower in diabetic patients in comparison with non-diabetic ones, and proportion in reduction of urea was significantly higher in diabetic patients than non-diabetics (Table 4).

The patients were divided into two groups according to their age; less than 50 years and more than 50 years. The serum levels of uric acid, creatinine and urea were significantly higher in group of < 50 than in group of >50 years in both pre- dialysis and post-dialysis samples. The percent reduction of creatinine, urea and uric acid was significantly lower in the young age group than the old one (Table 5). However, when we compared creatinine, uric acid and urea in hypertension patients with non-

Table 3: Kidney function parameters- Comparison of pre- and post-dialysis blood concentrations in males and females

	Males (n=102)			Females (n=135)		
	Pre	Post	% reduction	Pre	Post	% reduction
Creatinine	926.7 ± 294.6*	428.8 ± 173.16 *#	53.83± 10.01	708.31 ± 182.02	278.6 ± 90.9 #	60.14 ± 8.98*
Uric acid	6.68 ± 1.75*	2.73 ± 1.31 *#	59.65± 15.71	5.91 ±1.23	1.88 ± 0.94 #	67.13 ±20.19*
Urea	25.67 ± 9.42*	9.31 ± 4.77 *#	64.44± 11.57	20.95 ± 7.99	6.34 ± 2.84 #	68.75 ±11.06*

* Significant with respect to post-dialysis. # Significant with respect to the females

Table 4: Kidney function parameters- Comparison of pre- and post-dialysis blood concentrations in diabetic and non-diabetic patients

	Diabetics (n= 43)			Non-diabetics (n= 42)		
	Pre	Post	% reduction	Pre	Post	% reduction
Creatinine	753.1 ± 232.6*#	316.1 ± 131.9*	58.18 ± 8.91	839.3 ± 276.4#	361.8 ± 162.9	57.04 ± 10.81
Uric acid	6.05 ± 1.41#	2.14 ± 1.12	65.38 ± 12.83	6.39 ± 1.58#	2.29 ± 1.24	62.87 ± 23.49
Urea	23.12 ± 9.41#	7.11 ± 3.99	69.16 ± 11.68*	22.54 ± 8.35#	7.96 ± 3.98	64.83 ± 10.81

Significant with respect to post-dialysis * Significant with respect to the non-diabetic

Table 5: Kidney function parameters- Comparison of pre- and post-dialysis blood concentrations in patients of different age groups

	< 50 yrs (n= 102)			> 50 yrs (n= 135)		
	Pre	Post	% reduction	Pre	Post	% reduction
Creatinine	893.8 ± 240.9#*	400.3 ± 161.9*	55.54 ± 10.53*	708.4 ± 238.4#	283.9 ± 112.2	59.46 ± 8.92
Uric acid	6.55 ± 1.67#*	2.64 ± 1.31*	58.42 ± 23.5*	5.92 ± 1.29#	1.85 ± 0.90	69.22 ± 11.41
Urea	22.72 ± 7.85#	8.14 ± 4.1*	64.13± 12.35*	22.95 ± 9.74#	6.99 ± 3.86	9.92

*Significant with respect to post-dialysis # Significant with respect to the non-diabetic

Table 6: Kidney function parameters- Comparison of pre- and post-dialysis blood concentrations in hypertensive and non-hypertensive patients

	hypertensive (n=73)			Non- hypertensive (n= 12)		
	Pre	Post	% reduction	Pre	Post	% reduction
Creatinine	790.6 ± 266.9#	335.86 ± 149.2	57.56 ± 9.77	826.40 ± 179.3#	335.9 ± 152.8	57.96 ± 10.78
Uric acid	6.25 ± 1.58#	2.25 ± 1.22	63.81 ± 19.43	6.02 ± 0.83#	2.04 ± 0.91	66.13 ± 14.89
Urea	22.78 ± 8.92#	7.42 ± 3.80	67.16 ± 11.52	23.17 ± 8.8#	8.23 ± 5.12	66.20 ± 11.07

* Significant with respect to post-dialysis # Significant with respect to the non-hypertensive

hypertension ones, there was no significant difference in pre-dialysis samples (Table 6).

DISCUSSION

Hyperuricemia is common in patient with end-stage renal disease, which has been reported in up to 50% of subjects, probably due to deficiency in UA excretion[11]. The results of this study demonstrated elevated serum UA in the majority of the investigated patients. A strong correlation between serum UA levels and age among dialysis patients was also observed; there were significantly higher levels of UA in younger patients aged less than 50 years. Our findings are in agreement with those observed by Gouri *et al*. who showed a negative correlation of UA with age in HD patients[12]. Negative correlation of serum UA concentrations with age may be explained by slowing down of metabolism with age. However, other works by Chiou [13] and Rroji [14] found that UA values did not vary with age in both CKD and non-CKD patients. Age stratification (the median as cut off: 50 years) used in our study was different of that used in the later studies (using the median as cut-off: 72 years) and this possibly lead to different results.

Additionally, our results indicated more pronounced correlation of serum UA with creatinine and urea reductions in HD patients aged > 50 years in comparison with those less than 50 years old, i.e.; the proportion of reduction after dialysis process for creatinine and urea in the first age group were 59.46% and 69.6%, respectively in comparison with the second age group (55 % and 64 %, $p < 0.05$) respectively. Likewise, the proportion of reduction of UA was higher in age group > 50 years than < 50 years; the efficiency was 69 % and 58 %, respectively. Therefore, regardless of other chronic disorders as hypertension and diabetes or gender variation, the present results demonstrate that

serum UA is a reliable factor which can be used to monitor efficacy of HD process beside the conventional parameters. Furthermore, we hypothesize, if we lower or control UA levels in HD patients aged less than 50 years, there would be a conceivable reduction of urea and creatinine after HD process. This reduction in turn may decrease the mortality rate and improve the quality of life for CKD patients by lowering number of dialysis sessions.

We also found that hyperuricemia correlated significantly with kidney function parameters of creatinine and urea ($r= 0.736$ $p < 0.01$) and ($r= 0.615$ $p < 0.01$) respectively, as their statistical analysis revealed a positive correlation with high certainty. Similar results were reported by Beberashvili *et al* who demonstrated a positive correlation between UA and kidney nutritional markers such as albumin and creatinine [15]. Moreover, Ito *et al* demonstrated a direct relation between levels of UA, creatinine, urea and glomerular filtration rate; serum UA was involved in the progression of CKD and caused changes in the glomerular filtration rate influencing the rate of CVD prevalence[16], indicating a definitive contribution about the role of UA in renal pathogenesis.

In this study, we demonstrated a high prevalence of patients with cardiovascular events; we noticed that 86% of the entire study population suffered from hypertension. Iseki *et al* reported that the prevalence of hypertension in Japanese HD patients was 77.5% [17]. While the prevalence of hypertension in USA is reported to be 90 % of HD patients [18]. Gouri *et al* showed a significant correlation between levels of UA and hypertension in CKD patients ($p < 0.01$) as the incidence of hypertension has dramatically increased with higher UA levels [12]. Recently, Chen *et al* also showed that the association between UA and acute ischemic stroke was confounded by demographic characteristics and malnutrition-micro inflammation syndrome in Chinese HD patients [19]. This result is as an iceberg phenomenon for HD patients as they have a combinatorial synergistic effect on the mortality in this group. Jeon *et al*. reported increased mortality rate among diabetic patients with high UA and cardiovascular disease than in non-HUA patients with CVD 47 % and 19 %, respectively; whereas, mortality rate was lower in patients with higher UA without CVD 12% and non-high UA without CVD 6% [20]. Antunuvic *et al* reported that high uric acid causes low superoxide dismutase antioxidant activity on cardiovascular system in HD patients [10]. Accordingly, there should be updated medical guidelines for handling of HD patients with high UA levels, taking in considerations new monitoring parameters such as UA beside the conventional ones.

In contrast to our expectations, our data showed an elevated serum UA was not a predictor of cardiovascular events. Likewise, analysis in the subgroups of diabetics showed no significant differences relative to cardiovascular events in patients with high or normal UA levels. Levels of UA in hypertension and diabetic patients were totally concomitant confounder as we did not figure out an influence of uric acid on kidney function parameters in the both two types of patients. Our findings are in disagreement with other reports indicating the correlation of serum UA levels with hypertension and diabetes [19],[21]. We hypothesize that risk factors as hypertension and diabetes are predominantly more involved in the developmental process of kidney disorder in early stages whereas, in the end stages of kidney dysfunction, factors such as rate of glomerular filtration and inability of kidney to establish an adequate blood pressure between afferent and efferent veins may play a key role[22]. Indeed, hyperuricemia has been showed to aggravate renal dysfunction via preglomerular arteriolopathy characterized by hyalinosis and wall thickening[23].

Xia *et al* reported higher prevalence of HD in male (59%) CKD patients in comparison to female patients (41%) in China due to the independent factors of hypertension, smoking and alcohol consumption [24]. While, we observed that the prevalence of HD patients was higher in females than males with a percent of 60% to 40% respectively. It is possible that ethnic and other environmental factors may play an important role leading to this apparent disagreement. Meanwhile, we observed that the proportion of patients with increased serum UA were significantly higher in males. Our results were similar to those obtained by Barbieri et al who showed that uric acid levels were significantly higher in men [25]. However, it appears that the threshold of serum UA level as a risk factor for CKD is lower in female than in male which needs to be explored and confirmed.

CONCLUSION

Based upon the findings of this study, it may be concluded that uric acid lowering drugs can increase HD efficiency in subjects, particularly in the < 50 years of age.

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