Evaluation Of Uric Acid Among Sudanese Patients With Chronic Kidney Disease

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ABSTRACT: Background: Chronic kidney disease (CKD) is an international public health problem affecting 5-10% of the world population. As kidney function declines **Methods:** This study is case-control study conducted in Ibn sina hospital, Military hospital and Ribat specialized hospital within six months from October 2016 to March 2017. The aim of this study is to evaluate the effect of uric acid in Sudanese patients with chronic kidney disease. A total of 100 patients (60 male, 40 female) and 50 healthy individuals as control group (30 male, 20 female). **Results:** in this study the level of uric acid was significantly increased in CKD patients compared to control group, with the P-value (0.000). **Conclusion:** based upon the finding of this study, hyperuricemia as most cause of cardiovascular disease in patients with chronic kidney disease.

INTRODUCTION:

Chronic kidney disease (CKD) is an international public health problem affecting 5-10 of the world population. As kidney function declines, (KDIGO, 2009). Increase in incidence of Diabetes mellitus, hypertension, obesity and an aging population there is increase in progression of chronic kidney disease to end stage renal disease (ESRD). (Sumanth and Shobharani, 2015). Uric acid (UA) is an emerging risk factor for renal disease, hypertension, and cardiovascular disease and it is the breakdown product of purines from DNA, RNA, ATP and cAMP. In this process hypoxanthine is converted by the enzyme xanthine oxidase to xanthine and further to uric acid. Both steps induce the release of free radicals. Uric acid may accumulate in the body due to increased production (cell death, intake of alcohol or purine rich diet) or decreased elimination (impaired renal function, use of diuretics). (**Ingrid** et al., 2013). So the Kidneys excrete approximately 60% to 70% of total uric acid from body. Uric acid is a small molecule that can be partially removed by hemodialysis as for urea. Paradoxical results were gained between hyperuricemia and outcomes in chronic kidney disease (CKD) patients. (**Elaheh** et al., 2015). Therefore the most studies documented that an elevated serum uric acid level independently predicts the development of CKD. Raising the uric acid level in rats can induce glomerular hypertension and renal disease as noted by the development of arteriolosclerosis, glomerular injury and tubulointerstitial fibrosis. (**Richard** et al, 2013). Hyperuricemia is common in patients with chronic kidney disease (CKD) and evidence that hyperuricemia may also play a causal role in hypertension, vascular disease and progression of CKD is accumulating (**Hakan** et al., 2014). At this point the potential mechanisms to account for these associations may be diverse; i.e., endothelial dysfunction, the activation of the intrarenal renin-angiotensin system, a vascular smooth muscle cell proliferation, the increased synthesis of interleukin-6, insulin resistance, and impaired endothelial nitric oxide production. (**Tatsuo** et al., 2015). Premature cardiovascular disease (CVD), including stroke, peripheral vascular disease, sudden death, coronary artery disease, and congestive heart failure, is a notorious problem in patients with chronic kidney disease (CKD). Because the presence of CVD is independently associated with kidney function decline. (Peter et al., 2008).

Cardiovascular diseases are main morbidity and death causes in CKD patients, and especially to ESRD ones, with an annual frequency of 9%. (Sofia and Petros, 2013). The incidence of CAD in patients initiating dialysis is up to 38%, with a relative risk of 5- to 20-fold that of the general population. (Navdeep et al., 2016). Inflammation and oxidative stress have been linked to the pathogenesis of plaque formation and plaque rupture; both are associated with worse cardiovascular outcomes. The role of mineralocorticoid excess in the development of cardiovascular complications is increasingly recognized. (Charles et al., 2011). The purpose of the present study was to address uric acid as putative cardiovascular risk factor in a Sudanese people with Chronic Kidney Disease patients.

Materials and Methods:

This is case-control study conducted in Ibn sina hospital, Military hospital and Ribat specialized hospital. Study subject Sudanese Patients clinically diagnosed with CKD attending to be dialyzed in ibn sina hospital and Military hospital in Khartoum state were included in this study. Age matched individuals without chronic kidney disease are selected as control group. And Patients with CKD that are: Patients on dialysis, above than 70 years, Less than 10years, Smoking or drinking alcohol, pregnant women, patients infected by hepatitis B or C Virus were been excluded from this study. This study was conducted on 100 subjects with CKD as case (60male and 40female) and 50 subjects from healthy individual as control (30male and 20female). Data was collected by structured questionnaire including: age, BMI, gender, duration of disease and others. Ethical clearance received from research committee of Omdurman the informed consent Have been obtained from all participants; measure the level of uric acid in the study group. The plasma uric acid estimated by uricase peroxidase method, Data were entered to statistical package for social sciences SPSS software version 20. Descriptive analysis was performed for all variables, Results were expressed as (mean ± SD), and they were analyzed by using independent t-test, frequency test and Pearson correlation test. P-value less than 0.05 was considered significant. Charts and tables were developed, as convenient for better presentation of data.

RESULTS:

The present study involved100 cases of pre dialysis patients with CKD were (60% male and 40% female). In addition to 50 control matching with case were (30% male and 20% female). Our study found that the levels of uric acid was highly significant increase in CKD patients compared to control. Results expressed as (mean ± SD). (See table 1). Our study show that there were insignificant difference in CKD patients who were ≤ 40 years and ≥ 41 years in uric acid. (See table 2). Our study show significant increase of uric acid in CKD males compared to females. (See table 3). Our study show that there were no significant difference between CKD patients with normal weight and overweight patients. Results expressed as (mean ± SD). (See table 4). Our study show that there were no significant difference between CKD patients with diabetic and non-diabetic patients in serum uric acid. Results expressed as (mean ± SD). (See table 5). Our study show that there were no significant difference between CKD patients with hypertension and non-hypertension patients in serum uric acid.. Results expressed as (mean ± SD). (See table 6). In this study, all parameters show insignificant difference between CKD patients with duration less than 5 years compared to those with more than 5 years disease duration. (See table 7).

Table (1): *Comparison between control and dialysis patients for Uric Acid:*

Parameters	Sample condition		P – value
	Control	Cases	
Uric acid (mg/dl)	4.59±1.26	6.09±1.77	0.000

Table (2): *Levels of Uric Acid for dialysis patients as affected by age:*

Parameters	Age		P – value
	< 40 year	>40 year	
Uric acid (mg/dl)	6.28±1.59	5.99±1.85	0.000

Table (3): *Levels of Uric Acid for dialysis patients as affected by gender:*

Parameters	Gender		P – value
	Male	Female	
Uric acid (mg/dl)	6.28	5.78	0.048

Table (4): *Levels of Uric Acid for dialysis patients as affected by BMI:*

Parameters	BMI		P – value
	Normal (19-25)	Over weight (> 25)	
Uric acid (mg/dl)	6.16±1.57	6.24±1.93	0.021

Table (5): *Levels of Uric Acid for dialysis patients as affected by diabetes mallets of CKD:*

Parameters	DM		P – value
	Yes	No	
Uric acid (mg/dl)	5.99±198	6.11±1.72	0.000

Table (6): *Levels of Uric Acid for dialysis patients as affected by hypertension of CKD:*

Parameters	Hypertension		P – value
	Yes	No	
Uric acid (mg/dl)	6.08±1.80	6.10±1.69	0.044

Table (7): Levels of Uric Acid for dialysis patients as affected by Duration of CKD:

Parameters	Duration		P – value
	< 5 year	>5 year	
Uric acid (mg/dl)	6.2 ± 1.8	5.8 ± 1.6	0.011

Table (8): Levels of biochemical parameters for dialysis patients as affected by time of dialysis in CKD patients:

Parameters	No. of dialysis/week		P – value
	≤ 2/week	>2/week	
Uric acid	6.13±1.88	5.93±1.25	0.510

DISCUSSION:

CKD is a worldwide public health problem with growing incidence, prevalence, morbidity, and mortality and because of this, has a high cost to society. (**Arthur et al., 2014**). Increased CV risk in individuals with CKD is due partly to the high prevalence of traditional risk factors. Also, non-traditional kidney specific mechanisms make notable contributions to cardiovascular (CV) risk (**Damir and Senija, 2014**). **The present study in table (1):** we found that the level of High serum uric acid levels in CKD patients as compared to control group. **In concerning to age in table (2):** Uric acid level was insignificantly higher in CKD patients who were ≤ 40years than those who were ≥ 41 years with p-value (0.290). Our study agree with the study done by (**Mohd et al., 2016**) which found uric acid level was significantly lower in the young age group than the old one. Our justification of this results is due to slowing down of uric acid metabolism with age. Since the interactions between gender and BMI levels on the risks of all-cause and CVD mortality were not statistically significant. In this study we found significant increase of uric acid in males of CKD patients compared to females with p-value (0.048), This result deals with previous finding of (**Guilherme et al., 2012**) which said that Men have higher urate levels than women and an increased prevalence of gout at all ages, though less pronounced in older age. **In concerning to BMI in table (4):** Our study found significant in the levels of Uric acid in CKD patients with normal weight and overweight patients with P-value (0.752). This result deals with the previous finding which revealed that there was association between serum uric acid with body mass index according to (**Jamshid et al., 2015; Jøran et al., 2010**) respectively**. In concerning to duration in table (7):** Uric acid level show insignificant difference between CKD patients who were duration of dialysis was < 5 years and with those > 5 years with p-value (0.181). Our study agree with recent study by (**Jamshid et al., 2015**) which found no relationship between uric acid and duration of dialysis. **In concerning to number of dialysis in table (8):** Uric acid level was insignificantly reduced in CKD patients who have dialysis ≤ 2 time per week when compared with patients who have >2 times per week with p-value (0.510). Our finding agree with recent study done by (**Jamshid et al., 2015**) which found no relationship between uric acid levels and efficacy of dialysis.

CONCLUSIONS:

Based up on the findings of this study, CKD was common and associated with an increased frequency of cardiovascular out comes, that requires special attention and monitoring. The study conclude serum uric acid, is higher in pre-hemodialysis patients compared with control group. So the hyperuricemia it is most cause of cardiovascular disease in chronic kidney disease patients.

REFERENCES:

[1] **Addadi F., Alatab S., Pasha F., Ganji M.R., Soleimanian T. (2014).** The Effect of Treatment with N acetylcysteine on the Serum Levels of C - reactive protein and Interleukin-6 in Patients on Hemodialysis. Saudi Journal of Kidney Diseases and Transplantation. 25(1): P.66-72.

[2] **Adejumo A.O, Okaka I.E., Okwuonu G.C., Ikponmwosa O. Iyawe and Oluwole O.O.,** (2016). Serum C-reactive protein levels in pre-dialysis chronic kidney disease patients in southern Nigeria. 50(1). P.31-38.

[3] **AL-Sharqi A. H. S., AL-Najar SH. W. E. and AL-Jaff H. K. S.** (2015). Lipid profiles and kidney function in chronic renal failure Iraqi patient pre peritoneal dialysis or hemodialysis. International Journal of Advanced Research, Volume 3, Issue 11, P. 776 – 780.

[4] **Alaraj. M., Al-Tamimi N., Abu Rayyan W., Alshammari F., Hossain A., Al Hadires T., Alanazi M., Al-Trad B., Alfouzan F., Abu Rayyan A., Al-Shammary A., Alanazi1 M., Ginawi I., Al Hazmi A.** (2016). Role of Age and Uric Acid Levels on Dialysis Efficacy among End Stage Renal Disease Patients in Saudi Arabia. Journal of Research in Medical and Dental Science. Vol. 4. Issue 2. P. 92-96.

[5] **Albertoni A. G., Borges T. F., and Schor N.** (2012). Uric Acid and Renal Function, Diseases of Renal Parenchyma, Prof. Manisha Sahay (Ed.), InTech. P. 57-74.

[6] **Bhatti K.N, Galougahi K.K, Paz Y, Nazif T, Moses W.J, Leon B.M, Stone W.G, Kirtane J.A, Karmpaliotis D, Bokhari S, Hardy A.M, Dube G, Mohan S, Ratner E.L, Cohen J.D, Ali A.Z and DPhil.** (2016). Diagnosis and Management of Cardiovascular Disease in Advanced and End-Stage Renal Disease. P.1-14.

[7] **Bishop M L, Fody E and Schoeff L E.** (2010). Bishop's clinical chemistry. 6th ed. China: Lippinocott Williams and Wilkins. P. 220-368, 570-587.

[8] **Denise C. C., Dorin T., Raluca P., Mirela G., Emilian C. And Grigore D.** (2016). Body Mass Index and the Relationship with Chronic Kidney Disease in a Tertiary Care Hospital in Romania. Acta Medica Marisiensis. 62(2): P. 225-229.

[9] **Ding, D., Wang M., Su D., Hong C., Li X., Yang Y., Zhang Y., Hu G. and Ling W.** (2015). Body Mass Index, High-Sensitivity C - reactive protein and Mortality in Chinese with Coronary Artery Disease.

[10] **Dungey M, Hull L.K, Smith C.A, Burton O.J and Bishop C.N. (2013).** Inflammatory Factors and Exercise in Chronic Kidney Disease. International Journal of Endocrinology. P.1-12.

[11] **Elzain S., Balla H. and Ismail A**. (2016). Impact of Hemodialysis on Serum Zinc and Copper Level in CKD Patients. Journal of Applied Pharmaceutical Science. 6. (04). p. 165-168.

[12] **Goldberg I. and Krause I.** (2016). The role of gender in chronic kidney disease. European Medical Journal.1. (2): P. 58-64.

[13] **Herzog , Asinger W.R, Berger K.A, Charytan M.D, Dı´ez J, Hart G.R, Eckardt K, Kasiske L.B, McCullough A.P, Passman S.R, DeLoach S.S, Pun H.P and Ritz. E. (2011)**. Cardiovascular disease in chronic kidney disease. A clinical update from Kidney Disease: Improving Global Outcomes. International Society of Nephrology. P.1-15.

[14] **Higgins And Chris.** (2016). Urea and the clinical value of measuring blood. Acute care testing, p. 1-6.

[15] **Hjelmesæth J., Røislien J., Nordstrand N., Hofsø D., Hager H. and Hartmann A.** (2010). Low serum creatinine is associated with type 2diabetes in morbidly obese women and men: across-sectional study. BMC Endocrine Disorders. 10(6). P. 1-6.

[16] **KDIGO.** Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention, and Treaatment of chronic kidney disease-meniral and bone disorder (CKD-MBD). (2009). Official Journal Of The International Society of Nephrology. Vol.76. supplement 113, chapter 1. P.3.

[17] **Kumar S. B, Shobharani.B.** (2015). Comparative Study of Hscrp in Chronic Kidney Disease. IOSR Journal Of Pharmacy, July, Volume 5(7), P. 08-12.

[18] **McFarlin K. B.,Flynn G. M., Campbell W. W., Craig A. B., Robinson P. J., Stewart K. L., Timmerman L. K., and Coen M. P.** (2006). Physical Activity Status, But Not Age, Influences Inflammatory Biomarkers and Toll-Like Receptor 4. Journal of Gerontology. 2006, Vol. 61A, No. 4, P. 388–393.

[19] **Mendelssohn C. D., Brownscombe M. L., Greenberg E. D. And Levin A.** (1999). Elevated levels of serum creatinine:. Canadian Medical Association, 161 (4), p. 413-417.

[20] **Noor U. A., Mahmood T. M., Asad J. M., Zafar M. And Raja M. A**. (2014). Evaluating Urea and Creatinine Levels in Chronic Renal Failure Pre and Post Dialysis:. Journal Of Cardiovascular Disease, 2(2), p. 2330-4596.

[21] **Parmar A. J., Sagar R. A., Kapadia S., Joshi A. and Chakrabarti M.** (2014). Study of Parathyroid Hormone, Total Calcium, Creatinine and Urea in Chronic Kidney Disease. Int J Res Med. 3(2). P. 116-118.

[22] **Rebić D. and Rašić S**. (2014). Cardiovascular Remodelling In Chronic Kidney Disease. European Medical Journal. 1: P. 113-119.

[23] **Roozbeh J., Sagheb M. M., Vafaie E.** (2015). The association between blood pressure level and serum uric acid concentration in hemodialysis patients. Journal of Nephropathology. 4(3): P. 85-90.

[24] **Sathi1 S, Sunder S, MahapatraH, Rajesh J, Sharma N, Verma H, Venkataramanan K, Gupta A, Prabhu K, Daksh S, Ram P and Wardhan H.** (2014).Role of novel cardiac biomarkers in prediction of cardiovascular risk in pre-dialysis CKD patients by their correlations with left ventricular mass index. Clinical Nephrology and Urology Science. 1: (8). P.1-8.

[25] **Shi B., Zhaohui Ni Z., Hong Cai H.,Minfang Zhang M., Wang S. Q. And Cao L.** (2010). High-Sensitivity C-Reactive Protein: An Independent Risk Factor. Journal of Biomedicine and Biotechnology, Volume 2010, p. 1-5.

[26] **Stenvinkel P, Carrero J.J, Axelsson J, Lindholm B, Heimbu¨ rger O, and Ziad Massy.** (2008). Emerging Biomarkers for Evaluating Cardiovascular Risk in the Chronic Kidney Disease Patient. American Society of Nephrology. 3: P.505-521.

[27] **Zahed N., Ghassami M. and Nikbakht H.** (2016). Effects of coenzyme Q10 supplementation on C-reactive protein and homocysteine as the inflammatory markers in hemodialysis patients; a randomized clinical trial. Journal of Nephropathology. 5(1). P. 38-43.