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Assessment of Hyperurcemia in Patient with End Stage Chronic Kidney Disease

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Abstract

Chronic kidney disease (CKD) has become a global public health problem because of its high prevalence and the accompanying increase in the risk of end-stage renal disease, cardiovascular disease, and premature death. Progression of CKD is associated with a number of serious complications including increased incidence of cardiovascular disease, hyperlipidemia, anemia and metabolic bone disease. Hyperurcemia may be a major contributor to the development of progression of chronic kidney disease (CKD). Although there is no clear cutoff uric acid (UA) value associated to the risk for kidney damage, it appears to be an increased risk as UA rises.

Key words: *Chronic kidney disease (CKD), Uric acid (UA), Hyperurcemia.*

Introduction

CKD is characterized by progressive deterioration of kidney function, which develops eventually into a terminal stage of chronic kidney failure (CKF). CKF has traditionally been categorized as mild, moderate, or severe [1].

During the last few years, an international consensus has emerged categorizing CKF into five stages according to the glomerular filtration rate (GFR) and presence of signs of kidney damage: stage 1: GFR > 90 ml/min and signs of kidney damage, stage 2: GFR = 60-89 ml/min and signs of kidney damage, stage 3: GFR = 30-59 ml/min, stage 4: GFR = 15-29 ml/min, and stage 5: GFR < 15 ml/min [2]. Stage 5 represents the total inability of kidneys to maintain homeostasis, and this metabolic state is incompatible with life. Thus, at this stage, it is necessary to use methods that substitute for kidney function to ensure patient survival; these methods include peritoneal dialysis& hemodialysis [3].

CKF is associated with many kinds of metabolic changes caused by the kidney disease and also attributable to dialysis treatment. Phenomena such as accumulation or deficit of various substances and dysregulation of metabolic pathways combine in the pathogenesis of these changes [4]. In the process of accumulation, decreased urinary excretion plays a crucial role and leads to retention of metabolites in the organism (e.g. creatinine, urea, uric acid, electrolytes, water). The increased formation of metabolites through catabolic processes and alternative metabolic pathways also exerts an influence. Regular dialysis treatment partly decreases this accumulation, but cannot avert the overall deficit [5].

Chronic kidney disease leading to chronic kidney failure is an urgent medical problem in the context of demographic trends. In addition to the basic kidney disease, many metabolic disorders develop in the course of CKF. Particularly, patients in the terminal stage of CKF are endangered [6]. Regular dialysis treatment decreases the accumulation of metabolites; however, it contributes to a deficit of some important metabolic regulators and to the development of a chronic inflammation state. These factors can lead to serious secondary complications in CKF, including atherosclerosis and related cardiovascular disease, malnutrition, anemia, renal bone disease, and other problems [7]. These complications markedly and negatively affect the prognosis and quality of life of patients with CKF and increase costs for their treatment. The prognosis of CKD patients can be improved if kidney disease is diagnosed early and

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properly cured, including secondary complications. Appropriate treatment encompasses consistent control of blood pressure, prevention of malnutrition, anemia, and hyperparathyroidism, and treatment of metabolic disorders [8].

Because humans lack uricase, they cannot convert the uric acid generated during purine metabolism into a soluble form. This can lead to an increased risk for hyperurcemia and monosodium uric acid crystallization in joints and tissues [9]. Because approximately 70% of uric acid is excreted from the kidney, hyperurcemia occurs when renal function deteriorates. Hyperurcemia is defined as a level of serum uric acid greater than or equal to 7.0 mg/dl (420 µmol/l) in man and 6.0 mg/dl (360 µmol/l) in women. CKD is associated with decreased excretion of uric acid and resultant hyperurcemia. Other mechanisms may be implicated in CKD since variations in serum uric acid do not account for most of the risk for developing gout [10]. Hyperurcemia can be caused by the overproduction of uric acid, but is more often the result of insufficient kidney uric acid excretion. Observational data also suggest that hyperurcemia, even in the absence of gout, may independently worsen CKD, possibly via a pathogenic role in hypertension (Figure 1), and diabetic nephropathy, the two leading causes of CKD [11,12].

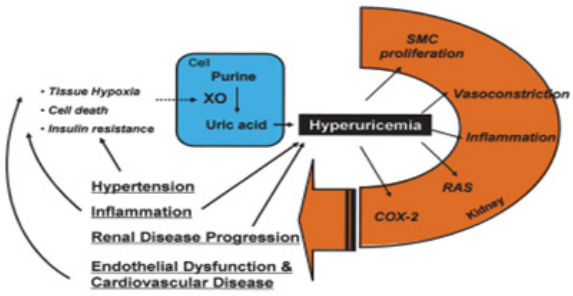

Figure 1: The potential interrelationships of uric acid, xanthine oxidase activity, and clinical endpoints of cardiovascular and renal disease.

Hyperurcemia may be a consequence of decreasing of glomerular filtration rate (GFR), reflecting tissue hypoxia or cell lysis associated with renal disease [13].

Materials and Method

Subjects:- Between 1st October 2019 and 1st December 2019,100 subjects were recruited to this study, 50 consecutive patients aged between 25- 70 years old, diagnosed by expert physicians as having CKF from kidney dialysis unit (KDU) in Al-kafeel hospital in Karbala City, in addition to age and sex matched (50 subjects) without CKF with similar risk factors considered as control group. This study was matched for gender, the ratio of male: female was 2:1 for both sexes. This study was performed in the Biochemistry laboratory in Pharmacy Department in Alsafwa collage.

Ethical Issues: The objectives and methodology were explained to all participants in the current study and their verbal consent was gained.

Sample collection:- Five ml of blood were obtained from each subject by vein puncture in sitting or lying position, and then pushed slowly into disposable tubes containing separating gel. Blood in the gel containing tubes was allowed to clot at room temperature for 2 hours and then centrifuged at 1000 ×g for approximately 15 minutes then the supernatant were obtained and stored at -20˚C until analysis.

Materials:- Uric acid biochemical kit (Biolab).

Methods:- uric acid serum level assayed by Biolab biochemical kit.

Statistical analysis:- The collected data were tabulated and analyzed by using the Statistical Package for Social Sciences (SPSS) for Windows version 20th version. Data were expressed as (mean ± SD). Independent sample t-test was used to compare means between two groups. P values less than (0.05) were considered significant.

Results

a. **Differences of Patients with Chronic Kidney Failure and control by Socio-Demographic Characteristics:**

The overall mean age of patients with ACS and control were (40.28±12.02) and (38.21±11.61) years old, respectively and the extremes were 25 to 70 years . There was no significant mean difference between the mean age of patients and control. This age matching helps to eliminate differences in parameters' results. This study was matched for gender, the ratio of male: female was 2:1 for both sexes.

b. Differences of patients and control by uric acid serum level

There were significant differences of **UA** serum level by patients and control subjects as shown in table (1).

Table (1): Mean differences of patients and control by UA serum level

Variable	Group	N	Mean	S.D	P value
Uric acid	case	50	17.78	7	**<0.001***
	control	50	7.3	2.5	

*p value ≤ 0.05 is significant

Discussion

This study revealed that hyperurcemia is clinically significant in the setting of CKD, especially when drugs used for their management can further impair kidney function. The established role of CKD as an independent risk factor for hyperurcemia may therefore warrant screening for CKD when gout is first diagnosed as presented by Juraschek SP *etal* [14]. The role of hyperurcemia as an independent risk factor for CKD, however, is still being debated. Large randomized controlled trials can provide definitive answers about its relationship to CKD, and how its treatment might forestall CKD progression in populations such as those with hypertension and diabetic nephropathy. The finding of this study agreed with Tae Ryom Oh *etal* [15] who reported that in the case of CKD, renal excretion of uric acid is decreased, resulting in hyperurcemia. It is thought that the interstitial accumulation of sodium urate induces the deterioration of the disease. This suggests that patients with renal impairment are more likely to be exposed to higher uric acid concentrations, which means that the multisystem effect of uric acid can be further strengthened. A recent study by Verzola D *etal* [16] utilizing immortalized proximal tubular epithelial cells from normal adult human male kidney has demonstrated that increasing levels of uric acid cause NAPDH-dependent oxidative changes which promote apoptosis. This finding sheds light on the connection between hyperuricemia and tubule-interstitial renal damage. The association of hyperurecemia with CKD also was reported by Jalal DI *etal* [17] & Momeni A. Momeni (2012)[18] who concluded that hyperurcemia is frequently found in patients who are found having chronic renal failure. Epidemiological studies have detected an association of hyperurcemia and risk of heart and vascular disease in the general population and in chronic renal insufficiency patients.

Conclusion

- There is significant elevation of serum uric acid in CKD patients.
- The challenge remains that the significance of elevations in uric acid is difficult to assess in those with chronic kidney disease because, as clearance decreases, the levels of serum uric acid naturally increase.
- Hyperurcemia may be used as a disease marker for the potential to develop renal disease in the future as well as predict risk for a patient with renal disease to develop worsening renal function.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. DIAZ-BUXO JA, WOODS HF: Protecting the endothelium: A new focus for management of chronic kidney disease. Hemodial Int 2006;10: 42-48,.
2. LEVEY AS, ECKARDT KU, TSUKAMOTO Y, LEVIN A, CORESH J, ROSSERT J, ZEEUW D, HOSTETTER TH, LAMEIRE N, EKNOYAN G: Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005. 67: 2089-2100,
3. DE DEYN PP, VANHOLDER R, D'HOOGE R: Nitric oxide in uremia: Effects of several potentially toxic guanidino compounds. Kidney Int 2003 63 (Suppl 84): S25-S28,.

4. CIBULKA R, RACEK J, VESELA E: The importance of L-carnitine in patients with chronic renal failure treated with hemodialysis (in Czech). Vnitr Lek 2005. 51: 1108-1113,
5. DIRICAN M, AKCA R, SARANDOL E, DILEK K: Serum paraoxonase activity in uremic predialysis and hemodialysis patients. J Nephrol 2004 17: 813-818,.
6. KALANTAR-ZADEH K, STENVINKEL P, BROSS R, KHAWAR OS, RAMMOHAN M, COLMAN S, BENNER D: Kidney insufficiency and nutrient-based modulation of inflammation. Curr Opin Clin Nutr Metab Care 2005. 8: 388- 396,
7. SNYDER S, PENDERGRAPH B: Detection and evaluation of chronic kidney disease. Am Fam Physician 2005. 72: 1723- 1732,
8. Krishnan E. Chronic kidney disease and risk of incident gout among middle-aged men: a seven-year prospective observational study. Arthritis Rheum. 2013; 65:3271-3278.
9. Juraschek SP, Kovell LC, Miller ER, et al. Association of kidney disease with prevalent gout in the United States in 1988-1994 and 2007-2010. Semin Arthritis Rheum. 2013;42:551-561.
10. Roddy E, Choi HK. Epidemiology of gout. Rhem Dis Clin N Am. 2014;40:155-175.
11. Bellomo G. Uric acid and chronic kidney disease: a time to act? World J Nephrol. 2013;2:17-25.
12. Feig DI. Serum uric acid and the risk of hypertension and chronic kidney disease. Curr Opin Rheumatol. 2014;26:176-185.
13. Elsayed, N.M., Nakashima, J.M. and Postlethwait, E.M. Measurement of Uricacid as a Marker of Oxygen Tension in the Lung. Archives of Biochemistry and Biophysics, (1993) 302, 228-232
14. Juraschek SP, Kovell LC, Miller ER, et al. Dose-response association of uncontrolled blood pressure and cardiovascular disease risk factors with hyperuricmemia and gout. PLoS ONE; 2013. 8:Article ID e56546.
15. Tae Ryom Oh, Hong Sang Choi, Chang Seong Kim, Eun Hui Bae, Seong Kwon Ma, Su-Ah Sung, Yong-Soo Kim, Kook Hwan Oh, Curie Ahn & Soo Wan Kim; Hyperuricemia has increased the risk of progression of chronic kidney disease: propensity score matching analysis from the KNOW-CKD study; *Scientific Reports* (2019). **9**, Article number: 6681
16. Verzola D, Ratto E, Villaggio B, Parodi EL, Pontremoli R, Garibotto G, *et al.* Uric acid promotes apoptosis in human proximal tubule cells by oxidative stress and the activation of NADPH oxidase NOX 4. PLoS One 2014; 9: e115210.
17. Jalal DI, Chonchol M, Chen W, Targher G. Uric acid as a target of therapy in CKD. Am J Kidney Dis. 2013; 61(1):134- 46.
18. Momeni A. Serum uric acid and diabetic nephropathy. J Renal Inj Prev. 2012;1(1):37-38.