



Ukrainian Journal of Nephrology and Dialysis

Scientific and Practical, Medical Journal

Founders:

- State Institution «Institute of Nephrology NAMS of Ukraine»
- National Kidney Foundation of Ukraine

ISSN 2304-0238;
eISSN 2616-7352

Journal homepage: <https://ukrjnd.com.ua>

Research Article

M.Y.N. Al Atbee, I.E. Hassan, H.N. Mnahi, H.A. Nassir, A.A. Yahya,
Z.M. Abdulbari

doi: 10.31450/ukrjnd.3(79).2023.05

Prevalence of hyperuricemia among patients undergoing hemodialysis: Approach to understanding the risk factors

College of Medicine, University of Basrah, Iraq

Citation:

Al Atbee MYN., Hassan IE, Mnahi HN, Nassir HA, Yahya AA, Abdulbari ZM. Prevalence of hyperuricemia among patients undergoing hemodialysis: Approach to understanding the risk factors. Ukr J Nephrol Dial. 2023;3(79): 32-38. doi: 10.31450/ukrjnd.3(79).2023.05.

Abstract. *Chronic Kidney Disease (CKD) is closely associated with hyperuricemia. Elevated urate levels and hyperuricemia are common in patients with impaired renal function. Kidney replacement therapies, such as hemodialysis and kidney transplantation, are conventional treatment strategies for end-stage kidney disease (ESKD). The present study aimed to determine the prevalence of hyperuricemia and investigate its correlation with demographic characteristics, clinical comorbidities, and biochemical parameters in patients undergoing hemodialysis.*

Method. *In this retrospective study, we assessed the prevalence of hyperuricemia in 102 hemodialysis patients at the Nephrology and Dialysis Department of Basra Teaching Hospital in Basra, Iraq. We recorded demographic characteristics, such as age and gender, and examined whether there was any correlation with hyperuricemia. Additionally, we assessed the association of hyperuricemia with clinical comorbidities like diabetes and cardiovascular diseases in these patients. Clinical chemistry and electrolyte parameters were analyzed using a high-performance serum work area platform, COBAS C 111.*

Results. *Among all the assessed biochemical parameters, magnesium showed a significant association with hyperuricemia in patients undergoing hemodialysis. We also found a statistically significant association between hyperuricemia and cardiovascular diseases in these patients. These findings underscore the significance of hyperuricemia as both a risk factor and a potential target for therapeutic interventions in managing these comorbidities.*

Conclusion. *This study highlights the importance of monitoring uric acid levels in patients undergoing hemodialysis to gain a more comprehensive understanding of their health, from the cellular to the organ level.*

Key words: hyperuricemia, hemodialysis, CKD, hypomagnesemia.

Conflict of interest. The authors declare no conflict of interest.

© M.Y.N. Al Atbee, I.E. Hassan, H.N. Mnahi, H.A. Nassir, A.A. Yahya, Z.M. Abdulbari, 2023.

Correspondence should be addressed to Mohammed Younus Naji Al Atbee:
mohammed.naji@uobasrah.edu.iq

Article history:

Received June 09, 2023,

Received in revised form
July 15, 2023

Accepted July 15, 2023



© Аль Атбі М. Й. Н., Хасан І. Е., Мнахі Х. Н., Насір Х. А., Яхья А. А., Абдулбарі З.М., 2023

УДК 616.61-085.38-073.27:616.633.857.5]-08

М.Й.Н. Аль Атбі, І.Е. Хасан, Х.Н. Мнахі, Х.А. Насір, А.А. Яхья, З.М. Абдулбарі

Поширеність гіперурикемії серед хворих, які лікуються методом гемодіалізу: підхід до розуміння факторів ризику

Медичний коледж Університету Басри, Ірак

Резюме. Хронічна хвороба нирок (ХХН) значною мірою пов'язана з гіперурикемією. Підвищена концентрація уратів і гіперурикемія поширені у пацієнтів з порушенням функції нирок. Метою цього дослідження було визначити поширеність гіперурикемії та дослідити її кореляцію з демографічними характеристиками, супутніми захворюваннями та біохімічними показниками у хворих, які лікуються методом гемодіалізу.

Методи. У цьому ретроспективному дослідженні визначали поширеність гіперурикемії у 102 пацієнтів, які лікувались методом гемодіалізу у відділенні нефрології та діалізу навчальної лікарні Басри, Басра, Ірак. Демографічні та клінічні характеристики цих пацієнтів також оцінювали залежно від наявності гіперурикемії.

Результати. Встановлено статистично значущу асоціацію між концентраціями магнію та сечової кислоти крові. Також спостерігався статистично значущий зв'язок між гіперурикемією та серцево-судинними захворюваннями у пацієнтів, які лікувались методом гемодіалізу.

Висновок. Це дослідження підкреслює важливість моніторингу концентрації сечової кислоти крові у пацієнтів на гемодіалізі для більш повного огляду стану пацієнта від клітинного до органного рівня.

Ключові слова: гіперурикемія, гемодіаліз, ХХН, гіномагніємія

Introduction. Uric acid (UA) is a sparingly soluble, weak acidic metabolite of purine metabolism. Due to its high dissociation constant and weak acidic properties, UA circulates predominantly as urate (a monovalent sodium salt) in the plasma at the physiologic pH of 7.4. Urate production depends on the balance between purine ingestion, de novo synthesis in the cells, recycling, and the enzymatic conversion of xanthine by xanthine oxidase in purine metabolism [1].

The evolutionary loss of the uricase enzyme in humans restricts the conversion of urea to the more water-soluble allantoin, which is easily disposed of through urine. As a result, UA becomes the end product of purine metabolism occurring in the liver, intestines, and vascular endothelium, resulting in higher UA levels in humans than in other mammals. Though UA is routinely disposed of through the kidneys (65-75%) and intestines (25-35%), the kidneys reabsorb almost 90% of it [2]. The loss of the uricase enzyme, reabsorption, and excess consumption of high-purine foods all act in concert to induce hyperuricemia. Several factors, including age and gender, influence the reference range for normal or high UA levels in the blood plasma of humans. UA levels of 6.0 mg/dL in women and 7.0 mg/dL in men are conventionally considered hyperuricemic [3]. Though the role of diet in elevating UA levels has not yet been fully elucidated, the consumption of fructose-rich industrialized food, high-purine foods, and high

alcohol consumption have all been implicated in effectively increasing the UA levels in circulation.

Prolonged malfunctioning or failure of the kidneys to eliminate waste products and electrolytes from the blood and regulate the body's fluid and pH balance are manifestations of acute or chronic renal failure [4]. High urate levels have been observed to be prevalent in Chronic Kidney Disease (CKD), with almost 90% of impaired renal function patients afflicted with hyperuricemia [5]. Urinary protein excretion levels and estimated glomerular filtration rate (eGFR) are used to determine the five stages of CKD (Stages 1-5), the final being End Stage Kidney Disease (ESKD) [6]. The onset of ESKD indicates a reduction in renal function to only 10- 15% of its normal capacity. A complicated interaction of several classic and nontraditional risk factors characterizes end-stage kidney disease (ESKD). Around 70% of patients with stage 4 or 5 CKD have hyperuricemia, which is significantly more common in patients with progressing disease conditions [7, 8].

About 60% of people afflicted with CKD develop hyperuricemia, while 25% develop gout [9]. However, treating hyperuricemia as an etiological agent of renal and metabolic complications is still contested. Extensive clinical trials are required to determine the effectiveness of lowering uric acid levels in hyperuricemic patients with renal and cardiometabolic complications.

Several studies have highlighted the prevalence and significance of electrolyte abnormalities in patients with CKD undergoing treatment [10-13]. Hypernatremia and hypokalemia were found to be strongly associated with the prevalence of hyperuricemia in CKD patients, regardless of their glomerular filtration rate (GFR) [14]. Hypercalcemia was also prevalent in predialysis CKD patients with mineral and bone disorders (MBD) [15]. Serum potassium level aberrations have

Mohammed Younus Naji Al Atbee
mohammed.naji@uobasrah.edu.iq

been linked to adverse outcomes, including cardiovascular disease, increased mortality risk, and hospitalization in CKD patients [16]. The role of magnesium (Mg) as a risk factor in cardiovascular diseases and mortality in CKD patients has been extensively studied, with both hypermagnesemia and hypomagnesemia being observed in dialysis patients [17]. Increased magnesium intake has shown potential in preventing hyperuricemia [18]. Additionally, interactions between serum electrolyte levels, such as phosphate and magnesium, have been implicated in CKD progression [19].

The healthcare costs and financial burden associated with CKD are immense and unsustainable, even in advanced Western nations [20]. Along with the growing global prevalence of CKD, the escalating rates of cardiovascular disease-associated mortality and morbidity, which often culminate in expensive kidney transplantation or dialysis, have significantly aggravated the disease burden worldwide. According to a 2013 survey, chronic renal disease is less prevalent (6.8%) in the province of Basrah than in West Malaysia (9.07%) [21].

Currently, the conventional interventions for treating ESKD are renal replacement therapy (dialysis and renal transplantation) and maintenance hemodialysis (HD). Physicians must now consider alternative treatment strategies and explore drugs in addition to conventional treatments to manage the manifold adverse effects and reduce disease burden effectively.

This retrospective study determines the prevalence of hyperuricemia in patients undergoing hemodialysis. It explores the significant correlations of hyperuricemia with other co-morbidities in these patients. In doing so, **the study aims** to emphasize the role of hyperuricemia as a remedial risk factor in progressing renal and co-existent cardiometabolic diseases.

Methods. Study Design. This is a retrospective study undertaken to determine the prevalence of hyperuricemia among patients undergoing hemodialysis at the Nephrology and Dialysis Department of the Basra Teaching Hospital, Basra, Iraq. Along with ethical approvals from the University of Basrah, College of Medicine, while conducting the study, informed consent was obtained from the 102 participating patients.

Participant details. The study enlisted 102 patients, 55 males, and 47 females, undergoing hemodialysis and examined the prevalence and effects of hyperuricemia in them. The cohort included patients aged

11 to 86 years and was divided into three age groups, each spanning 25 years, viz., 11-36, 36-61, and 61-86 years. The recruited patients were further grouped based on their diagnosis of hyperuricemia into groups referred to as 'hemodialysis' and 'normal uric acid.' The correlations between hyperuricemia and underlying co-morbidities, such as hypertension and cardiovascular diseases, were determined by comparing their individual and combined prevalences in the recruited hemodialysis patients.

Selection Criteria. Patients undergoing hemodialysis were included in the study all patients from 11 years to 86 years underwent hemodialysis for more than 6 months on B Braun Dialog plus machine with a high flux hemodialyzer.

Sample collection and preparation. A gel and clot activator tube was availed for collecting specimens and preparing samples. Following collection, the blood samples were allowed to clot at room temperature for 10 minutes. The clotted blood was centrifuged at 3000-4000 rpm for 10 minutes, and the supernatant was collected without sediment. The COBAS C 111 random access analyzer, manufactured by Roche, Germany, was employed to evaluate the electrolyte parameters and clinical chemistry of the serum obtained after the centrifugation. The following COBAS C 111 analyzer kit was used- PHO\$2, CREJ2, ALT, AST, MG-2, CA2, BILT3. The automated serum work area platform provides precise results within 15 minutes of loading samples.

Statistical analysis. The statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) 21. All obtained data were summarized and analyzed through descriptive statistics comprising means, standard deviations, proportions, and correlation calculations. The categorical variables were compared using the Pearson chi-square (χ^2) test. Cox analysis was used to determine the risk of patients' age, gender, and comorbid conditions on hyperuricemia by hazard ratio and 95% confidence interval. Pearson correlation and two-tailed significance tests were conducted to determine the correlations between the levels of electrolytes and other serum constituents of the patients. The P-value <0.05 was considered statistically significant.

Results. The study population comprised 102 patients undergoing hemodialysis whose demographics have been provided in Table 1.

Table 1

Prevalence of hyperuricemia in the study cohort stratified by age and gender

Variables		Hyperuricemia	Normal uric acid	p-value
		n (%)		
Age (yrs.)	11-36	11 (10.9)	7 (6.9)	0.982
	36-61	37 (36.6)	25 (24.8)	
	61-86	13 (12.9)	9 (7.9)	
Gender	Male	35 (34.3)	20 (19.6)	0.523
	Female	27 (26.5)	20 (19.6)	

The recruited patients ranged from 11 to 86 years of age and were categorized into three age- groups: 11-36, 36-61, and 61-86 years (see Table 1). No statistically significant differences were ($p=0.982$) observed in the distribution of patients among the three age groups of either the hyperuricemic patients or those with normal UA levels. Corresponding to previous reports [22], this study also recorded higher incidences of hyperuricemia in males (35, 34.3%) compared to females (27, 26.5%). However, our study's male predominance was not statistically significant ($p=0.523$).

However, it was interesting to note that the middle-aged group, aged 36-61 years and undergoing hemodialysis, had the highest number of hyperuricemic

and normal UA-level patients. Thirty-seven of the 61 hyperuricemic hemodialysis patients and 25 of the 40 normal UA patients were middle-aged, corresponding to 36.6 and 24.8% of the total patients, respectively.

Hyperuricemia is often concomitant with chronic conditions such as diabetes, cancer, hypertension, and cardiovascular diseases. Underlying conditions of hypertension, hyperglycemia, and cardiovascular diseases were identified in the hemodialysis patients recruited for this study. Table 2 represents the correlations between hyperuricemia and clinical co-morbidities with age and gender of patients. Hypertension was the most prevalent co-morbidity, followed by hyperglycemia.

Table 2

Comorbidities and hyperuricemia in the study cohort

Variables	Hyperuricemia	Normal uric acid	Hazard ratio	95%CI	p-value
	M±SD / n (%)				
Age	51.42±7.85	49.65±8.69	1.133	0.92 – 1.98	0.888
Gender (M:F)	1.3:1	1:1	1.045	0.88 – 1.77	0.867
Hypertension (HT)	43 (42.2)	30 (29.4)	3.433	-5.43 – 7.9	0.966
Hyperglycemia	23 (22.5)	13 (12.7)	2.8	-6.1 – 8.14	0.965
Cardiovascular diseases	18 (17.6)	3 (2.9)	0.687	0.87 – 1.11	0.042

However, no statistically significant correlation between age (HR: 1.133, 95%CI: 0.92 – 1.98, $p=0.888$), gender (HR: 1.045, 95%CI: 0.88 – 1.77, $p=0.867$), HT (HR: 3.433, 95%CI: -5.43 – 7.9, $p=0.966$) and hyperglycemia (HR: 2.8, 95%CI: -6.1 – 8.14, $p=0.965$) and hyperuricemia could be deduced. In contrast, cardiovascular

diseases, the least prevalent co-morbidity observed in the study population, showed a distinct correlation with hyperuricemia (HR: 0.687, 95%CI: 0.87 – 1.11, $p=0.042$).

The levels of the serum's various constituents in hyperuricemic patients and those with normal UA levels were compared to detect significant differences (Table 3).

Table 3

Blood biochemical data of the study cohort stratified by the presence of hyperuricemia

Items, n (%)	Hyperuricemia	Normal uric acid	p-value
Positive HCV	11 (10.8)	10 (9.8)	0.376
Positive HBV	1 (0.98)	-	-
Secondary hyperparathyroidism	44 (43.6)	33 (32.7)	0.467
Vit D deficiency	49 (48.0)	29 (28.4)	0.448
Hypocalcemia	25 (24.5)	15 (14.7)	0.598
Raised AST	5 (4.9)	3 (2.9)	0.270
Raised TSB	5 (4.9)	2 (2.0)	0.742
Raised ALT	5 (4.9)	2 (2.0)	0.495
Hypomagnesemia	14 (13.7)	6 (5.9)	0.005
Hyperphosphatemia	48 (47.0)	27 (26.5)	0.463
Hyponatremia	16 (15.7)	9 (8.8)	0.893
Hyperkalemia	26 (25.5)	12 (11.8)	0.467
Metabolic acidosis	26 (25.5)	19 (18.6)	0.581
Hyperchloremia	14 (13.7)	12 (11.8)	0.392
Leukocytosis	6 (5.9)	5 (4.9)	0.310
Raised Ferritin (male)	2 (3.6)	1 (1.8)	0.532
Raised Ferritin (female)	4 (8.5)	4 (8.5)	-
Anemia	61 (59.8)	39 (38.2)	0.633

Abbreviations: AST, aspartate aminotransferase; ALT, alanine transaminase; HBV, hepatitis B virus; HCV, hepatitis C virus; TSB, total serum bilirubin.

The analysis evaluated electrolyte levels (Ca²⁺, Mg²⁺, Na⁺, K⁺, Cl⁻, PO₄³⁻), metabolic acidosis (raised blood pH), leukocytosis, and anemia. The patients' renal damage was assessed through their secondary hyperparathyroidism and Vitamin D deficiency levels. Raised aspartate aminotransferase (AST), alanine transaminase (ALT), and total serum bilirubin (TSB) levels and detection of pathogenic etiology (Positive HCV and HBV) indicated potential liver damage. Raised ferritin protein levels were also assessed separately for males and females. None of the variables except magnesium displayed any significant association with elevated UA levels. Lower magnesium levels (hypomagnesemia) were observed to be significantly more prevalent in hyperuricemic hemodialysis patients (13.7%) as compared to those with normal UA levels (5.9%) ($p=0.005$).

Discussion. The study population consisted of 102 patients undergoing hemodialysis, ranging from 11 to 86 years old, categorized into three age groups. There were no significant differences in the distribution of patients among the age groups or in the gender ratio. The middle-aged group (36-61 years) had the highest number of both hyperuricemic and normal uric acid level patients. Cardiovascular diseases showed a significant association with hyperuricemia. In terms of serum chemistry, lower magnesium levels were significantly more common in hyperuricemic patients compared to those with normal uric acid levels. Other variables did not show a significant association with elevated uric acid levels.

Multiple studies have suggested that elevated levels of uric acid can contribute to the development of various chronic diseases, including diabetes, hypertension, metabolic syndrome, non-alcoholic fatty liver disease, and chronic kidney disease (CKD) [23]. In a study conducted by Barman et al., a multivariate logistic regression analysis revealed an independent association between hyperuricemia and CKD, and it was observed that males had a higher prevalence of hyperuricemia compared to females in the adult population of Bangladesh [24]. Similar results were found in the current study where the male-to-female ratio of hyperuricemia prevalence in hemodialysis patients is 1.3, which implies a higher incidence of hyperuricemia among men than women.

Elevated UA levels have been linked to hypertension, a major risk factor for cardiovascular diseases [25]. Impaired nitric oxide bioavailability, oxidative stress, renin-angiotensin system activation, and inflammation are implicated in the development of hypertension due to hyperuricemia. In hemodialytic patients, the coexistence of hypertension and hyperuricemia exacerbates vascular dysfunction, reduces blood flow, and increases peripheral vascular resistance [26]. These detrimental effects further compromise cardiovascular health and dialysis adequacy. Managing UA levels through lifestyle changes and pharmacological interventions may hold promise for mitigating the adverse effects associated

with hyperuricemia and hypertension in this population. However, in the current study, no significant correlation between hypertension and hyperuricemia was found in the hemodialysis patients.

Cardiovascular diseases, especially myocardial infarction (heart attack), are highly prevalent among end-stage kidney disease (ESKD) patients with hyperuricemia who undergo regular hemodialysis sessions [27]. This population is particularly vulnerable to cardiovascular complications due to the combined effects of hyperuricemia, impaired kidney function, and the stress placed on the cardiovascular system during dialysis treatment. Therefore, effective management of hyperuricemia and comprehensive cardiovascular care is essential in reducing the incidence and severity of cardiovascular events in this high-risk population. The current results show a significant association of cardiovascular diseases with hyperuricemia in hemodialysis patients.

The abnormal renal function observed in hemodialysis patients with hyperuricemia disrupts the body's electrolyte balance, leading to various morbidities such as hyperphosphatemia and hyperkalemia [7]. Furthermore, there is a growing body of evidence from observational studies in CKD and ESKD indicating an association between hypomagnesemia and cardiovascular disease and mortality [28]. Despite these associations, the specific mechanisms underlying these relationships have not been fully elucidated. Further research is needed to comprehensively understand the underlying mechanisms by which these electrolyte imbalances, particularly hypomagnesemia, contribute to the development and progression of cardiovascular disease in patients with hyperuricemia and impaired renal function.

The current study showed a statistically significant association between hypomagnesemia and hyperuricemia in the recruited hemodialysis patients. The development of hypomagnesemia in patients with CKD and ESKD may be attributed to the use of certain drugs, including diuretics, calcineurin inhibitors, proton pump inhibitors, and epidermal growth factor inhibitors [29]. Recently, a published protocol outlines a randomized, double-blinded, care-controlled trial aimed at determining the safety and feasibility of gradually increasing magnesium concentrations in hemodialysis-treated patients [30]. However, to comprehensively investigate the effects of magnesium levels in CKD patients and assess its potential as a therapeutic tool for regulating hyperuricemia, further studies, including randomized controlled trials, are warranted. Such studies would contribute to our understanding of the optimal management of magnesium levels and its potential benefits in the treatment of hyperuricemia in CKD patients.

Limitations. This study has several limitations. The sample size was relatively small with only 102 hemodialysis patients, which may limit the generalizability of the findings. In addition, being a single-center study, the results may not fully represent the broader population. The cross-sectional design of the study re-

stricted the ability to establish causal relationships. The lack of longitudinal data and the absence of a control group further limit the study's ability to track long-term outcomes and make robust comparisons. These limitations highlight the need for larger, multicenter studies with longitudinal designs and comprehensive analyses to further understand the associations between hyperuricemia, clinical co-morbidities, and potential interventions in CKD patients.

Conclusion. Despite being a well-established prognostic marker of CKD and renal disorders, the implementation of urate-lowering therapy for impeding renal degeneration in CKD patients is still disputed. Males and middle-aged individuals (36-61 years) are more predisposed toward developing hyperuricemia. Moreover, clinical co-morbidities, such as hypertension, diabetes mellitus, cardiovascular diseases, hypomagnesemia, and hyperphosphatemia, significantly correlate with hyperuricemia. Though hyperuricemia is still a debatable etiologic agent of renal diseases, CKD, and underlying cardiometabolic disorders, its association with these co-morbidities is undeniable. We suggest a

mandatory follow-up of UA levels in hemodialysis patients besides the renal function test since the UA level is a crucial indicator of an individual's cellular function and physiological conditions.

Conflict of interest statement. The authors declare no conflict of interest

Funding. None

The authors' contribution.

M.Y.N. Al Atbee: conceptualization, methodology, formal analysis, investigation, resources, data curation, original draft writing;

I.E. Hassan: investigation, resources, data curation, original draft writing;

H.N. Mnahi: methodology, formal analysis, investigation, resources, data curation, writing and editing;

H.A. Nassir: supervision, investigation, resources, data curation, original draft writing and editing;

A.A. Yahya: investigation, resources, original draft writing;

Z.M. Abdulbari: methodology, formal analysis, investigation, resources, data curation.

References:

1. *Maiuolo J, Oppedisano F, Gratteri S, Muscoli C, Mollace V.* Regulation of uric acid metabolism and excretion. *Int J Cardiol.* 2016 Jun 15;213:8-14. doi: 10.1016/j.ijcard.2015.08.109.
2. *de Oliveira EP, Burini RC.* High plasma uric acid concentration: causes and consequences. *Diabetol Metab Syndr.* 2012;4:12. doi: 10.1186/1758-5996-4-12.
3. *De Giorgi A, Fabbian F, Pala M, Tiseo R, Parisi C, Misurati E, Manfredini R.* Uric acid: friend or foe? Uric acid and cognitive function «Gout kills more wise men than simple». [Інтернет]. *Eur Rev Med Pharmacol Sci.* 2015 Feb;19(4):640-6. Available from: <https://pubmed.ncbi.nlm.nih.gov/25753882/>. (Last accessed: 06.06.2023).
4. *Ricci Z, Ronco C.* New insights in acute kidney failure in the critically ill. *Swiss Med Wkly.* 2012 Aug 14;142:w13662. doi:10.4414/smw.2012.13662.
5. *Becker BF.* Towards the physiological function of uric acid. *Free Radic Biol Med.* 1993;14 (6): 615-631. doi:10.1016/0891-5849(93)90143-i.
6. *Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco AL, De Jong PE, et al.* Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. [Інтернет]. *Kidney international supplements.* 2013 Jan 1;3(1):1-50. Available from: https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf. (Last accessed: 21.07.2023).
7. *Prasad Sah OS, Qing YX.* Associations Between Hyperuricemia and Chronic Kidney Disease: A Review. *Nephrourol Mon.* 2015 May 23;7(3):e27233. doi: 10.5812/numonthly.7(3)2015.27233.
8. *Dousdampanis P, Trigka K, Musso CG, Fourtounas C.* Hyperuricemia and chronic kidney disease: an enigma yet to be solved. *Ren Fail.* 2014 Oct;36(9):1351-9. doi: 10.3109/0886022X.2014.947516.
9. *Johnson RJ, Sanchez Lozada LG, Lanaspa MA, Piani F, Borghi C.* Uric Acid and Chronic Kidney Disease: Still More to Do. *Kidney Int Rep.* 2022 Dec 5;8(2):229-239. doi:10.1016/j.ekir.2022.11.016.
10. *Voormolen N, Noordzij M, Grootendorst DC, Beetz I, Sijkens YW, van Manen JG, et al.* PREPARE study group. High plasma phosphate as a risk factor for decline in renal function and mortality in pre-dialysis patients. *Nephrol Dial Transplant.* 2007 Oct;22(10):2909-16. doi: 10.1093/ndt/gfm286.
11. *Nakhoul GN, Huang H, Arrigain S, Jolly SE, Schold JD, Nally JV, et al.* Serum Potassium, End-Stage Renal Disease and Mortality in Chronic Kidney Disease. *Am J Nephrol.* 2015;41: 456-463. doi:10.1159/000437151.
12. *Mandai S, Kanda E, Iimori S, Naito S, Noda Y, Kikuchi H, et al.* Association of serum chloride level with mortality and cardiovascular events in chronic kidney disease: the CKD-ROUTE study. *Clin Exp Nephrol.* 2017;21:104-111. doi: 10.1007/s10157-016-1261-0.

13. *Kestenbaum B, Sampson JN, Rudser KD, Patterson DJ, Seliger SL, Young B, et al.* Serum phosphate levels and mortality risk among people with chronic kidney disease. *J Am Soc Nephrol.* 2005 Feb;16(2):520-8. doi: 10.1681/ASN.2004070602.
14. *Sofue T, Nakagawa N, Kanda E, Nagasu H, Matsushita K, Nangaku M, et al.* Prevalences of hyperuricemia and electrolyte abnormalities in patients with chronic kidney disease in Japan: A nationwide, cross-sectional cohort study using data from the Japan Chronic Kidney Disease Database (J-CKD-DB). *PLoS One.* 2020 Oct 15;15(10):e0240402. doi: 10.1371/journal.pone.0240402.
15. *Seng JJB, Tan YLC, Lim RW, Ng HTS, Lee PH, Wong J.* Prevalence and risk factors for hypercalcemia among non-dialysis patients with chronic kidney disease-mineral and bone disorder. *Int Urol Nephrol.* 2018 Oct;50(10):1871-1877. doi: 10.1007/s11255-018-1906-x.
16. *Gilligan S, Raphael KL.* Hyperkalemia and Hypokalemia in CKD: Prevalence, Risk Factors, and Clinical Outcomes. *Adv Chronic Kidney Dis.* 2017 Sep;24(5):315-318. doi:10.1053/j.ackd.2017.06.004.
17. *Coburn JW, Popovtzer MM, Massry SG, Kleeman CR.* The physicochemical state and renal handling of divalent ions in chronic renal failure. *Arch Intern Med.* 1969;124:302-11.
18. *Zhang Y, Qiu H.* Dietary Magnesium Intake and Hyperuricemia among US Adults. *Nutrients.* 2018 Mar 2;10(3):296. doi:10.3390/nu10030296.
19. *Sakaguchi Y, Iwatani H, Hamano T, Tomida K, Kawabata H, Kusunoki Y, et al.* Magnesium modifies the association between serum phosphate and the risk of progression to end-stage kidney disease in patients with non-diabetic chronic kidney disease. *Kidney Int.* 2015;88:833-42. doi:10.1038/ki.2015.165.
20. *Ojo A.* Addressing the global burden of chronic kidney disease through clinical and translational research. [Интернет]. *Trans Am Clin Climatol Assoc.* 2014;125:229-43; discussion 243-6. Available from: <https://pubmed.ncbi.nlm.nih.gov/25125737/>. (Last accessed: 21.07.2023).
21. *Hooi LS, Ong LM, Ahmad G, Bavanandan S, Ahmad NA, Naidu BM, et al.* A population-based study measuring the prevalence of chronic kidney disease among adults in West Malaysia. *Kidney Int.* 2013 Nov;84(5):1034-40. doi: 10.1038/ki.2013.220.
22. *Xiaoyun Lin, Xiqian Wang, Xin Li, Lili Song, Zhaowei Meng, Qing Yang, et al.* Differences in the Association of Hyperuricemia and Hypertension: A Cross-Sectional Study". *International Journal of Endocrinology.* 2019, Article ID 7545137. doi:10.1155/2019/7545137.
23. *Kanbay M, Jensen T, Solak Y, Le M, Roncal-Jimenez C, Rivard C, et al.* Uric acid in metabolic syndrome: From an innocent bystander to a central player. *Eur J Intern Med.* 2016 Apr;29:3-8. doi:10.1016/j.ejim.2015.11.026.
24. *Barman Z, Hasan M, Miah R, Mou AD, Hafsa JM, Trisha AD, et al.* Association between hyperuricemia and chronic kidney disease: a cross-sectional study in Bangladeshi adults. *BMC Endocr Disord.* 2023 Feb 21;23(1):45. doi:10.1186/s12902-023-01304-7.
25. *Johnson RJ, Tittle S, Cade JR, Rideout BA, Oliver WJ.* Uric acid, evolution and primitive cultures. *Semin Nephrol.* 2005 Jan;25(1):3-8. doi: 10.1016/j.seminephrol.2004.09.002.
26. *Feig DI.* Hyperuricemia and hypertension. *Adv Chronic Kidney Dis.* 2012 Nov;19(6):377-85. doi:10.1053/j.ackd.2012.05.009.
27. *Mohammed Walid Khalil Abushunnar.* The Correlation between Hyperuricemia and Cardiovascular Morbidities among Hemodialysis Patients Attending the Academy Charity Teaching Hospital From Jan 2019 - Dec 2019. [Интернет]. *Cardiology and Cardiovascular Medicine.* 2022; 6: 390-397. Available from: <https://fortuneonline.org/articles/the-correlation-between-hyperuricemia-and-cardiovascular-morbidities.pdf>. (Last accessed: 21.07.2023).
28. *Van Laecke S, Nagler EV, Verbeke F, Van Biesen W, Vanholder R.* Hypomagnesemia and the risk of death and GFR decline in chronic kidney disease. *Am J Med.* 2013 Sep;126(9):825-31. doi:10.1016/j.amjmed.2013.02.036.
29. *De Baaij JH, Hoenderop JG, Bindels RJ.* Magnesium in man: implications for health and disease. *Physiol Rev.* 2015 Jan;95(1):1-46. doi: 10.1152/physrev.00012.2014.
30. *Leenders NHJ, Douma CE, Hoenderop JGJ, Vervloet MG.* Magnesium in chronic haemodialysis (MAGIC-HD): a study protocol for a randomised controlled trial to determine feasibility and safety of using increased dialysate magnesium concentrations to increase plasma magnesium concentrations in people treated with haemodialysis. *BMJ Open.* 2022 Nov 21;12(11):e063524. doi:10.1136/bmjopen-2022-063524.