НИРКИ KIDNEYS

DOI: https://doi.org/10.22141/2307-1257.14.3.2025.538

Arwa M. Nasser[1], Essam F. Al-Jumaili[2]

[1]Scientific Research Commission, Research and Technology Center of Environment, Water and Renewable Energy, Iraq

[2]Institute of Genetic Engineering and Biotechnology, University of Baghdad, Baghdad, Iraq

The level of blood lead, zinc and relationship with the metallothionein gene polymorphism in chronic kidney failure

For citation: Kidneys. 2025;14(3):191-198. doi: 10.22141/2307-1257.14.3.2025.538

Abstract. ***Background.*** *Chronic kidney disease is defined by renal damage or an estimated glomerular filtration rate less than 60 ml/min/1.73 m^2. Lead is a ubiquitous environmental factor that can contribute to lengthy clinical complications in individuals with chronic kidney disease. They can be exposed to changes in zinc homeostasis. The MT2A gene also expresses a wide range of physiological and pathological effects.* ***Materials and methods.*** *This study involved 60 blood samples from individuals with kidney disease on hemodialysis, and 60 samples from apparently healthy individuals as a control. The purpose was to identify the molecular character of the genotype of the MT2A gene SNP (A>G) (rs28366003) in a cohort of chronic kidney disease subjects and apparently healthy controls.* ***Results.*** *Blood lead and zinc serum levels were compared between patients and healthy controls by flame atomic absorption spectrophotometry. Lead contents were significantly and considerably higher, with significant differences (p > 0.01) between the patient cohort and the healthy controls, while serum zinc was significantly decreased. Males are more affected than females with chronic kidney disease, and individuals older than 40 years had a greater risk of complications. Hypertension has a meaningful positive relation to chronic kidney disease, and it is therefore considered a possible risk factor. The rs28366003 A>G genotype associated with increased risk of kidney disease in Iraqi patients demonstrated considerable variation. The median age of kidney disease patients was 20 to 69 years. Genotypes and allele frequencies of rs28366003, A>G in the kidney disease population: 51.7 % (n = 31) were wild-type (AA), 33.3 % (n = 20) were heterozygous (AG) and 15 % (n = 9) were homozygous (GG). The allele frequencies of A and G were 68.3 and 31.7 %.* ***Conclusions.*** *Thus, the drop in zinc levels and the harmful increase in blood lead in chronic kidney failure patients who possess SNP variants of the MT2A gene, specifically rs28366003, may be involved in kidney disease susceptibility.*

Keywords: *chronic kidney disease; metallothionein gene polymorphism; lead exposure, zinc deficiency; gene SNP rs28366003; hemodialysis*

Introduction

Chronic kidney disease (CKD) is a serious threat to global health as more than two million of us get CKD annually [1]. It is a primary source of illness and mortality globally and is becoming more acknowledged as a global public health concern, particularly in developing nation [2]. There are five stages of chronic renal failure (CRF) based on glomerular filtration rate (GFR), and stage 5, is also called end-stage renal disease (ESRD). CKD is present when damage to the kidney exists with persistence for approximately three months or longer; it also poses an especially large burden in low- and middle-income countries [3]. It is now recognized that even slight changes in kidney structure and function are associated with increased risk of mortality and implications for other organ systems [4]. Dialysis therapies replace some functions of the healthy kidney by removal of fluid and waste products [5]. Maintenance hemodialysis is considered a life sustaining treatment for patients with such disease. It also requires adherence to recommended attendance for hemodialysis, guidelines for dietary and fluid intake, and adherence to medication regimens to perpetuate its benefits [6]. In the population

For correspondence: Essam F. Al-Jumaili, Institute of Genetic Engineering and Biotechnology, University of Baghdad, Baghdad, Iraq; e-mail: Prof.dr.essamal-jumaily@ige.uobaghdad.edu.iq

Full list of authors' information is available at the end of the article.

of patients receiving maintenance hemodialysis, nutritional therapy focuses on ensuring an appropriate intake of protein and calories [7]. Major causes of CKD are diabetes, hypertension, chronic glomerulonephritis, chronic pyelonephritis, chronic use of anti-inflammatory medications, autoimmune diseases, polycystic kidney disease and long-term acute renal disease [8]. Zinc (Zn) is a trace element involved in multiple physiological functions in the body. It is essential for cell viability, growth, and replication, and the activation of 300 or more enzymes [9]. A deficiency of trace elements, particularly Zn, can lead to cardiovascular disease; lower serum Zn levels were associated with increased premature death and diminished physical activity [10]. Zinc stimulates the production of metallothionein, which are proteins that are effective in diminishing hydroxyl radicals and sequestering any reactive oxygen species (ROS) produced during stress conditions [11]. Lead has a high affinity for low-molecular-weight proteins which are easily filtered through the glomerulus then reabsorbed in proximal tubules, establishing primary tubular toxicity. This may culminate into albuminuria and progressive kidney disease towards ESRD [12]. The first identified case of Pb-related nephrotoxicity was reported in the 19th century. Since then, exposure to high concentrations of Pb has been regarded as an environmental risk factor for hypertension and kidney injury [13]. Metallothionein is a protein rich in cysteine with large amounts of metals that can be found in all organisms. Apart from heavy metal detoxification, metallothionein is one of the most powerful antioxidants where it is capable of regulating and mediating several cellular processes [14]. Any mutation of this gene will affect the function metallothionein proteins increasing the effects of heavy metals. ROS, the SNP A-G (rs28366003) in promotor of metallothionein gene, A to G allele conversion appearance, thereby decrease transcription qualification [15]. The location of the SNP A-G (rs28366003) in promotor of a metallothionein gene, this polymorphism exists away of five base pairs upstream of their initiation site; this polymorphism includes changing an A nucleotide to G nucleotide in promotor of MT gene, later caused a decreased in production of metallothionein and a decrease in the role of metallothioneins to protect the cell from dangerous products of metabolism, exercise or cellular injury [16].

Materials and methods

Study design

From December 2020 to March 2021, blood samples were collected from patients with CKD under hemodialysis and a healthy control group. A total of 7 ml of blood was taken from each patient, 5 ml in plain vacutainer tubes and 2 ml in EDTA. DNA was extracted from the Iraqi Dialysis Center and the Medical City Center The study consisted of 120 blood samples from two groups as follows: group 1, 60 samples of Iraqi patients with chronic kidney disease, and group 2, 60 samples from healthy controls which included no history of kidney disease. We prepared a questionnaire with information including age, chronic diseases, blood pressure, and gender.

Ethical commission

The study was approved by Scientific Research Commission, Research and Technology Center of Environment, Water and Renewable Energy and Institute of Genetic Engineering and Biotechnology, University of Baghdad (No. 335 in 22/1/2025).

Survey administration

Verbal consent was obtained from patients undergoing hemodialysis sessions and they were asked whether they agreed to participate in the current study. If they agreed, the survey questions were explained to the patients as they completed the research questionnaire.

Exclusion criteria

Patients under 20 years old, patients who need immunosuppressive treatment for kidney disease and patient with polycystic kidney disease

Lead and zinc measurement

5 ml of blood collected in plain vacutainer tubes were was used to determine the concentrations of zinc and the blood lead with flame atomic absorption spectrophotometry (FAAS), an analytical technique used to determine the concentration of metal. It utilizes the principle of atomic absorption, where excited atoms in a flame absorb light at specific wavelengths, leading to a decrease in the intensity of the transmitted light.

Molecular methods

DNA extraction. 2 ml in EDTA (Ethylene Diamine Tetracetic Acid) blood samples from patients and controls were kept at –20° C. ReliaPrep™ Blood gDNA Miniprep System was utilized to extract genomic DNA. In the case of DNA purity genotyping of polymorphism metalothionein (rs28366003) by using high resolution melting (HRM). Used master mixes were containing EVA-Green, HRM Master Mix Synthetic SNP sequences. The DNA was extracted, using DNA extraction kit EasyPure® Genomic (TransGen Biotech, EE101-01) (Fig. 1). Primer sequences were designed according to their reference sequence (rs) in the National Center for Biotechnology Information database (NCBI) in Table 1 forward-primer CTTGGGATCTCCAACCTCAC and the reverse-primer ACTTCTCTGATGCCCCTTTG the thermal cycle in Table 2.

Table 1. Specific primers for MT single nucleotide polymorphisms

	Primer sequence (5'-3')	Primer size, bp	Product size, bp
F-rs28366003	CTTGGGATCTCCAACCTCAC	20	200
R-rs28366003	ACTTCTCTGATGCCCCTTTG	20	200

Analysis of data

The Statistical Package for the Social Sciences (2019) program was utilized to determine the effect of difference groups on study variables [17]. For the normally distributed quantitative data of study groups, parametric (independent samples t-test, ANOVA, standard error) were used. Qualitative data (categorical variables) were presented as the frequency (percentage), and the significant differences between their distributions in study groups were evaluated by a chi-square test of independence (χ^2-test) or Fisher's exact tests, where applicable. The allelic and genotypic frequencies were calculated using direct gene counting method. The differences were determined by chi-square test of independence, odds ratios (ORs) and its 95% confidence interval (CI) were estimated to determine the association MT2A SNPs with chronic kidney failure and treatment response using WINPEPI program for epidemiologists (2002, 2020).

Ethics statement

This study was approved by the Ethics Committee of the Institute of Genetic Engineering and Biotechnology for postgraduate studies, all participants gave informed consent, the study followed the Declaration of Helsinki principles.

Results

Age and hypertension

Table 3 illustrates the chronic kidney patients aged 50 to 59 had the highest prevalence of 43.33 % when compared with other groups while only 1.67 % of patients within age group 20–29 and 6.67 % with in age group 30–39 and 15 % of patients within age group 40–49 while in age group above 60 years, 33.33 %. There are highly significant differences between the incidences of the different age groups among chronic kidney disease patients ($p < 0.01$) (Table 2).

Another study found there was no difference between the ages of patients compared to healthy people, and this study does not agree with our study [18]. Also, Table 3

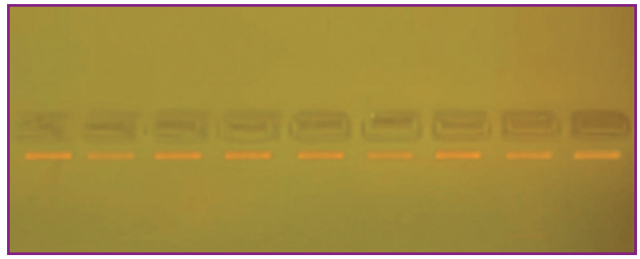

Figure 1. Genomic DNA gel electrophoresis for 9 samples on agarose gel with a concentration of 1 % for 70 min and 70 V

Table 2. The cycling protocol

Step	Temperature	Time, sec	Cycles
Enzyme activation	94	30	1
Denaturation	94	10	40
Annealing	60	15	
Extension	72	20	
HRM	55–95	0.5 for 1 °	

Table 3. Distribution of sample study according to age, gender and hypertension in different groups

Variables/factors		Patients (N = 60)		Controls (N = 60)	
		Abs.	%	Abs.	%
Age (years)	20–29	1	1.67	9	15.00
	30–39	4	6.67	13	21.67
	40–49	9	15.00	22	36.67
	50–59	26	43.33	9	15.00
	≤ 60	20	33.33	7	11.67
	Total	60	100	60	100
	p-value	0.0001**		0.0174*	
Sex	Male	31	51.67	36	60.00
	Female	29	48.33	24	40.00
	p-value	0.796 NS		0.121 NS	
Hypertension	Positive	48	80.00	14	23.33
	Negative	12	20.00	46	76.67
	p-value	0.0001**		0.0001**	

Notes: * — p ≤ 0.05; ** — p ≤ 0.01; NS — non-significant.

showed there was a very significant ($p \leq 0.0001$) difference between the same group 96 % of patients in CKD group had hypertension patently. and this result concurs with [19] who recorded hypertension prevalence (80 %) in CKD.

Lead and zinc

Table 4 showed significant decrease between the level of zinc in patients and control group the mean of the Zn in the patients 63.86 ± 1.06, while the control 99.41 ± 2.01 and this result agree with [20]. Also, the result shown the high significant increase in lead in the CKD patients ($p \leq 0.01$) the mean of the CKD patients 23.05 ± 0.75 while the control group 16.50 ± 0.42 and this result agree with [21].

SNP polymorphism MT2A gene

A single nucleotide polymorphism of *MT2A* gene in this study the genotypes and allele frequencies of SNP rs28366003 A>G in Hardy-Weinberg equilibrium (HWE) in patient with kidney disease groups 51.7 % (n = 31) wild (AA), and 33.3 % (n = 20) heterozygous (AG) and 15 % (n = 9) homozygous (GG). The genotypes and allele frequencies (HWE) in healthy control was 36 % (n = 60) wild (AA), and 40 % (n = 24) heterozygous (AG) and 0 % (n = 0) homozygous (GG). Allele frequencies for A and G were 68.3 and 31.7 %, respectively, as shown in Table 5.

DNA samples of all study groups were genotyped of *MT2A* SNP (rs28366003), detection was achieved by using HRM real-time PCR. The resulting output of thermocycler of the HRM analysis process for SNP (rs28366003) three genotypes is shown in Fig. 2.

Table 4. Comparison between different groups in Zn and Pb

Group	Mean ± SE	
	Zn	Pb
Patients	63.86 ± 1.06	23.05 ± 0.75
Controls	99.41 ± 2.01	16.50 ± 0.42
T-test	15.6	7.6
p-value	0.0001*	0.0001*

Note: * — p ≤ 0.01.

The relationship between MT2A rs28366003 and blood lead and zinc

As shown in Table 6, there was no significant difference in Zn in the group of patient, control and the rs28366003 while observed group of patients is a significant difference in the value of lead.

Discussion

Age and hypertension

CKD is a primary source of illness it is slow, steady progression characterizes it and is irreversible [22]. Age, sex and socioeconomic status are considered to be influential in the development, progression and outcomes from CKD [23]. The prevalence of chronic kidney disease increases markedly with old age. The reason for this because the patients with advanced age may suffer from systemic and chronic diseases, stress, and an increasing rate of catabolism. Moreover, elderly patients suffer from a decrease in the glomerular filtration rate (GFR) due to diseases that complicate aging, such as atherosclerosis and high blood pressure. In addition, there is an increase in catabolism rates and a decrease in metabolism

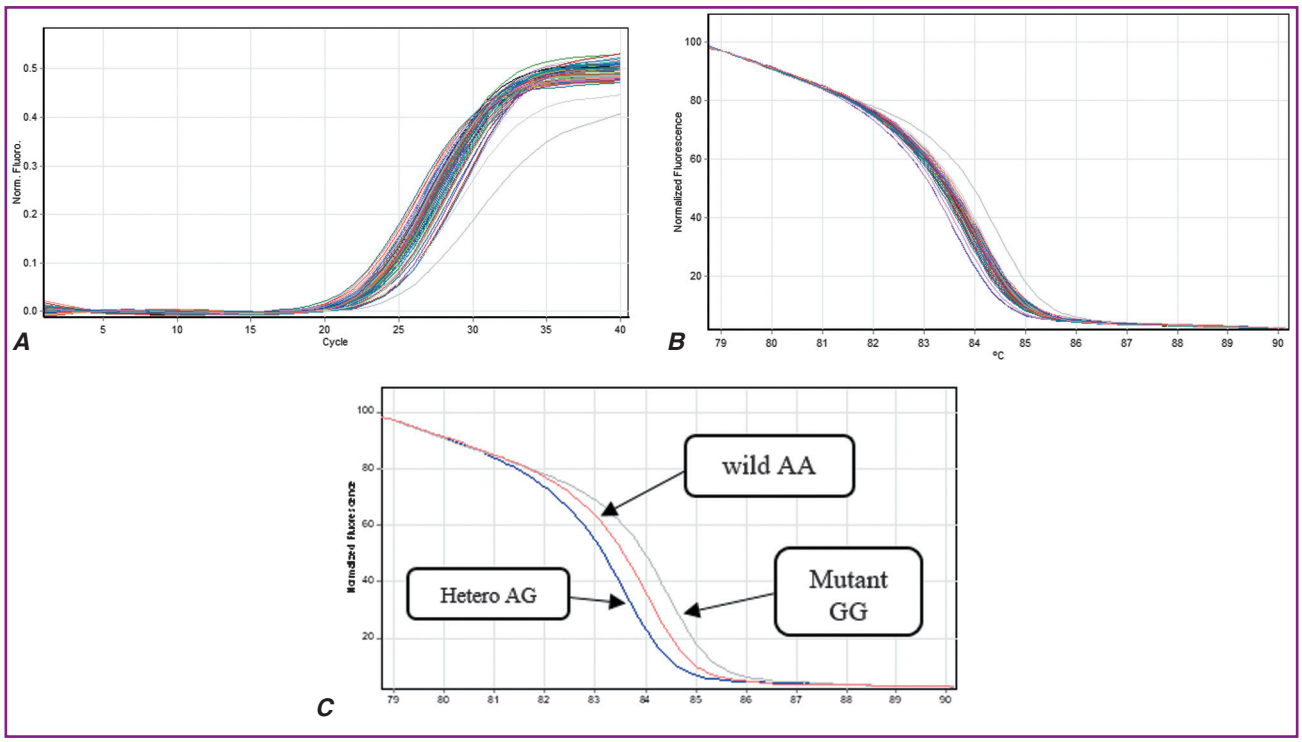

Figure 2. The genotype result for SNP rs28366003: A, B — the HRM result, C — the wild, heterozygous and mutant genotypes

rates, which makes the elderly vulnerable to many chronic diseases and health problems [24]. The encompassing factors of male sex hormones, gender neutrality of occupation role, stress expressed as performance, and chronic disease distribution all contribute to the fact that males are at a higher risk of CKD than female gender. In addition, differences in lifestyle (e.g. smoking cigarettes; drinking alcohol) might also help explain this gender gap [25]. Of the highest prevalence of chronic kidney disease, the female gender was the greatest risk factor for chronic kidney disease. This could be based on biological differences between men and women in glomerular structure; glomerular hemodynamics; muscle mass; and hormone metabolism [26]. Hemodialysis patients had high blood pressure (hypertension) immediately after their first time experiencing hemodialysis. Patients undergoing dialysis often experience high blood pressure — difficult to treat and causes a range of adverse effects including increased risk of heart disease [27]. Hypertension is one of the leading factors for the development of CKD, given the adverse effects of enhanced blood pressure on kidney vasculature. Over the long-term, uncontrolled high blood pressure translates into high intraglomerular pressures that lead to impairment in glomerular filtration. Damage to the glomeruli lead to an increase in protein filtration, resulting in abnormally increased amounts of protein in the urine [28].

Lead and zinc

Zn, the second among the most critical trace elements in the human body, is crucial in regulating cellular and subcellular processes across various tissues. Zn deficiency is linked to the advancement of CKD and related consequences. As CKD progresses to ESRD [29]. Zinc deficiency is a risk factor for ESRD and indicate association between zinc deficiency and organ damage due to fibrosis. Thus, zinc deficiency may affect kidney function via oxidative stress and fibrosis. Zn concentrations are decreased in CKD [30]. Increased zinc excretion causes zinc deficiency in patients with kidney diseases as well as in those on hemodialysis. CKD patients have higher urinary zinc excretion, which tends to increase as the CKD stage progresses [31]. Chronic kidney disease is susceptible to zinc deficiency, which may be caused by an inadequate dietary intake due to uremia-related anorexia and dietary restriction, reduced gastrointestinal zinc absorption, adsorption of zinc by phosphate binders, and removal of zinc by dialysis procedure [32] lead (Pb) binding to low-molecular-weight proteins, probably enters kidney proximal tubule cells through endocytosis. It seems to inhibit kidney mitochondria's respiratory function inside the cells, which causes the formation of oxidative stress, reactive oxidative species, and intracellular depletion of glutathione [33]. Exposure to Pb is linked to an elevated CKD risk as assessed by proteinuria, and a greater risk of decreased GFR [34].

SNP polymorphism MT2A gene

Single nucleotide polymorphisms (SNPs) are the most common type of variation in the human genome. The vast majority of SNPs identified in the human genome do not

Table 5. Comparison of the genotype and allele frequency of SNP (rs28366003) between patients and controls, n (%)

	Genotype	Controls	Patients	χ^2	OR (95% CI)	p-value
Genotype	AA reference	36 (60)	31 (51.7)	0.03	1.00 (reference)	0.9 NS
	AG	24 (40)	20 (33.3)	0.47	0.9 (0.4471–2.065)	0.9 NS
	GG	0 (0)	9 (15)	9.1	22.02 (1.2315–.59)	0.03*
	Total	60	60			
Allele	A reference	96 (80)	82 (68.3)	0.011	1.00 (reference)	0.92
	G	24 (20)	38 (31.7)	4.3	1.8 (1.044–3.273)	0.03*
	Total	120	120			

Notes: * — p ≤ 0.05; NS — non-significant.

Table 6. Relationship between genotype of rs28366003 SNP with Zn and Pb in patients and control groups

Group	Genotype	Mean ± SE, ppm	
		Zn	Pb
Patients	AA	65.16 ± 1.45	22.19 ± 1.21[a]
	AG	63.30 ± 2.04	17.85 ± 0.81[b]
	GG	61.55 ± 1.62	19.67 ± 1.20[ab]
	L.S.D. (p-value)	5.839 NS (0.4549)	3.948 (0.0261)*
Controls	AA	96.94 ± 2.17	18.05 ± 0.55
	AG	99.62 ± 3.23	17.67 ± 0.61
	L.S.D. (p-value)	7.491 NS (0.4767)	1.678 NS (0.6445)

Notes: means with the different letters in same column differed significantly; * — p ≤ 0.05; NS — non-significant.

have any effect on the phenotype; however, some can lead to changes in the function of a gene or the level of its expression. Moreover, determination of associations of genetic variants with a disease does not provide information about the functionality of these variants, which is necessary to elucidate the molecular mechanisms of the development of pathology and to design effective methods for its treatment and prevention. Further scrutiny into the functionality of such SNPs will assist us in better understanding the associated differences between individuals and facilitate the development of alternative therapies targeting different groups of individuals with different SNP profiles [35]. Chronic kidney disease is a progressive disease that results from kidney damage and results in loss of kidney function. Genetic factors, such as allelic variants, can contribute to this disease. [36]. As is known, this mutation in the promotor of the metallothionein gene in the site A-G (rs28366003) lead to a defect in the function of the main protein that coding by metallothionein gene, this protein have able to combined the different type of heavy metals together by thiol group, and then remove it's from the body by filtration in the kidney and secreted with the urine, and because this mutation the heavy metals accumulate in the body of the patient and causes many health problems [37]. The effect of *MT2A* A-5G polymorphism in a general Japanese population, we observed significant associations with CKD the GG genotype was identified as a risk factor for CKD. The ORs for *MT2A* A-5G genotypes were statistically significant independently of age, sex and other potential confounders. This suggests that the vulnerability to these diseases due to *MT2A* A-5G polymorphism is independent of their major risk factors. *MT2A* A-5G may be associated with CKD and this polymorphism is a promising target for evaluations of CKD and with possible involvement of low-dose chronic exposure to environmental pollutant [38].

The relationship between MT2A rs28366003 and blood lead and zinc

Environmental pollution causes an increase in levels of heavy metals in the organism. Due to this mutation in the promotor of the metallothionein gene, the protein cannot remove all the amount of heavy metals from the body and consequently increase the toxicity of heavy metals [39]. Highly statistically significant associations were detected between the −5 A/G core promoter region SNP in the MT2A gene and Pb Individuals with the GG genotype had statistically lower Zn level and higher Pb levels in the blood samples than individuals with AA and AG genotypes. This study suggests that having the GG genotype individuals may be more sensitive for the metal toxicity and they should be more careful about protecting their health against the toxic effects of the heavy metals no detect changes in serum Zn level for the GA or GG genotype in population consider that MT2A A-5G polymorphism likely affects intracellular homeostasis rather than contributing to excretion of related molecules outside the cells [40].

Conclusions

This study showed that decreased zinc levels in patients with CKD are correlated with an elevated concentration of lead as a result of kidney's diminished ability to eliminate lead because of the decreased activity of metallothionein genes. In our study there was positive correlation between the GG genotype and the kidneys disorders; this shows us that male carried GG genotype have higher risk to suffer kidney problems.

References

1. *Hamid RH, Al-Jumaily RMKh. Evaluation of Oxidative Stress Activity, DNA Damage and Global DNA Methylation among Patients with Chronic Kidney Disease. Iraqi J Sci. 2024;65(9):4963-4972. doi: 10.24996/ijs.2024.65.9.13.*
2. *Mahdi Al-Shattawi SS, Al-Jumili EF, Al-Kawaz UMR. Pin1 Gene Expression and Some Biochemical Parameters in Iraqi Population with Chronic Kidney Disease. Iraqi J Biotechnol. 2024;23(2):105-111.*
3. *AL-Razak MJA, Al Saadi BQH, Al Saedi AJH. Investigate Some Biochemical Parameters and Impact of NOS3 Gene Polymorphism among Iraqi Patients with Chronic Kidney Disease. Iraqi J Biotechnol. 2025;24(1):243-252.*
4. *Al-Jumaili RA, Al-Jumaili EF, Ramadhan OM. Role of Calcium Sensing Receptor Gene Polymorphism r1801725 in the Evaluation of Kidney Disease. Iraqi J Biotechnol. 2024;23(1):235-240.*
5. *Attia RI, Naji Abed NA. Evaluation of Some Biochemical Parameters and the Effect of Oxidative Stress During Hemodialysis in Patients with Chronic Renal Disease. Biochem Cell Arch. 2021;21(1):405.*
6. *Abdul-Jabbar MA, Kadhim DJ. Adherence to Different Treatment Modalities among Patients on Maintenance Hemodialysis. Iraqi J Pharm Sci. 2022;31(1):95-101. doi: 10.31351/vol31iss1pp95-101.*
7. *Al-Shibly KH, Al-Diwan JK. Effect of the Dietary Protein Intake on Urea Reduction Rate in Patients on Maintenance Hemodialysis in Merjan Teaching Hospital. Med J Babylon. 2022;19(2):244-249. doi: 10.4103/MJBL.MJBL_19_22.*
8. *Narayanan M, Setia S. Chronic Kidney Disease. In: Jackson M, Huang R, Kaplan E, Mookherjee S, editors. Perioperative Medicine Consult Handbook. Cham: Springer; 2020. 301-305 pp. doi: 10.1007/978-3-030-19704-9_38.*
9. *Filler G, Felder S. Trace elements in dialysis. Pediatr Nephrol. 2014 Aug;29(8):1329-1335. doi: 10.1007/s00467-013-2585-6.*
10. *Jebur NJ, Yahya RN. The Actual Benefits of Zinc for Cardiovascular Diseases: Mini Review. Al-Rafidain J Med Sci. 2022 Jul-Dec;3:82-86. doi: 10.54133/ajms.v3i.92.*
11. *Marreiro DD, Cruz KJ, Morais JB, Beserra JB, Severo JS, de Oliveira AR. Zinc and Oxidative Stress: Current Mechanisms. Antioxidants (Basel). 2017 Mar 29;6(2):24. doi: 10.3390/antiox6020024.*
12. *Gao B, Chi L, Mahbub R, et al. Multi-Omics Reveals that Lead Exposure Disturbs Gut Microbiome Development, Key Metabolites, and Metabolic Pathways. Chem Res Toxicol. 2017 Apr 17;30(4):996-1005. doi: 10.1021/acs.chemrestox.6b00401.*
13. *Ekong EB, Jaar BG, Weaver VM. Lead-related nephrotoxicity: a review of the epidemiologic evidence. Kidney Int. 2006 Dec;70(12):2074-2084. doi: 10.1038/sj.ki.5001809.*
14. *Yang R, Roshani D, Gao B, Li P, Shang N. Metallothionein: A Comprehensive Review of Its Classification, Structure, Biological Functions, and Applications. Antioxidants (Basel). 2024 Jul 9;13(7):825. doi: 10.3390/antiox13070825.*

15. Hamed OM, Khalil MI, Alsaffar RS. Metallothionein Gene Polymorphism Is Considered to Be a Risk Factor for Chronic Diseases. Int J Health Sci. 2022;6(S5):1691-1692. doi: 10.53730/ijhs.v6nS5.9021.

16. Leierer J, Rudnicki M, Braniff SJ, et al. Metallothioneins and renal ageing. Nephrol Dial Transplant. 2016 Sep;31(9):1444-1452. doi: 10.1093/ndt/gfv451.

17. George D, Mallery P. IBM Statistics 26 Step by Step: A simple guide and reference. 16th ed. New York: Routledge; 2019. 402 p. doi: 10.4324/9780429056765.

18. Al-Jumaili RA, Al-Jumaili EF. Study of the causes of parathyroid hormone imbalance and some biochemical parameter in patients with chronic kidney disease. Rom J Diabetes Nutr Metab Dis. 2024;31(1):49-57. doi: 10.46389/rjd-2024-0049.

19. Rebhi F, Khadhar M, Sarra H, et al. Hypertension and Chronic Kidney Disease: A Close and Proportional Relationship. Nephrol Dial Transplant. 2023 Jun;38(Suppl 1):gfad063d_6789. doi: 10.1093/ndt/gfad063d_6789.

20. Elgenidy A, Amin MA, Awad AK, Husain-Syed F, Aly MG. Serum Zinc Levels in Chronic Kidney Disease Patients, Hemodialysis Patients, and Healthy Controls: Systematic Review and Meta-Analysis. J Ren Nutr. 2023 Jan;33(1):103-115. doi: 10.1053/j.jrn.2022.04.004.

21. Yao S, Xu D. Relationships between blood concentrations of cadmium, lead, mercury, selenium, and manganese and the risk of chronic kidney disease: a cross-sectional study based on NHANES 2011-2018. Arch Med Sci. 2024 Dec 13;20(6):1822-1830. doi: 10.5114/aoms/181508.

22. AlAni HT, Al-Lami MQ. Evaluation of Some Biochemical and Hematological Parameters in Patients with Chronic Kidney Disease. J Fac Med Baghdad. 2024;66(2):154-161. doi: 10.32007/jfacmedbagdad.2269.

23. Duff R, Awofala O, Arshad MT, et al. Global health inequalities of chronic kidney disease: a meta-analysis. Nephrol Dial Transplant. 2024 Sep 27;39(10):1692-1709. doi: 10.1093/ndt/gfae048.

24. Fradelos EC. The Effect of Clinical and Demographic Factors on Quality of Life in End-Stage Renal Disease: A Multicenter Cross-Sectional Study. J Ren Hepat Disord. 2020;4(1):1-9. doi: 10.15586/jrenhep.2020.58.

25. Baqer HM, Jabur F, Kadhum S. Impact of End Stage Renal Disease Upon Physical Activity for Adult Patients Undergoing Hemodialysis at AL-Najaf Governorate Hospitals. J Pharm Sci Res. 2018;10(5):1170-1174.

26. Saber A, Tahami AN, Najafipour H, Azmandian J. Assessment of Prevalence of Chronic Kidney Disease and Its Predisposing Factors in Kerman City. Nephro-Urol Monthly. 2017;9(2):e13113. doi: 10.5812/numonthly.41794.

27. Swastika KD, Tarigan RR. Hypertension on Dialysis Patients: Influence Factors and Management. J Endocrinol Tropic Med Inf Dis. 2022;4(4):176-190. doi: 10.32734/jetromi.v4i4.14734.

28. Ku E, Lee BJ, Wei J, Weir MR. Hypertension in CKD: Core Curriculum 2019. Am J Kidney Dis. 2019 Jul;74(1):120-131. doi: 10.1053/j.ajkd.2018.12.044.

29. Abdollahi A, Ghahramani A, Ghahramani N. Zinc and Kidney Disease: A Review. Iran J Kidney Dis. 2022 Mar;16(2):79-87.

30. Tokuyama A, Kanda E, Itano S, et al. Effect of zinc deficiency on chronic kidney disease progression and effect modification by hypoalbuminemia. PLoS One. 2021 May 11;16(5):e0251554. doi: 10.1371/journal.pone.0251554.

31. Damianaki K, Lourenco JM, Braconnier P, et al. Renal handling of zinc in chronic kidney disease patients and the role of circulating zinc levels in renal function decline. Nephrol Dial Transplant. 2020 Jul 1;35(7):1163-1170. doi: 10.1093/ndt/gfz065.

32. Toida T, Toida R, Ebihara S, et al. Association between Serum Zinc Levels and Clinical Index or the Body Composition in Incident Hemodialysis Patients. Nutrients. 2020 Oct 19;12(10):3187. doi: 10.3390/nu12103187.

33. Harari F, Sallsten G, Christensson A, et al. Blood Lead Levels and Decreased Kidney Function in a Population-Based Cohort. Am J Kidney Dis. 2018 Sep;72(3):381-389. doi: 10.1053/j.ajkd.2018.02.358.

34. Jalili C, Kazemi M, Cheng H, et al. Associations between exposure to heavy metals and the risk of chronic kidney disease: a systematic review and meta-analysis. Crit Rev Toxicol. 2021 Feb;51(2):165-182. doi: 10.1080/10408444.2021.1891196.

35. Ivanova M, Dyadyk O, Ivanov D, Clerici F, Smith A, Magni F. Matrix-assisted laser desorption/ionization mass spectrometry imaging to uncover protein alterations associated with the progression of IgA nephropathy. Virchows Arch. 2020 Jun;476(6):903-914. doi: 10.1007/s00428-019-02705-7.

36. Mira FS, Oliveiros B, Carreira IM, Alves R, Ribeiro IP. Genetic Variants Related to Increased CKD Progression-A Systematic Review. Biology (Basel). 2025 Jan 14;14(1):68. doi: 10.3390/biology14010068.

37. Kalantar-Zadeh K, Jafar TH, Nitsch D, Neuen BL, Perkovic V. Chronic kidney disease. Lancet. 2021 Aug 28;398(10302):786-802. doi: 10.1016/S0140-6736(21)00519-5.

38. Hattori Y, Naito M, Satoh M, et al. Metallothionein MT2A A-5G Polymorphism as a Risk Factor for Chronic Kidney Disease and Diabetes: Cross-Sectional and Cohort Studies. Toxicol Sci. 2016 Jul;152(1):181-193. doi: 10.1093/toxsci/kfw080.

39. Tamay-Cach F, Quintana-P rez JC, Trujillo-Ferrara JG, et al. A review of the impact of oxidative stress and some antioxidant therapies on renal damage. Ren Fail. 2016;38(2):171-175. doi: 10.3109/0886022X.2015.1120097.

40. Kayaalt Z, Aliyev V, S ylemezo lu T. The potential effect of metallothionein 2A -5A/G single nucleotide polymorphism on blood cadmium, lead, zinc and copper levels. Toxicol Appl Pharmacol. 2011 Oct 1;256(1):1-7. doi: 10.1016/j.taap.2011.06.023.

Received 02.07.2025
Revised 05.08.2025
Accepted 14.08.2025

Information about authors
Arwa M. Nasser, Scientific Research Commission, Research and Technology Center of Environment, Water and Renewable Energy, Iraq; https://orcid.org/0009-0007-9442-8057
Essam F. Al-Jumaili, Institute of Genetic Engineering and Biotechnology, University of Baghdad, Baghdad, Iraq; https://orcid.org/0000-0002-5161-3128

Conflicts of interests. Authors declare the absence of any conflicts of interests and own financial interest that might be construed to influence the results or interpretation of the manuscript.

Arwa M. Nasser[1], Essam F. Al-Jumaili[2]
[1]Scientific Research Commission, Research and Technology Center of Environment, Water and Renewable Energy, Iraq
[2]Institute of Genetic Engineering and Biotechnology, University of Baghdad, Baghdad, Iraq

Рівень свинцю й цинку в крові та зв'язок із поліморфізмом гена металотіонеїну при хронічній нирковій недостатності

Резюме. Актуальність. Хронічна хвороба нирок визначається пошкодженням нирок або розрахунковою швидкістю клубочкової фільтрації менше 60 мл/хв/1,73 м^2. Свинець є повсюдним фактором навколишнього середовища, що може призводити до тривалих клінічних ускладнень у людей із хронічною хворобою нирок. Вони можуть зазнавати змін у гомеостазі цинку. Ген MT2A також має широкий спектр фізіологічних та патологічних ефектів. **Матеріали та методи.** У цьому дослідженні вивчено 60 зразків крові від осіб із захворюваннями нирок, які перебувають на гемодіалізі, та 60 від практично здорових осіб (контрольна група). Мета: визначити молекулярний характер генотипу SNP (A>G) (rs28366003) гена MT2A у пацієнтів із хронічною хворобою нирок та в контрольній групі. **Результати.** Рівні свинцю в крові та цинку в сироватці крові порівнювали в обох групах за допомогою полум'яної атомно-абсорбційної спектрофотометрії. Уміст свинцю в крові був значно вищим, із суттєвими відмінностями ($p > 0,01$) між когортою пацієнтів та здоровими особами, тоді як рівень цинку в сироватці крові був значно знижений. Чоловіки частіше страждають на хронічну хворобу нирок, ніж жінки, а пацієнти старше 40 років мали більший ризик ускладнень. Виявлено значущий позитивний зв'язок гіпертензії із хронічною хворобою нирок, тому її вважають можливим фактором ризику розвитку останньої. Генотип rs28366003 A>G, пов'язаний із підвищеним ризиком захворювання нирок в іракських пацієнтів, продемонстрував значну варіабельність. Медіанний вік осіб із хворобами нирок становив від 20 до 69 років. Генотипи та частота алелів rs28366003, A>G у популяції із захворюваннями нирок: 51,7 % (n = 31) були дикого типу (AA), 33,3 % (n = 20) — гетерозиготними (AG) та 15 % (n = 9) — гомозиготними (GG). Частота алелів A та G становила 68,3 та 31,7 %. **Висновки.** Таким чином, зниження рівня цинку та шкідливе підвищення рівня свинцю в крові пацієнтів із хронічною нирковою недостатністю, які мають варіанти SNP гена MT2A, зокрема rs28366003, можуть бути пов'язані зі схильністю до хвороб нирок.

Ключові слова: хронічна хвороба нирок; поліморфізм гена металотіонеїну; вплив свинцю; дефіцит цинку; SNP гена rs28366003; гемодіаліз