ORIGINAL ARTICLE

OPEN ACCESS

Correlation with Adrenal Hormones and Kidney Stone Pathogenesis Biochemical and Immunological Parameters in Human Patients

Hasan Ali Mohamed Aljezani

Lecturer, Department of Microbiology, College of Science, Al-Karkh University for Science, Baghdad, Iraq

Abstract

Background: Kidney stones are solid deposits that form in the urinary system, especially the kidneys, from chemical substances like salts and minerals. The pathophysiology of stone development involves aldosterone hormones and renin., as biochemical indicators of the kidney's susceptibility to different types of stones. In this study, two types of stones were used in relation to their formation in patients (calcium oxalate and uric acid stones). TNF and IL-17 were also thought to affect stone formation. Significant characteristics like smoking, BMI, and sex were examined. **Objective:** Assessing hormones in patients with kidney stones of both types (calcium oxalate and uric acid) and their relationship to smoking, body mass index, gender, and immunological indicators like tumor necrosis factor and interleukin-17. **Methodology:** This case-control study took 98 blood samples from kidney stone patients and healthy people. From May 2022 to December 2022, 68 patients with urinary tract problems, specifically kidney stones, were identified, along with 30 healthy individuals as a control group. Serum was obtained from blood. The samples were categorized as (38) calcium oxalate stone patients, (30) uric acid stone patients, and (30) healthy persons. Vital and immunological parameters were evaluated using ELISA. **Results:** Patients with calcium oxalate stones differed significantly from smokers ($P<0.05$), while those with uric acid stones differed significantly from smokers in terms of body mass ($P<0.01$). Gender index did not differ significantly across groups, but hormones (aldosterone, renin) and immune factors (TNF, IL-17) differed significantly between calcium oxalate and uric acid stones and the healthy group ($P<0.01$). **Conclusion:** Hormones affected the production of calcium oxalate and uric acid stones. Aldosterone hormone release increased calcium oxalate stone development, while renin depression increased both forms of stones. Smoking had an effect on uric acid stone patients, and immune indicators like TNF and IL-17 were vital as stone formation increased their blood levels. *[Journal of Current and Advance Medical Research, July 2024;11(2):102-108]*

Keywords: Kidney stone; aldosterone; renin; TNF; IL-17

Correspondence: Dr Hasan Ali Mohamed Aljezani, Lecturer, Department of Microbiology, College of Science, Al-Karkh University for Science, Baghdad, Iraq; **Cell no.:** +9647708842945; **Email:** dr.hasanaljezani@kus.edu.iq; **ORCID:** https://orcid.org/0009-0003-6278-7961

Introduction

The kidneys are among the most important organs in the human body, as they are affected by the formation of stones due to the presence of substances that have the ability to clump together into stones in the urine[1]. Recently, the formation of stones has increased significantly in all countries of the world, with no difference between genders and age groups. The main reasons that contribute to the formation of stones include insufficient water intake, irregular use of medications, weight gain, and malnutrition[2,3]. Predicting the formation of stones is essential due to their harmful effects on the urinary system, especially the kidneys, and imaging techniques are used in the diagnosis of

stones [4,5,6]. Kidney stones form as a result of a chemical imbalance in the urine and depend on chemical precipitates of different sizes and shapes[7].

Calcium stone is one of the most common types of kidney stones, affecting a high percentage of patients, causing deformities and scratches on the urinary tract. It is composed of calcium phosphate and calcium oxalate, affecting more than 60.0% of patients suffering from kidney stones. It exists in two forms (calcium monohydrate and calcium dihydrate), with the former being more prevalent than the latter[8].

Uric acid stone constitutes 3.0% to 10.0% of kidney stone patients, and it differs from other types in its components, as it contains a high percentage of purines resulting from animal proteins, such as meat mainly as well as fish[9]. This type causes a decrease in urine volume, excess uric acid in the urine, and a decrease in its acidity. It is more common in males than females[9].

The renin-angiotensin-aldosterone system (RAAS) is a system that regulates blood pressure, fluid balance, and cardiovascular health. These two hormones are vital in the regulation of the functions of the body because they create a system that is known as the RAAS. They are also responsible for a significant part of the influence that they have on the proliferation of cells and the biology of cancer, including migration, death, and metastasis. In addition, they contribute to conditions such as inflammation, necrosis, and fibrosis[10,11,12]. In addition to its production in the kidneys, renin is an aspartate proteinase that is mostly produced by the cells that are located in close proximity to the glomeruli.

Its primary function is to induce the conversion of angiotensinogen to angiotensin. The adrenal gland, the placenta, the testes, the retina, and the salivary glands are among the organs that are responsible for its production. Among these organs, some are located outside of the kidneys[13]. Aldosterone is a steroid hormone produced by the adrenal cortex. It works to balance sodium and potassium ions in the blood, maintaining water and electrolyte balance by increasing sodium retention and potassium excretion in the kidneys. It is made by cholesterol through a special enzyme called aldosterone synthase in the glomerulus, and its secretion is regulated by the renin-angiotensin system[14].

Interleukin-17 is an inflammatory cytokine secreted by the helper gene Th-17, which is a coded gene located in the short arm of the T chromosome. It is considered a promoter of osteoporosis[15]. Tumour necrosis factor is an inflammatory cytokine produced by phagocytic cells during acute inflammation. It works to produce signals within cells, leading to necrosis or programmed cell death. It plays an important role in resisting infection, as it works to bind to the cell membrane receptor. It exists in two forms: the first is called Tumour Necrosis Factor I, and the second is Tumour Necrosis Factor II[16].

Methodology

Study Settings and Population: This case-control study took 98 blood samples from kidney stone patients and healthy people. From May 2022 to December 2022, 68 patients with urinary tract problems, specifically kidney stones, were identified, along with 30 healthy individuals as a control group.

Study Procedure: Samples were collected from Yarmouk Teaching Hospital and nearby private laboratories. The patient group suffered from urinary tract infections and problems, as diagnosed by a specialist physician. Blood samples were collected from all patients to measure aldosterone and renin levels, as well as the concentration of the immunological markers interleukin-17 and tumor necrosis factor (TNF). ESRA was used to measure aldosterone levels according to the manufacturer's kit (Demeditec Aldosterone Elisa DE5125) and renin levels according to the manufacturer's kit (Demeditec Renin Elisa DE5125). Kits from [Company Name] were used to measure interleukin-17 levels, and kits from [Sunlong Biotch-ELISA kit] were used to measure TNF levels (BLK-Labtech-cat ELK1190). Basic information was collected from the patients, including sex, Body mass index (BMI), and whether smoking was a negative risk factor.

Statistical Analysis: Data were statistically analyzed using the program Statistical Analysis System -SAS (2012). and compared the significant differences between the averages using the Duncan test[9] polynomial.

Ethical Consideration: The study followed ethical criteria set by the University of Baghdad. The researcher agreed to follow the ethical requirements for conducting the necessary experiments to finish this research. Furthermore, all follow-up processes and analyses followed the University of Baghdad's applicable regulations and statutes.

Results

The study relied on a blood sample taken from healthy patients. These samples were distributed into three groups. The first group consisted of a blood sample from patients with calcium stones, and their total percentage was 38.8%. The second group consisted of patients with uric acid stones (30) samples, and their percentage was 30.6%. The third group consisted of healthy individuals (30) samples, and their percentage was 30.61%. The number of males in the study was 55 samples, and their percentage was 56.1%, while the total number of females was 43 samples, and their percentage was 43.9%. The results regarding the effect of gender on kidney stone types were recorded and 25 blood samples were distributed among males with calcium stones (65.8%), while 13(43.3%) samples were among males with uric acid stones, and 17 samples (56.7%) were among healthy males. A significant difference was found between these two groups (Table 1).

Table 1: Distribution of Sex According to Types of Stone

Gender	Type of Stone		
	Calcium	**Uric acid**	**Control**
Male	25(65.8%)	13(43.3%)	17(56.7%)
Female	13(34.2%)	17(56.7%)	13(43.3%)
Total	**38(100.0%)**	**30(100.0%)**	**30(100.0%)**

Regarding females, 43 blood samples were distributed and 13 samples (34.2%) were among females with calcium stones, 17(56.7%) samples were among females with uric acid stones, and 13(43.3%) samples were among healthy females. No significant difference was found between these groups (Table 1).

Table 2: Relation between Body Index and Smoker to Types of Stones (Mean±Std. Error)

Type of stone	No.	Body index	Smoker
Calcium	38	23.87± 0.52[b]	1.65± 0.07[a]
Uric acid	30	30.68± 0.84[a]	1.40± 0.09[b]
Control	30	23.53± 0.64[b]	1.53± 0.09[ab]
Significant		**	*

The results for the body mass index recorded an arithmetic mean for patients with uric acid stones (30.68 ± 0.84) higher than for patients with calcium stones, whose arithmetic mean was 23.87 ± 0.52, while the healthy group recorded 23.53 ± 0.64,

where a highly significant difference was found between the two groups like patients with calcium stones and uric acid stones (Table 2).

Among the patients who had calcium stones (1.65± 0.07) and uric acid stones (1.40± 0.09), the smoking rate was observed. On the other hand, the smoking rate for the healthy group was reported as 1.53 ± 0.09. On the one hand, there is a substantial difference between the group of people who have calcium stones and the group of people who have uric acid stones, and on the other hand, there is a healthy group (Table 2).

Serum aldosterone and renin levels and their relationship to kidney stone types: Aldosterone levels were significantly higher in patients with calcium stones compared to the control group (20.67±2.02). Uric acid patients also showed a significant increase compared to the healthy control group. Renin levels were significantly higher (63.56±3.02).) in patients with calcium stones, while uric acid patients showed a significantly lower (2.28±0.25). A highly significant difference was found between the three groups (Table 3).

Type of stone	No.	Hormones	
		Aldosterone	Renin
Calcium	38	20.67±2.02[a]	63.56±3.02[a]
Uric acid	30	21.01±1.97[a]	2.28±0.25[c]
Control	30	5.81±0.43[b]	25.30±2.22[b]
Significant		**	**

Interleukin-17 (IL-17) levels in the blood serum of patients with both calcium and uric acid kidney stones were significantly higher than in the healthy control group. Tumor necrosis factor (TNF) levels for both types were also significantly higher than in the control group, showing a highly significant difference between them and the healthy group. (Table 4).

Table 4: Relation between IL-17 and TNF with types of stones in kidney (Mean±Std. Error)

Type of stone	No.	IL-17	TNF
Calcium	38	41.64±2.56[a]	59.49±3.44[a]
Uric acid	30	42.06±3.28[a]	68.19±3.32[a]
Control	30	11.40±0.73[b]	13.00±3.19[b]
Significant		**	**

Discussion

This study examined the relationship between sex, body mass, and smoking, as well as some vital and

immunological indicators in individuals with various types of kidney stones. Numerous studies have investigated the relationship between sex and kidney stone formation. One study indicated a higher incidence in women than men, but this study focused on age in the women's groups[17]. This suggests that the sex indicator (women) does not necessarily mean they are more susceptible than men, as the study focused on two groups of women and relied on age, which is inconsistent with our study. Other studies have demonstrated a higher risk of kidney stones in men, showing elevated calcium oxalate and uric acid levels, which can lead to the formation of this type of stone in urine. This is attributed to differences in the urine environment between males and females, as the chemical environment plays a key role in stone formation, as mentioned by[18].

The data from the experimental study corroborated the findings of the latter study, confirming its strengths in highlighting the higher susceptibility of men to kidney stones compared to women. Body mass index (BMI) is associated with kidney stone formation through metabolic and physiological changes such as hyperuricemia, acid-base imbalance, and hypercalciuria, as indicated in studies[19,20,21]. Another study confirmed that obesity is a risk factor[22]. The relationship between high BMI and an increased risk of kidney stones can be explained by various physiological processes associated with obesity. High BMI is linked to metabolic syndrome, characterized by hypertension, dyslipidemia, and insulin resistance[23,24]. Such metabolic disturbances lead to changes in urine chemistry, including increased excretion of calcium, uric acid, and oxalate, and decreased citrate levels, thus leading to the formation of calcium and uric acid stones[25,26]. Other studies have indicated that increased production of acid receptors and decreased ammonium excretion lead to a decrease in urine pH, ultimately resulting in the formation of uric acid stones[27]. This aligns with the study that addressed in the research, the body mass index increased in patients with uric acid stones, and this is consistent with the reasons mentioned. Moreover, dietary patterns associated with a high body mass index, such as the consumption of sodium and animal proteins, can exacerbate metabolic disorders in urine, leading to an increased risk of kidney stone formation[28].

This relationship justifies the essential role of obesity in the risk of increased stone formation, especially uric acid stones. Numerous studies have been conducted on the effects of smoking on health. One study demonstrated that repeated exposure to

secondhand smoke for more than an hour per week increases the risk of kidney stones by more than 1.4 times. Current literature has found that even short-term exposure, from minutes to hours, is more harmful than heavy smoking[29]. Another study showed that exposure to secondhand smoke leads to a higher rate of stone formation, suggesting that avoiding exposure offers protection against developing health problems[30]. This is attributed to the amount of nicotine and cadmium present.

Cadmium increases serum levels, which is linked to the formation of urinary tract stones[31]. This aligns with the study that found smokers had a higher incidence of both types of stones. Nicotine also plays a significant role by increasing serum vasopressin levels, leading to decreased urine production, a risk factor for stone formation[32]. Another theory suggests that smoking reduces calcium excretion in urine, thus contributing to the formation of calcium kidney stones[33]. This view is supported by the study's findings. The studies conducted provide a convincing explanation, while the other opinion is that smoking increases oxidative stress in the kidneys, causing damage to them[34]. This damage leads to the formation, retention, and accumulation of crystals, which in turn leads to the formation of stones, especially calcium stones[35]. Aldosterone has been identified as a steroidal salt hormone that maintains ionic balance.

Several studies have been conducted on its various effects on calcium regulation, as reported in [36,37]. Other studies found that aldosterone increases urinary calcium excretion in mice, leading to calcium loss in the blood. Other studies have demonstrated a close relationship between aldosterone and the parathyroid gland[38], where it stimulates the gland to secrete calcium. This view is very close to explaining the results, as the study showed elevated aldosterone levels in patients with calcium stones.

Thus, we agree with the study above, as the reason is that long-term increased aldosterone secretion leads to continued stimulation of the parathyroid gland to secrete calcium, which increases its level in the blood and causes increased absorption in the bones and intestines. This leads to calcium deposition within the renal tubules, which increases the likelihood of developing calcium stones[39]. Renin primarily functions in the formation of angiotensin A, which raises blood pressure. Angiotensin A, in turn, activates the RES system, increasing sodium reabsorption and potassium excretion.

Studies on the role of renin in animals with chronic kidney disease. Increased renin activates angiotensin, which in turn impairs the influx and expulsion of ions, leading to salt accumulation and stone formation. It also causes narrowing of small arteries[40]. Furthermore, excessive RES activity leads to inflammation, fibrosis, and stone formation[41,42]. This explains the elevated RES levels observed in experimental samples, particularly in patients with calcium stones. Conversely, results also showed a decrease in renin levels in patients with uric acid stones. This is attributed to acidity, which reduces renin activation, leading to increased sodium reabsorption and retention, thus lowering renin levels.

This view is widely accepted. Studies have shown that the formation of stones, especially calcium stones in the kidneys, leads to the stimulation of the immune system, especially interleukin-17, which plays a key role in activating calcium oxalate crystals and oxidative stress, which leads to the activation of interleukin-18, causing tubular damage and recurrence of stone formation[43]. Other studies were conducted on the role of interleukin-17 in kidney functions, where it was found to have a major role in the inflammatory response in the kidneys. Studies have been conducted on the role of tumour necrosis factor and its relationship to types of stones. The studies proved the relationship of tumour necrosis factor through oxidative stress, the increase of which increases the formation of stones inside the kidneys due to the free radicals that are present and work to damage cells[44,45].

This study was linked to the results of the experiment, and we find that patients with kidney stones had an increase in tumour necrosis factor. This explains that oxidative stress stimulates cells to secrete tumour necrosis factor, and in turn, it increases in the blood. Some studies found that an increase in the production of reactive oxygen species in mitochondria is an important secondary contributor to kidney injury that is related to the formation of stones[46,47].

Conclusion

In conclusion, oxidative stress, after destroying cells, gives a stimulus to secrete tumour necrosis factor at high levels, and this view is agreed upon. Hormones affected the production of calcium oxalate and uric acid stones. Aldosterone hormone release increased calcium oxalate stone development, while renin depression increased both forms of stones. Smoking had an effect on uric acid stone patients, and immune indicators like TNF and IL-17 were vital as stone formation increased their blood levels.

Data Availability
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

ORCID
Hasan Ali Mohamed Aljezani: https://orcid.org/0009-0003-6278-7961

References

1. Barnett AJ, Schwartz FR, Tao C, Chen C, Ren Y, Lo JY et al. A case-based interpretable deep learning model for classification of mass lesions in digital mammography. Nature Machine Intelligence. 2021;3(12):1061-70.
2. AlQudah M, Hale TM, Czubryt MP. Targeting the renin-angiotensin-aldosterone system in fibrosis. Matrix Biology. 2020;91:92-108.
3. Bamberger JN, Rosen DC, Khusid JA, Kaplan-Marans E, Gallante B, Kapoor A, et al. The impact of metabolic syndrome components on urinary parameters and risk of stone formation. World Journal of Urology. 2021;39(12):4483-90.]
4. Boldt AM, Di Sole F. Targeting the NLRP3 inflammasome for calcium oxalate stones: pathophysiology and emerging pharmacological interventions. Frontiers in Physiology. 2025;16:1614438.

5. Chaudhary A, Singla SK, Tandon C. In vitro evaluation of Terminalia arjuna on calcium phosphate and calcium oxalate crystallization. Indian journal of pharmaceutical sciences. 2010;72(3):340.

6. Coe FL, Evan A, Worcester E. Kidney stone disease. The Journal of clinical investigation. 2005;115(10):2598-608.

7. de Miranda FS, Guimarães JP, Menikdiwela KR, Mabry B, Dhakal R, Rahman R, et al. Breast cancer and the renin-angiotensin system (RAS): Therapeutic approaches and related metabolic diseases. Molecular and Cellular Endocrinology. 2021;528:111245.

8. Dinh HA, Volkert M, Secener AK, Scholl UI, Stölting G. T- and L-type calcium channels maintain calcium oscillations in the murine zona glomerulosa. Hypertension. 2024;81(4):811-22

9. Duncan DB. Multiple range and multiple F tests. biometrics. 1955;11(1):1-42.

10. Dursun M, Otunctemur A, Ozbek E. Kidney stones and ceftriaxone. UROLOGY. 2015 Jan

11. Ferraro PM, Bargagli M, Trinchieri A, Gambaro G. Risk of kidney stones: influence of dietary factors, dietary patterns, and vegetarian–vegan diets. Nutrients. 2020;12(3):779.

12. Ferraro PM, D'Addessi A, Gambaro G. When to suspect a genetic disorder in a patient with renal stones, and why. Nephrology Dialysis Transplantation. 2013;28(4):811-20.

13. Ferraro PM, Taylor EN, Curhan GC. Factors associated with sex differences in the risk of kidney stones. Nephrology Dialysis Transplantation. 2023;38(1):177-83.

14. Fischer E, Hannemann A, Rettig R, Lieb W, Nauck M, Pallauf A, et al. A high aldosterone to renin ratio is associated with high serum parathyroid hormone concentrations in the general population. The Journal of Clinical Endocrinology & Metabolism. 2014;99(3):965-71.

15. Hanna IR, Taniyama Y, Szöcs K, Rocic P, Griendling KK. NAD (P) H oxidase-derived reactive oxygen species as mediators of angiotensin II signaling. Antioxidants and Redox Signaling. 2002;4(6):899-914.

16. Ji P, Shi Q, Liu Y, Han M, Su Y, Sun R, et al. Ginsenoside Rg1 treatment alleviates renal fibrosis by inhibiting the NOX4–MAPK pathway in T2DM mice. Renal Failure. 2023 Dec 31;45(1):2197075.

17. El Beze J, Mazeaud C, Daul C, Ochoa-Ruiz G, Daudon M, Eschwège P, Hubert J. Evaluation and understanding of automated urinary stone recognition methods. BJU international. 2022;130(6):786-98.

18. Chen C, Li O, Tao D, Barnett A, Rudin C, Su JK. This looks like that: deep learning for interpretable image recognition. Advances in neural information processing systems. 2019;32

19. Khan SR. Renal tubular damage/dysfunction: key to the formation of kidney stones. Urological research. 2006;34(2):86-91.

20. Kobori H, Nangaku M, Navar LG, Nishiyama A. The intrarenal renin-angiotensin system: from physiology to the pathobiology of hypertension and kidney disease. Pharmacological reviews. 2007;59(3):251-87.

21. Black KM, Law H, Aldoukhi A, Deng J, Ghani KR. Deep learning computer vision algorithm for detecting kidney stone composition. BJU international. 2020;125(6):920-4.

22. Lavoie JL, Sigmund CD. Minireview: overview of the renin-angiotensin system—an endocrine and paracrine system. Endocrinology. 2003;144(6):2179-83.

23. Liu M, Wu J, Gao M, Li Y, Xia W, Zhang Y, et al. Lifestyle factors, serum parameters, metabolic comorbidities, and the risk of kidney stones: a Mendelian randomization study. Frontiers in endocrinology. 2023;14:1240171.

24. Lovegrove CE, Bešević J, Wiberg A, Lacey B, Littlejohns TJ, Allen NE, et al. Central adiposity increases risk of kidney stone disease through effects on serum calcium concentrations. Journal of the American Society of Nephrology. 2023;34(12):1991-2011.

25. Maalouf NM, Sakhaee K, Parks JH, Coe FL, Adams-Huet B, Pak CY. Association of urinary pH with body weight in nephrolithiasis. Kidney international. 2004;65(4):1422-5.

26. Ma Y, Cheng C, Jian Z, Wen J, Xiang L, Li H, Wang K, Jin X. Risk factors for nephrolithiasis formation: an umbrella review. International Journal of Surgery. 2024;110(9):5733-44.

27. Corrales M, Doizi S, Barghouthy Y, Traxer O, Daudon M. Classification of stones according to michel daudon: a narrative review. European Urology Focus. 2021;7(1):13-21.

28. Meulmeester FL, Luo J, Martens LG, Mills K, van Heemst D, Noordam R. Antioxidant supplementation in oxidative stress-related diseases: What have we learned from studies on alpha-tocopherol? Antioxidants. 2022;11(12):2322.

29. Daudon M, Dessombz A, Frochot V, Letavernier E, Haymann JP, Jungers P, Bazin D. Comprehensive morpho-constitutional analysis of urinary stones improves etiological diagnosis and therapeutic strategy of nephrolithiasis. Comptes Rendus Chimie. 2016 Nov 1;19(11-12):1470-91.

30. Daudon M, Jungers P, Bazin D, Williams Jr JC. Recurrence rates of urinary calculi according to stone composition and morphology. Urolithiasis. 2018 Oct;46(5):459-70.

31. Mulrow PJ. The intrarenal renin-angiotensin system. Current opinion in nephrology and hypertension. 1993 Jan 1;2(1):41-4.

32. Peto R, Lopez AD. The future worldwide health effects of current smoking patterns. Tobacco and public health: Science and policy. 2004 Jan 1;281(6):281-6.

33. Re RN. Cellular biology of the renin-angiotensin systems. Archives of internal medicine. 1984 Oct 1;144(10):2037-41.

34. Al-Lami RS, Al-Hilfy JH. Role of Interleukins-8,-17 and-22 in Iraqi postmenopausal women with Osteoporosis. Cytokine. 2025;187:156853.

35. Rivera ME, Krambeck AE. Overweight/obesity: metabolic benefits to reduce stone risk. InNutrition Therapy for Urolithiasis 2017 Nov 24 (pp. 147-155). Cham: Springer International Publishing.

36. Rosenberg J, Pines M, Hurwitz S. Response of adrenal cells to parathyroid hormone stimulation. Journal of endocrinology. 1987;112(3):431-7.

37. Sakhaee K. Unraveling the mechanisms of obesity-induced hyperoxaluria. Kidney international. 2018;93(5):1038-40.

38. Singh R, Singh AK, Leehey DJ. A novel mechanism for angiotensin II formation in streptozotocin-diabetic rat glomeruli. American Journal of Physiology-Renal Physiology. 2005;288(6):F1183-90.

39. Skolarikos A, Straub M, Knoll T, Sarica K, Seitz C, Petřík A, Türk C. Metabolic evaluation and recurrence prevention for urinary stone patients: EAU guidelines. European urology. 2015;67(4):750-63.

40. Song S, Cai X, Hu J, Zhu Q, Shen D, Heizhati M, Yang W, Hong J, Li N. Correlation between plasma aldosterone concentration and bone mineral density in middle-aged and elderly hypertensive patients: potential impact on osteoporosis and future fracture risk. Frontiers in endocrinology. 2024;15:1373862.

41. Sulaiman SK, Enakshee J, Traxer O, Somani BK. Which type of water is recommended for patients with stone disease (hard or soft water, tap or bottled water): evidence from a systematic review over the last 3 decades. Current urology reports. 2020;21(3):6.

42. Tomaschitz A, Ritz E, Pieske B, Rus-Machan J, Kienreich K, Verheyen N, et al. Aldosterone and parathyroid hormone interactions as mediators of metabolic and cardiovascular disease. Metabolism. 2014;63(1):20-31.

43. VanderWeele T, Vansteelandt S. Mediation analysis with multiple mediators. Epidemiologic methods. 2014;2(1):95-115.

44. Estrade V, Daudon M, Richard E, Bernhard JC, Bladou F, Robert G, et al. Towards automatic recognition of pure and mixed stones using intra-operative endoscopic digital images. BJU International. 2022;129(2):234-42.

45. Wang X, Derakhshandeh R, Liu J, Narayan S, Nabavizadeh P, Le S, Danforth OM, Pinnamaneni K, Rodriguez HJ, Luu E, Sievers RE. One minute of marijuana secondhand smoke exposure substantially impairs Vascular endothelial function. Journal of the American Heart Association. 2016;5(8):e003858.

46. Ye Z, Wu C, Xiong Y, Zhang F, Luo J, Xu L, et al. Obesity, metabolic dysfunction, and risk of kidney stone disease: a national cross-sectional study. The Aging Male. 2023;26(1):2195932

47. Baker ME, Katsu Y. Evolution of the mineralocorticoid receptor. Vitamins and hormones. 2019;109:17-36