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THE ROLE OF ESSENTIAL AND TOXIC TRACE ELEMENTS IN THE DEVELOPMENT OF KIDNEY STONE DISEASE. LITERATURE REVIEW

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Abstract

Relevance. A literature review focused on the impact of essential and toxic trace elements on the development of kidney stone disease. Special attention is given to the relationship between trace element imbalance, mineral metabolism disorders, oxidative stress, and inflammatory processes, which play a key role in the mechanisms of stone formation.

Search Strategy: A systematic search of scientific publications was conducted in the PubMed, Scopus, Web of Science, Google Scholar, and Science Direct databases. The search period covered 10 years. A total of 60 articles, containing data on the role of essential and toxic trace elements in the pathogenesis of kidney stone disease, were included in the analysis.

Results: Data on the impact of essential trace elements (calcium, magnesium, zinc, selenium) and toxic metals (lead, cadmium, mercury, arsenic) on the stone formation processes are presented. It was found that trace element imbalance may contribute to disturbances in mineral metabolism, the development of oxidative stress, and inflammatory reactions, which play a key role in the pathogenesis of kidney stone disease. The findings confirm the significant involvement of trace elements in the mechanisms of urolith formation.

Conclusion: Monitoring the levels of trace elements in the body and reducing exposure to toxic metals may contribute to the prevention of kidney stone disease. Further research is needed to develop effective prevention and treatment strategies, focusing on studying the mechanisms through which trace elements influence stone formation processes.

Keywords: *kidney stone disease, essential trace elements, toxic trace elements, heavy metals.*

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Резюме

РОЛЬ ЭССЕНЦИАЛЬНЫХ И ТОКСИЧНЫХ МИКРОЭЛЕМЕНТОВ В РАЗВИТИИ МОЧЕКАМЕННОЙ БОЛЕЗНИ. ОБЗОР ЛИТЕРАТУРЫ.

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Актуальность. Обзор литературы, посвящен влиянию эссенциальных и токсичных микроэлементов на развитие мочекаменной болезни. Особое внимание уделено взаимосвязи между микроэлементным дисбалансом, нарушением минерального обмена, окислительным стрессом и воспалительными процессами, играющими ключевую роль в механизмах камнеобразования.

Стратегия поиска: Проведен систематический поиск научных публикаций в базах данных PubMed, Scopus, Web of Science, Google Scholar и ScienceDirect. Глубина поиска составила 10 лет. В анализ включены 60 статей, содержащих данные о роли эссенциальных и токсичных микроэлементов в патогенезе мочекаменной болезни.

Результаты: Представлены данные о влиянии эссенциальных микроэлементов (кальций, магний, цинк, селен) и токсичных металлов (свинец, кадмий, ртуть, мышьяк) на процессы камнеобразования. Установлено, что дисбаланс микроэлементов может способствовать нарушению минерального обмена, развитию окислительного стресса и воспалительных реакций, которые играют ключевую роль в патогенезе мочекаменной болезни. Полученные данные подтверждают значительное участие микроэлементов в механизмах формирования уролитов.

Заключение: Контроль уровня микроэлементов в организме и снижение воздействия токсичных металлов могут способствовать профилактике мочекаменной болезни. Для разработки эффективных стратегий предотвращения и лечения заболевания необходимы дальнейшие исследования, направленные на изучение механизмов влияния микроэлементов на процессы камнеобразования.

Ключевые слова: *мочекаменная болезнь, эссенциальные микроэлементы, токсичные микроэлементы, тяжелые металлы*

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Түйіндеме

ЭССЕНЦИАЛДЫ ЖӘНЕ УЫТТЫ МИКРОЭЛЕМЕНТТЕРДІҢ НЕСЕП ТАС АУРУЫ ДАМУЫНДАҒЫ РӨЛІ. ӘДЕБИЕТТІК ШОЛУ.

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Өзектілігі. Бұл зерттеу эссенциальді және токсикалық микроэлементтердің несеп тас ауруының дамуына әсерін қарастыратын әдебиеттер шолуын ұсынады. Микроэлементтердің дисбалансы, минералды алмасудың бұзылуы, оксидативті стресс және қабыну процестерінің арасындағы өзара байланыстың маңыздылығына ерекше көңіл бөлінген, олар тас қалыптасу механизмдерінде маңызды рөл атқарады.

Іздеу стратегиясы: PubMed, Scopus, Web of Science, Google Scholar және ScienceDirect деректер базаларында ғылыми жарияланымдарды жүйелі іздеу жүргізілді. Іздеу тереңдігі 10 жылды құрады. Анализге эссенциалды және уытты микроэлементтердің несеп тас ауруының патогенезіндегі рөлі туралы деректерді қамтитын 60 мақала енгізілді.

Нәтижелер: Эссенциалды микроэлементтердің (кальций, магний, цинк, селен) және уытты металдардың (қорғасын, кадмий, сынап, мышьяк) тас түзілу процестеріне әсері туралы деректер ұсынылған. Микроэлементтердің тепе-теңдігінің бұзылуы минералды алмасудың бұзылуына, оксидативті күйзелістің дамуына және қабыну реакцияларының пайда болуына ықпал етуі мүмкін екені анықталды, олар несеп тас ауруының патогенезінде маңызды рөл атқарады. Алынған деректер микроэлементтердің НТА түзілу механизмдеріндегі маңызды рөлін растайды.

Қорытынды:Ағзадағы микроэлементтердің деңгейін бақылау және уытты микроэлементтердің әсерін азайту несеп тас ауруының алдын алуға көмектесуі мүмкін. Аурудың алдын алу және емдеудің тиімді стратегияларын әзірлеу үшін қосымша зерттеулер қажет.

Түйінді сөздер: *несеп тас ауруы, эссенциалды микроэлементтер, уытты микроэлементтер, ауыр металдар.*

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Introduction

Kidney stone disease (KSD) is one of the most common pathologies of the urinary system, significantly affecting the quality of life of patients. In the CIS countries, the proportion of urolithiasis among urological diseases ranges from 33.9% in Russia to 58.2% in Kyrgyzstan, while in Tajikistan, Uzbekistan, and Kazakhstan, this figure stands at 42.2–56.1%, with a trend toward an increase in incidence [6]. On a global scale, the prevalence of KSD ranges from 1% to 20%, with significantly higher risks in regions with hot climates and high levels of environmental pollution, which are associated with increased fluid loss and salt concentration in urine [4, 35].

KSD is a pathological condition characterized by the formation of solid concretions (stones) in the kidneys and urinary tract due to a disruption in mineral metabolism. The main predisposing factors include an imbalanced diet, low fluid intake, genetic predisposition, and environmental factors. The stones can have various compositions, including calcium oxalates, phosphates, uric acid, and cystine, which determine their physicochemical properties and treatment approaches [51].

In recent years, researchers have focused on the role of essential and toxic trace elements in the pathogenesis of KSD. Essential elements such as calcium, magnesium, zinc, selenium, and copper are necessary for the normal functioning of the body, regulating mineralization processes and preventing stone formation. At the same time, toxic metals, including lead, cadmium, mercury, arsenic, and cobalt, have nephrotoxic effects, promoting lithogenesis [17,46]. Toxic trace elements actively participate in the development of nephropathies, causing damage to renal tubules, disrupting filtration processes, and triggering inflammatory reactions. Prolonged exposure to these metals can lead to chronic kidney failure, particularly in children, whose kidneys are more susceptible to toxins. It has been established that the accumulation of lead and cadmium in the kidneys is associated with kidney dysfunction and the development of nephrolithiasis [3,54].

Studies show that elevated concentrations of toxic elements are found in urinary stone samples from patients in industrial regions. Specifically, lead, cadmium, and vanadium, which are present in contaminated water and food, contribute to the mineralization of urinary salts and the increase in the size of concretions [55]. Additionally, cobalt, despite its important role in the composition of vitamin B12, has a toxic effect in its free form, damaging renal tissue and promoting stone formation [39].

In addition to toxic elements, essential trace elements that are involved in mineral metabolism also have a significant impact on the stone formation process. For example, magnesium reduces the risk of calcium oxalate crystallization, while zinc and selenium deficiencies contribute to oxidative stress and inflammatory processes, creating favorable conditions for the formation of concretions [17,45].

Recent studies highlight the significant role of essential and toxic trace elements in the pathogenesis of KSD. In particular, elements such as calcium, magnesium, zinc, lead, cadmium, and arsenic can influence the stone formation process through various mechanisms, including changes in mineral metabolism, oxidative stress, and inflammatory processes [46].

The chemical composition of drinking water significantly affects the prevalence of kidney stone disease (KSD). In regions where the levels of calcium, magnesium, and heavy metals in water exceed normative values, the incidence of nephrolithiasis rises substantially [27]. Furthermore, the presence of arsenic and mercury in water may exacerbate nephrotoxic processes, impairing renal filtration and promoting the deposition of mineral salts in the kidneys [2].

Thus, contemporary research underscores the critical role of trace elements in the development of KSD. Their influence on lithogenesis warrants further investigation to devise new preventive and therapeutic strategies aimed at correcting mineral metabolism and mitigating the impact of toxic environmental factors.

The aim of this review is to analyze the existing data on the impact of essential and toxic trace elements on the development of kidney stone disease.

Search Strategy.

To write this review, a systematic search of scientific publications was conducted in leading databases, such as PubMed, Google Scholar, Scopus, Web of Science, and ScienceDirect. The search employed key terms, with primary queries including combinations such as "kidney stones" AND ("trace elements" OR "heavy metals"), "urolithiasis" AND ("magnesium" OR "zinc" OR "calcium" OR "copper" OR "selenium"), as well as combinations with metals like lead and cadmium. As a result, 3,779 articles were identified, and after the initial analysis, 60 publications met the inclusion criteria and were selected for final analysis. The search covered a period of 10 years.

Inclusion Criteria:

The analysis included articles published in peer-reviewed journals containing data on the role of trace elements in the pathogenesis of kidney stone disease. Both clinical and experimental studies were considered. Only full-text articles in English and Russian, freely accessible, and published between 2015 and 2025, were included.

Exclusion Criteria:

Sources that were not peer-reviewed, as well as materials that did not contain information on trace elements in the context of kidney stone disease, were excluded. This included works that focused solely on the surgical or therapeutic aspects of the disease.

Results

Essential Trace Elements and Their Role in Kidney Stone Disease

Calcium (Ca) is a primary component of kidney stones, including oxalate and phosphate stones (2.64%–27.68%) [50,56]. Moderate calcium intake does not increase the risk of kidney stone disease, while its deficiency promotes lithogenesis [2]. Studies confirm that optimal calcium intake (1000–1200 mg/day) reduces the risk of stone formation by binding oxalates in the intestine [11]. Hypercalciuria, however, is a risk factor for stone formation [28].

Magnesium (Mg) plays an important role in preventing the crystallization of calcium oxalates by forming soluble complexes with them [28,44]. Magnesium deficiency contributes to an increased frequency of kidney stone disease, especially among patients with metabolic syndrome [1,7,60]. Low magnesium levels in children with KSD also confirm its importance in mineralization and calcium metabolism [2]. Consuming water deficient in magnesium increases the risk of stone formation, while hard water, which contains excess calcium, neutralizes the protective effect of magnesium [58].

Zinc (Zn) has a dual role in kidney stone disease. On one hand, it protects the kidneys from oxidative stress, while on the other hand, high concentrations of zinc can contribute to stone formation by altering the structure of struvite stones and increasing their size [48]. Excessive zinc intake can disrupt the balance of trace elements and stimulate lithogenesis [48]. In patients with urolithiasis, the zinc levels in stones are higher than in healthy individuals [17,21].

Selenium plays a crucial role in the prevention of kidney stone disease by reducing oxidative stress and preventing apoptosis of renal cells. It protects the kidneys from the toxicity of heavy metals such as cadmium, lead, and mercury, due to its antioxidant properties and involvement in detoxification mechanisms [47,5].

Essential metals are those required for the normal functioning of the human and animal body. These include copper (Cu), iron (Fe), sodium (Na), silicon (Si), potassium (K), calcium (Ca), manganese (Mn), selenium (Se), cobalt (Co), magnesium (Mg), boron (B), chromium (Cr), and molybdenum (Mo). Toxic metals, on the other hand, are those that can lead to adverse effects when continuously ingested. These include cadmium (Cd), lead (Pb), arsenic (As), aluminum (Al), mercury (Hg), zinc (Zn), lithium (Li), nickel (Ni), titanium (Ti), and antimony (Sb).

Table 1.

Reference Values of Essential and Toxic Trace Elements.

Essential trace elements	Reference values	Toxic trace elements	Reference values
Copper (Cu)	575-1725 µg/L	Molybdenum (Mo)	0,1-3 µg/L
Iron (Fe)	270-2930 µg/L	Cadmium (Cd)	0,013-2µg/L
Sodium (Na)	2900-3335 mg/L.	Lead (Pb)	0,15-4 µg/L
Silicon (Si)	0-500 µg/L	Arsenic (As)	2-62 µg/L
Potassium (K)	132-195 mg/L.	Aluminum (Al)	0-15 µg/L
Calcium (Ca)	86-102 mg	Mercury (Hg)	0,21-5,8 µg/L
Marganese (Mn)	0-2 µg/L	Zinc (Zn)	600-2910 µg/L
Selenium (Se)	23-190 µg/L	Lithium (Li)	0.7–84 µg/L
Cobalt (Co)	0,1-0,4 µg/L	Nickel (Ni)	0,6 - 7,5 µg/L.
Magnesium (Mg)	12,15-31,59 mg/L.	Titanium (Ti)	0,1-50 µg/L
Boron (B)	0-100 µg/L	Antimony (Sb)	0,027–0,71 µg/L
Chromium (Cr)	0,05-2,1. µg/L		

Toxic trace Elements and Their Role in Kidney Stone Disease

Lead (Pb) significantly influences the development of urolithiasis (kidney stone disease), particularly in the formation of phosphate stones. The concentration of lead in the blood and urinary stones of patients with nephrolithiasis is significantly higher than in healthy individuals. High lead levels are associated with nephrotoxicity, damage to renal tubules, and increased crystallization of calcium phosphates. Lead, as a cumulative toxin, disrupts mineralization and promotes the formation of phosphate stones [1,7,17,29].

The accumulation of toxic trace elements such as barium, lead, and cadmium damages the renal epithelium and promotes the formation of Randall's plaques, thereby increasing the risk of nephrolithiasis. The combined exposure to lead and cadmium induces oxidative stress and damages renal tissues [1,25].

Cadmium increases the risk of urolithiasis, particularly among workers exposed to it professionally. Patients with elevated cadmium levels in urine have a 32% higher risk of stone formation [24].

Arsenic and other toxic elements induce oxidative stress and calcification of the kidneys, increasing the risk of urolithiasis. Elevated arsenic levels impair kidney filtration, exacerbating stone formation. This is also associated with the combined effects of cadmium, chromium, and lead, which disrupt mineral metabolism and promote the crystallization of urinary salts [14,15,31]. Long-term exposure to arsenic through contaminated water is linked to an increased risk of stone formation [14,42].

Cobalt (Co) and mercury (Hg) influence the development of urolithiasis by altering urine pH and promoting the deposition of phosphate and oxalate salts. Elevated levels of mercury and cobalt in urine correlate with an increased risk of nephrolithiasis [28,32,34]. Exposure to cobalt and other toxic metals enhances lithogenic effects [26]. Mercury disrupts kidney filtration, leading to the accumulation of calcium and other minerals, creating conditions conducive to stone formation [15,49].

Workers in the metallurgical industry are at increased risk of urolithiasis due to exposure to mercury and other toxic metals. This underscores the need for monitoring mercury levels and reducing its impact on health [26]. The effect of mercury on children is especially pronounced, as their kidney filtration and detoxification mechanisms are not fully developed.

Mercury exposure during early childhood has a particularly significant effect, contributing to the development of chronic kidney diseases, including urolithiasis. Children are especially vulnerable to the toxic effects of heavy metals due to their underdeveloped renal filtration and detoxification mechanisms. Children exposed to mercury through contaminated water and food show alterations in mineral metabolism, which promote the crystallization of urinary salts. This underscores the need for stringent monitoring of mercury levels in the environment and early detection of renal impairments in children [52].

Discussion

The data obtained indicate that the elemental composition of urine and blood plays a significant role in the pathogenesis of urolithiasis. Essential trace elements such as magnesium and selenium may exert protective effects, while calcium and zinc have a complex impact, depending on their concentrations. At the same time, toxic metals, including cadmium and lead, can increase the risk of stone formation through oxidative stress and damage to renal tubules. The role of trace elements in the pathogenesis of urolithiasis has been actively studied in recent decades. Полученные данные свидетельствуют о том, что микроэлементный состав мочи и крови играет важную роль в патогенезе мочекаменной болезни.

The study by *Ahmad et al.* (2025) showed that an imbalance in mineral ionic trace elements, including calcium, magnesium, phosphorus, zinc, and selenium, plays a key role in the development of chronic diseases, including urolithiasis. Magnesium deficiency and excess calcium can disrupt kidney metabolism and increase the risk of lithogenesis. The authors also highlight that endocrine regulation of mineral metabolism, particularly the levels of vitamin D and parathyroid hormone (PTH), affects stone formation, emphasizing the importance of monitoring these parameters for urolithiasis prevention [10].

In the study by *Razzaque et al.* (2025), the authors confirm that optimal calcium intake (1000–1200 mg/day) reduces the risk of urolithiasis by binding oxalates in the gastrointestinal tract [41]. *Kosiba et al.* (2020) identified the key role of the calcium-sensing receptor (CaSR) in nephrotoxicity induced by heavy metals such as cadmium (Cd), lead (Pb), arsenic (As), and mercury (Hg). They found that impaired CaSR function in the kidneys contributes to nephrolithiasis by altering the balance of calcium and phosphate ions, increasing oxidative stress, and activating mitogen-activated protein kinase (MAPK) signaling pathways. The authors suggest that modulation of CaSR activity could be a promising approach for preventing and treating nephrotoxicity caused by heavy metals [28]. In a study conducted in Jordan, patients with urolithiasis exhibited elevated concentrations of trace elements in their kidney stones [8]. Using X-ray fluorescence (XRF) and atomic absorption spectroscopy (AAS), 110 stone samples were analyzed, revealing elements such as calcium (Ca), sodium (Na), potassium (K), magnesium (Mg), iron (Fe), aluminum (Al), zinc (Zn), copper (Cu), manganese (Mn), phosphorus (P), sulfur (S), strontium (Sr), molybdenum (Mo), chromium (Cr), cobalt (Co), and nickel (Ni). Calcium was found to be the main component of most stones, particularly in the form of oxalates and phosphates. However, toxic trace elements such as lead (Pb), cadmium (Cd), and arsenic (As) were not detected in the analyzed samples. The authors conclude that the accumulation of certain metals, such as Mo, Cr, Co, and Ni, may play a role in the stone formation process, although their concentrations in the samples were low [8].

Ferraro et al. (2020) demonstrated that excessive consumption of meat and animal proteins lowers urine pH, increases calcium levels, and decreases citrate concentration, which promotes stone formation [21]. In contrast, a balanced vegetarian diet with a high intake of fruits and vegetables reduces the risk of urolithiasis. Furthermore, balanced calcium intake is essential, as its deficiency increases oxalate excretion and promotes lithogenesis [21].

The study by *Keshavarzi et al.* (2014) identified that calcium and phosphorus are the main components of urinary stones, with calcium binding to oxalates and phosphates binding to metals [27]. High concentrations of zinc and strontium in phosphate stones may be associated with lithogenesis, highlighting the role of trace elements in stone formation [27].

Abdel-Gawad et al. (2022) confirmed the role of heavy metals and trace elements in the pathogenesis of urolithiasis. Elevated levels of aluminum, arsenic, selenium, zinc, and nickel were found in calcium-oxalate stones, while magnesium, cadmium, lead, and barium were predominant in phosphate stones. Geographic differences in stone composition suggest the influence of environmental factors on the development of the disease [9]. Research from the Medical University of Iran explored the concentrations of heavy metals and other urolithic elements in both blood and urinary stones to examine their relationship with environmental factors and diet in individuals with urinary stones in Ardabil. The results showed significant differences in nickel and copper concentrations in individuals who consumed vegetables daily, and among people with various types of kidney stones [17].

According to *Hamzah et al.* (2024), zinc and copper levels in patients with chronic kidney disease significantly differ from the control group. Zinc deficiency is associated with impaired antioxidant defense, which may contribute to stone formation. At the same time, excess copper may exacerbate inflammatory processes in the kidneys, creating a favorable environment for stone formation [12].

Ramli et al. (2025) found that methamphetamine abuse increases the risk of kidney diseases, including urolithiasis.

This is associated with increased oxidative stress and an imbalance of trace elements such as calcium and magnesium, which may contribute to the precipitation of salts in the urinary tract [40]. Ruidiaz Gómez et al. (2024) confirm that geographic location affects the content of trace elements in urinary stones. For example, regions with high magnesium content in water have a lower frequency of nephrolithiasis, whereas areas with elevated levels of lead and cadmium show a higher disease prevalence [23].

Quiroz et al. (2025) identified that patients with chronic kidney diseases have higher concentrations of toxic metals, such as cadmium and lead, compared to healthy individuals. This highlights their potential role in the development of nephrolithiasis and emphasizes the need for monitoring these elements in the body [38].

The study by *Qin et al.* (2025) demonstrated that hypoxia, associated with chronic kidney diseases, leads to altered levels of zinc and iron. This can contribute to mineral metabolism imbalance and increase the risk of stone formation [37].

Dietary habits play an essential role in the pathogenesis of urolithiasis. Excessive intake of sodium and oxalates combined with magnesium and citrate deficiency promotes the formation of calcium oxalate stones. Overuse of calcium supplements and vitamins without professional supervision can disrupt mineral balance, increasing the risk of stone formation. The study emphasizes the importance of a personalized approach to the nutrition of patients with kidney stones, including reducing salt intake, increasing magnesium levels, and ensuring adequate hydration to prevent recurrences [13].

The study by *Sanders et al.* (2019) examined the combined impact of heavy metals such as lead (Pb), cadmium (Cd), mercury (Hg), and arsenic (As) on kidney function in adolescents aged 12–19 years. Analysis of data from the U.S. National Health and Nutrition Examination Survey (NHANES) from 2009 to 2014 revealed that increased levels of these metals in urine and blood were associated with changes in kidney parameters, including estimated glomerular filtration rate (eGFR), blood urea nitrogen (BUN) levels, and urinary albumin levels. Arsenic had the most significant effect on BUN, while mercury and cadmium primarily affected eGFR. These findings highlight the potential risk of combined exposure to heavy metals on kidney health at an early age and underscore the need for further research to assess the long-term consequences of such exposures [43].

Conclusions

Current research confirms the significant role of trace elements in the pathogenesis of nephrolithiasis (NKD). Essential elements such as calcium, magnesium, and selenium contribute to maintaining mineralization and preventing stone formation, whereas their deficiency may enhance crystallization of urinary salts and inflammatory processes. In contrast, excess levels of toxic metals (lead, cadmium, arsenic, cobalt, and mercury) adversely affect kidney tissue, increasing the risk of lithogenesis. Maintaining optimal levels of essential trace elements and minimizing exposure to toxic metals are critical preventive measures and should be part of comprehensive NKD treatment. Further detailed clinical studies aimed at correcting mineral metabolism and protecting the kidneys from toxic factors are necessary for a deeper understanding of stone formation mechanisms and the development of effective therapeutic strategies.

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