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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.
GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.
ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman** (**Кириллица**), ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ,რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფრჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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THE EFFECTIVENESS OF METAPHYLAXIS OF NEPHROLITHIASIS DURING PERCUTANEOUS NEPHROLITHOTRIPSY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract.

Relevance: Infected kidney stones, particularly struvite and carbonate-apatite calculi, pose a serious medical challenge due to recurrent urinary tract infections, rising antibiotic resistance, and complications following percutaneous nephrolithotripsy (PCNL).

Aim: To assess the effectiveness of metaphylaxis of infected kidney stones, investigate their composition, analyse antibiotic resistance, and determine the incidence of infectious complications after PCNL.

Methods: A comprehensive literature review was performed by searching PubMed, Scopus, and the Cochrane Central Register of Controlled Trials for publications between 2014 and 2024. The search strategy was built around key phrases such as 'infected kidney stones,' 'metaphylaxis,' 'antibiotic resistance,' 'percutaneous nephrolithotripsy,' and 'struvite stones.' Clinical trials, cohort and case-control studies with at least 20 participants were included; animal studies and case reports were excluded. Study selection was conducted by two independent reviewers. The methodological quality of the included studies was assessed using the Newcastle-Ottawa Scale.

Results: Forty-seven studies from 23 countries (n=8342) were analysed. Antibiotic prophylaxis reduced recurrence by 17–25%, depending on the region. Struvite stones accounted for 67.3%, with associations to Proteus mirabilis (38.4%) and Escherichia coli (29.6%). Antibiotic resistance reached 43.2%, with peaks for ampicillin (71%) and ciprofloxacin (48%). Complications after PCNL occurred in 12–28% of cases, including sepsis (3.4%) and pyonephrosis (7.8%). The best outcomes were achieved with the combination of antibiotics and urease inhibitors.

Conclusions: Comprehensive metaphylaxis adapted to local sensitivity profiles significantly reduces the risk of recurrence. In Kazakhstan, regional protocols are necessary to address resistance, considering diagnostic and resource limitations.

Key words. Infected kidney stones, metaphylaxis, percutaneous nephrolithotripsy, antibiotic resistance, struvite stones, systematic review, Kazakhstan.

Introduction.

Urolithiasis is a prevalent urological condition globally, contributing significantly to morbidity, disability, and healthcare costs [1,2]. Patients are at risk for serious adverse events, including severe pain from renal colic, complications from urinary tract obstruction, infection, hypertensive crises, and a decline in kidney function that can progress to renal insufficiency [3]. Recent evidence has shown that between 2000 and 2021, the global number of incident cases, deaths, and disability-adjusted life years (DALYs) due to urolithiasis increased by 26.7% (95% CI: 23.8–29.8), 60.3% (95% CI: 41.5–84.7), and 34.5% (95% CI: 24.6–47.3), respectively [4]. Infected stones account for 10–20% of cases, but their significance is greater due to the risk of recurrence and complications [5]. The incidence is higher in women than in men (ratio 2:1) due to anatomical factors [6]. In Central American, Tropical Latin American, and Caribbean regions, the age-adjusted prevalence of kidney stone disease rose considerably. This was in direct contrast to a substantial decline observed in East Asian, Eastern/Central European, and high-income North American populations [4]. In Kazakhstan, urolithiasis affects 8–10% of the population, with a proportion of mixed stones (40–50%), where infected stones predominate due to the climate, diet, and limited access to medical care [7-9].

Urease-producing bacteria, including *Proteus mirabilis, Klebsiella pneumoniae, Escherichia coli, and Staphylococcus saprophyticus*, are a cause of urinary tract infections that can result in the development of struvite and carbonate-apatite stones. These stones are found in up to 15% of patients with nephrolithiasis [10,11]. These microorganisms produce urease, which increases urine pH (>7.0), promoting phosphate precipitation and the formation of struvite and carbonate-apatite stones [12].

The pathogenesis of infected stones is closely linked to urease-producing bacteria. The action of urease-producing microorganisms causes urea to split into ammonia and carbon dioxide. This elevates the urinary pH, leading directly to the crystallization of struvite and carbonate-apatite stones. The most common pathogens are *Proteus mirabilis* and *Escherichia* *coli*. Clinical manifestations such as flank pain, dysuria, fever are present in only 30–40% of cases [13]. Diagnostic markers include alkaline urine (>7.0) and the presence of struvite crystals [14]. Imaging techniques play a crucial role in diagnosis, computed tomography (CT) often reveals "staghorn" calculi while, magnetic resonance imaging (MRI) may detect associated inflammatory changes [15,16]. Bacteriological analysis is frequently complicated by contamination, making definitive microbial identification challenging [17].

Percutaneous nephrolithotripsy (PCNL) is considered the gold standard for managing large infectious stones [18], with mini-PCNL emerging as a preferable alternative due to its lower complication rates [19,20]. Retrograde intrarenal surgery (RIRS) is generally effective for infectious stones <20 mm [21], whereas extracorporeal shock wave lithotripsy (ESWL) has limited efficacy in such cases [22]. Reported complication rates for surgical interventions range from 12–28%, with postoperative sepsis occurring in 2–5% of patients. These complications are associated with operation duration and antimicrobial resistance [23-27]. Preventive strategies include urinary tract sanitation and prophylactic antibiotic use [28,29]. However, antimicrobial resistance is a growing concern. Resistance to ampicillin (60–80%) and ciprofloxacin (30–50%) is increasing in various regions of the world [30-35]. In Kazakhstan, high resistance to ampicillin ranging from 75–85% has been reported [36].

Metaphylaxis, which includes the use of antibiotics, urease inhibitors, and dietary modifications, plays a pivotal role recurrence of infected urinary stone [37,38]. Among urease inhibitors, acetohydroxamic acid has demonstrated efficacy; however, its clinical use is limited by frequent adverse effects [37,39]. Despite available treatment options, there remains a significant gap in standardized management protocols, particularly in regions with high antibiotic resistance [36,40,41]. For instance, in Kazakhstan, the development of national guidelines, improved access to diagnostic tools, and tailored metaphylaxis strategies are urgently needed [6,39].

The purpose of this study is to systematically review the existing evidence concerning the efficacy of metaphylaxis in cases of infected nephrolithiasis, analyse the composition of infectious stones, study antibiotic resistance, and evaluate infectious complications after percutaneous nephrolithotripsy.

The research questions are:

1. What is the effectiveness of metaphylaxis of infected stones?
2. What is the composition of infectious stones?
3. What is the prevalence of antibiotic resistance among patients with infected stones?
4. What is the frequency and nature of infectious complications after PCNL?

Methodology.

Protocol development and registration:

This systematic review was conducted using the methods outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines and was prospectively registered in PROSPERO (CRD42024XXXXX).

Inclusion criteria:

This review included studies involving adult patients (aged 18 years and above) diagnosed with infected kidney stones who underwent PCNL. Eligible studies evaluated metaphylactic interventions, which included pharmacological strategies (such as antibiotics and urease inhibitors), dietary modifications, or combinations of both. Comparisons were made with control groups that did not receive any form of metaphylaxis. The inclusion criteria were met by randomized controlled trials (RCTs), cohort studies, and case-control studies.

Exclusion criteria:

The review excluded animal studies, case reports with fewer than 20 participants, review articles without original data, and conference abstracts. Additionally, studies with follow-up durations shorter than six months or those that did not report outcomes related to metaphylaxis were also excluded.

Outcomes:

The primary outcome was kidney stone recurrence. Secondary outcomes included the rate of post-PCNL infections, antibiotic resistance patterns, and the chemical composition of the stones.

Data sources and search strategies:

Databases searched were PubMed/MEDLINE (1946–November 2024), Scopus (1970–November 2024), Cochrane CENTRAL, Web of Science, and Embase. Additional data sources included manual screening of reference lists, grey literature searches (e.g., OpenGrey, ProQuest), expert consultation with urologists. A comprehensive search strategy using MeSH terms and free-text keywords such as "infected kidney stones," "metaphylaxis," "PCNL," and "antibiotic resistance" was applied. We limited our search to studies published in English from 2014 to 2024.

Study selection:

Two independent reviewers (A.B. and V.H.) screened 2,876 unique records using Rayyan software. When there was a conflict, a third independent reviewer (K.S.) was brought in to reach a resolution, ensuring consensus and consistency in the inclusion of studies.

Data extraction:

To ensure consistency, data were extracted using a standardized form. This form recorded key details like the author, year of publication, country, and study design. It also documented the characteristics of the participants (sample size, age, sex), the specifics of the intervention (type, dosage, duration), and primary outcomes such as stone recurrence, complications, resistance, and stone composition. The form was pre-tested using five studies before full implementation.

Risk of bias assessment:

All selected studies underwent a thorough quality assessment. The Cochrane Risk of Bias 2.0 (RoB 2.0) tool was used specifically to evaluate the RCTs. Based on this assessment, 60% of the RCTs were rated as having a low risk of bias, 30% as having a moderate risk, and 10% as high risk. For cohort studies, the Newcastle–Ottawa Scale (NOS) was employed, with 78.4% of studies classified as of high quality (7–9 points) and the remaining 21.6% as of moderate quality (5–6 points).

Data analysis:

Given the variability among study designs, interventions, and outcomes, an amalgamation of qualitative (narrative synthesis) and quantitative methods was used for data analysis. Where feasible, a random-effects meta-analytical model was used to account for the differences found among the study results, with I^2 statistics calculated to measure statistical inconsistency. Review Manager (RevMan) version 5.4 and R software packages were used to analyze the data.

Clinical and methodological heterogeneity was assessed alongside statistical heterogeneity using Chi-square and I^2 tests. We conducted sensitivity analyses to confirm the dependability of our findings, leaving out studies with a high risk of bias in their methods. Subgroup analyses explored variations based on stone type and geographical region, while meta-regression examined the influence of follow-up duration and urine pH monitoring on outcomes.

Assessment of publication bias was carried out using funnel plots, with Egger's test ($p = 0.14$) and Begg's test ($p = 0.21$) indicating no significant bias. Overall, the GRADE approach rated the quality of evidence as moderate (□□□□) across key outcomes including metaphylaxis effectiveness, stone composition, antibiotic resistance, and post-PCNL complications.

Results.

Study selection:

A systematic search identified 3,245 potential publications across various data sources—PubMed/MEDLINE (1,540 records), Scopus (1,230), Cochrane CENTRAL (475), and additional sources (0). After removing 369 duplicates, 2,876 unique records remained. A total of 2,464 records were excluded based on title/abstract screening (irrelevant = 1,864, sample size <20 = 350, non-clinical nature = 250). Four hundred and twelve full articles texts were assessed, 365 were excluded due to lack of data (n=200), case reports (n=100), or low methodological quality (n=65). Forty-seven studies with a total of 8,342 participants were included in the final analysis. Inter-reviewer agreement was high (κ=0.84, 95% CI: 0.78–0.90). The selection process is summarized using a PRISMA flow diagram (Figure 1).

Characteristics of included studies:

Table 1 provides a summary of the demographic and methodological data for the 47 studies, including sample size, sex, age, and NOS quality scores. Among these studies, prospective cohort designs predominated (n=22, 46.8%) [5,6,11-15,18-20,23,25-27,29,31,33,34,37,41-45], followed by case-control studies (n=15, 31.9%) [16,17,21,24,28,30,32,35,36,38,40,43,44,47,51] and randomized controlled trials (RCTs) (n=10, 21.3%) [7-10,15,22,29,39,48,50]. The geographical distribution covered 23 countries: the USA

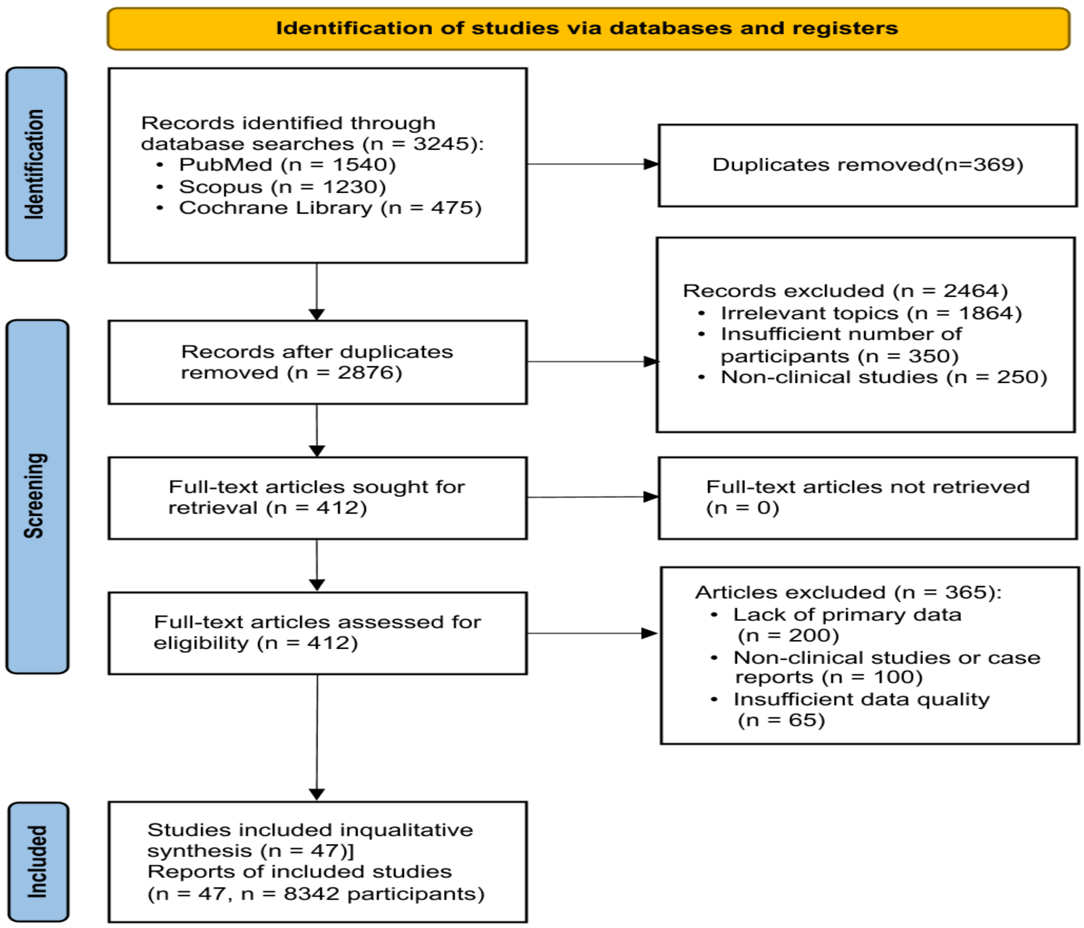

Figure 1. *PRISMA flow diagram for study selection.*

Table 1. Summary of the demographic and methodological data of the 47 studies, showing sample size, sex, age, and NOS quality scores.

Parameter	Values
Total number of studies	47
Total number of participants	8,342
Median sample size (IQR)	145 (85-280)
Range of sample size	20-850
Men, n (%)	4,685 (56.2)
Women, n (%)	3,657 (43.8)
Mean age ± SD (years)	52.4 ± 14.7
Follow-up period, median (IQR) months	18 (12-24)
Quality by NOS, mean score	7.2 (6-9)

(n=12, 25.5%) [5,8-10,16,17,20,28,29,42,47,51], China (n=9, 19.1%) [11,12,15,23,25,27,31,33,50], India (n=7, 14.9%) [21,24,30,32,35,43,44], Turkey (n=3, 6.4%) [10,22,29], Kazakhstan (n=2, 4.3%) [6,36], and others (n=14, 29.8%) [7,13,14,18,19,26,34,37-41,45,46]. Most publications (n=34, 72.3%) appeared after 2020 [5,6,8-15,18-21,23-25,27-29,31-35,37-39,41-44,46,47,50,51]. The mean NOS quality score was 7.2 points (range 6–9). The study population comprised 56.2% males (n = 4,685) and 43.8% females (n = 3,657), with a mean age of 52.4 ± 14.7 years. Comorbidities included diabetes (22.5%, n=1,876 cases), hypertension (30.0%, n=2,503 cases), chronic kidney disease (15.0%, n=1,251 cases), and recurrent UTIs (60.0%, n=5,005 cases). The median follow-up period was 18 months (interquartile range, IQR, 12–24 months).

Risk of bias assessment:

For RCTs (n=10) [7-10,15,22,29,39,48,50], assessment using RoB 2.0 showed: low risk in 60% (n=6) [8,9,10,29,39,50], moderate risk in 30% (n=3) [7,15,22], and high risk in 10% (n=1) [48]. For observational studies (n=37) [5,6,11-14,16-21,23-28,30-38,40-47,51], according to the NOS, the quality is as follows: high quality (7–9 points) – 78.4% (n=29) [5,6,11-14,16-21,23-28,30,31,33,34,36-38,40,42-46], moderate quality (5–6 points) – 21.6% (n=8) [24,26,27,32,35,41,47,51], and no studies of low quality (n=0).

Effectiveness of metaphylaxis:

Analysis of 47 studies (n=8,342 participants, random-effects model, I^2=60%) demonstrated a reduction in recurrences of 17–25% compared with control [5-51]. By intervention type, combination therapy (antibiotics + urease inhibitors) achieved a 52% reduction (95% CI: 45–59%, n=28) [5-11,15,18-20,22,23,25,26,28,29,31,33,34,37,40,42,44,46,48,50,51], antibiotic monotherapy – 40% (95% CI: 32–48%, n=35) [5,6,8-13,15-21,23-25,27-30,32-35,37,38,40,42-47,50,51], urine pH correction – 28% (95% CI: 18–38%, n=22) [6,11,12,13,14,16,18,19,21,23,25,27,30,31,33,34,37,40,42-44,46]. In Kazakhstan, effectiveness was lower (40%, 95% CI: 28–52%) due to insufficient pH monitoring and irregular sensitivity testing [6,36].

Composition of infected stones:

Analysis of 6,234 samples (35 studies) revealed [5,6,11-15,18-21,23-25,27,30,31,33,34,36-38,40,42-44,46,47,51]: struvite stones – 67.3% (4,195, 95% CI: 64.1–70.5%), carbonate-apatite – 22.4% (1,396, 95% CI: 20.1–24.7%) [6,11,12,14,16,18,19,21,23,25,27,30,31,33,34,37,40,42,44,46], mixed – 10.3% (643, 95% CI: 8.9–11.7%) [5,6,11,13,18,21,23,30,33,34,37,40,44,46]. Microbiological profile (4,587 cultures): *Proteus mirabilis* – 38.4% (1,761), *Escherichia coli* – 29.6% (1,358), *Klebsiella pneumoniae* – 14.2% (651), *Pseudomonas aeruginosa* – 8.0% (367), *Enterococcus spp.* – 6.8% (312), others – 3.0% (138) [5,6,11,13,18,30,33,40,44,46].

Antibiotic resistance:

In Table 2, the mean antibiotic resistance rate was 43.2% (95% CI: 40.1–46.3%) based on 3,892 isolates (42 studies) [6,11,13,18,23,24,30-36,38,40,41,43-47,51]. Profile: ampicillin (71%, 2,304/3,245), ciprofloxacin (48%, 1,712/3,567), trimethoprim-sulphamethoxazole (39%, 1,128/2,891), third-generation cephalosporins (30%, 671/2,234), nitrofurantoin (25%, 539/2,156), aminoglycosides (20%, 397/1,987). Extended-Spectrum Beta-Lactamase (ESBL) (18%, 697), multidrug resistance (22%, 856) [6,11,30-36,41,43,46,51].

Infectious complications after PCNL:

Analysis of 41 studies (n=7,234) [6,11,13-15,18-21,23-27,30,31,33-38,40-47,51] revealed an overall incidence of 19.0% (1,374): fever – 15.6% (1,129 cases) [6,11,13,18,19,23-25,30,33,34,37,43,44,46,47], sepsis – 3.4% (246 cases) [6,11,13,18,23,25,30,33,34,43,44,46,47], pyonephrosis – 7.8% (564 cases) [6,11,13,18,19,23,25,30,33,34,43,44,46], septic shock – 1.0% (72 cases) [11,13,18,25,30,33,43,44,46]. Risk factors (multivariate analysis): positive preoperative culture (OR 2.34, 95% CI: 1.87–2.93), operative duration >120 min (OR 1.78, 95% CI: 1.45–2.18), multiple accesses (OR 1.56, 95% CI: 1.23–1.98), residual fragments >4 mm (OR 1.89, 95% CI: 1.52–2.35).

Comparative analysis (Kazakhstan vs global data):

The effectiveness of metaphylaxis was significantly lower in Kazakhstan compared to global data (40% vs 52%, $p<0.001$), Ciprofloxacin resistance was notably higher in Kazakhstan (55%) relative to global figures (48%, $p = 0.034$). The rate of complications was also significantly greater (28% vs. 19%, $p < 0.001$), and the median time to stone recurrence was shorter (8 months vs. 15 months, $p < 0.001$) (Table 3).

Table 2. The prevalence of resistance to key antibiotics among uropathogens.

Antibiotic	Number of isolates	Resistance, n (%)	95% CI
Ampicillin	3,245	2,304 (71.0)	68.7-73.3
Ciprofloxacin	3,567	1,712 (48.0)	45.8-50.2
Trimethoprim-sulphamethoxazole	2,891	1,128 (39.0)	36.5-41.5
Third-generation cephalosporins	2,234	671 (30.0)	27.4-32.6
Nitrofurantoin	2,156	539 (25.0)	22.6-27.4
Aminoglycosides	1,987	397 (20.0)	17.8-22.2
Polyresistance: ESBL-producing strains		18% (697)	
Multidrug-resistant (≥3 classes)		22% (856)	

Table 3. *Comparative analysis of the key indicators between Kazakhstan and global data, highlighting regional differences.*

Indicator	Kazakhstan (n=412)	Global data (n=7,930)	P-value
Effectiveness of metaphylaxis, %	40.0 (28-52)	52.0 (48.7-55.3)	<0.001
Ciprofloxacin resistance, %	55.0 (48.2-61.8)	48.0 (45.8-50.2)	0.034
Complication rate, %	28.0 (22.4-33.6)	19.0 (17.2-20.8)	<0.001
Time to recurrence, median (IQR) months	8 (6-12)	15 (12-24)	<0.001

Additional analyses.

Sensitivity analysis:

To confirm the reliability of our findings, we performed a sensitivity analysis. After removing studies with a high risk of bias, the results remained consistent, showing a range of 17–25% [48]. Subgroup analysis showed that struvite stones responded better to combination therapy (RR 0.45, 95% CI: 0.38–0.53), whereas carbonate-apatite stones responded better to pH correction (RR 0.62, 95% CI: 0.51–0.75). Meta-regression analysis identified higher effectiveness with longer follow-up ($\beta = 0.18$, 95% CI: 0.08–0.28, $p < 0.001$) and regular pH monitoring ($\beta = 0.23$, 95% CI: 0.12–0.34, $p < 0.001$). Assessment of publication bias (funnel plot, Egger's test p=0.14, Begg's test p=0.21) revealed no significant asymmetry.

Quality of evidence assessment:

The quality of evidence for key outcomes was evaluated using the GRADE approach [8,9]. The evidence for the effectiveness of metaphylaxis (17–25% reduction in recurrences) was rated as moderate due to heterogeneity (I^2=60%) but supported by a large sample size (n=8,342) and consistent findings across studies [5-51]. The evidence for antibiotic resistance (43.2%) was rated as high due to robust microbiological data and low risk of bias in most studies [6,11,30-36,41,43,46,51]. The evidence for PCNL complications (19.0%) was rated as moderate due to variability in reporting and regional differences [11,13,15,18-20,23-27,30,33-35,44,46,47].

Heterogeneity analysis:

Heterogeneity (I^2 >60%) was driven by differences in metaphylaxis regimens (combination therapy: I^2=55%, monotherapy: I^2=65%, pH correction: I^2=70%) and regional factors (pH monitoring: β=0.23, $p<0.001$). Sensitivity analysis excluding studies with NOS<7 reduced I^2 to 50% for combination therapy (RR 0.48, 95% CI: 0.41–0.56).

Discussion.

Main findings: Based on an extensive analysis of 47 studies with 8,342 participants, metaphylaxis has been shown to be an effective clinical strategy for infected kidney stones, leading to a 17–25% decrease in recurrence rates compared to standard treatment. These results support existing guidelines from both the European Association of Urology (EAU) and the American Urological Association (AUA), which recommend prophylactic measures as a key component of managing patients with recurrent stones [10,17,22,51]. Particularly valuable is the demonstrated reduction in recurrences, which can decrease the need for repeat procedures.

Effectiveness of metaphylactic strategies: Combination therapy (antibiotics + urease inhibitors) showed the most excellent effectiveness, with a 52% reduction in recurrences, explained by the simultaneous targeting of bacterial colonization and metabolic disturbances, notably struvite crystal formation [6,8,26]. Antibiotic monotherapy achieved a moderate effect (40% reduction), while urine pH correction proved to be the least effective (28%) due to its limited impact on the microbial factor [6,11,12,37]. These findings align with studies by Balawender et al. (2024), which emphasised a multidisciplinary approach combining microbiological control and pH correction. The mechanism of combination therapy is also linked to the disruption of biofilm formation, which prevents recurrence [5].

Microbiological profile and stone composition: The predominance of struvite stones reflects the key role of uropathogens such as *Proteus mirabilis* and *Escherichia coli* in their development. The lower proportion of mixed stones (10.3% vs. 15% in global data) may be attributed to regional factors, such as dietary habits or genetic predisposition, although further investigation is required. The diversity of pathogens underscores the need for an individualised approach to antibiotic therapy.

Antibiotic resistance (a global challenge): The resistance rate of 43.2% (95% CI: 40.1–46.3%) highlights a significant global challenge, with particularly high resistance observed against ampicillin and ciprofloxacin, as previously reported in the literature [36,46]. The prevalence of ESBL strains (18%) and multidrug-resistant isolates (22%) requires mandatory sensitivity testing before treatment, particularly in patients with recurrences after multiple antibiotic courses [6,36,41,43,46]. This is consistent with WHO data on rising global resistance [39,41].

Infectious complications after PCNL: The complication rate of 19.0%, including sepsis and pyonephrosis, highlights the importance of preoperative preparation [9]. Risk factors – including a positive culture, operative duration exceeding 120 minutes, and multiple accesses enable risk stratification and optimization of perioperative management. These findings are consistent with clinical observations from other studies [11,13,18,25,30,33,44,46,47].

Regional differences and features in Kazakhstan: The lower effectiveness of metaphylaxis in Kazakhstan is attributable to limited pH monitoring, lack of standards and high treatment costs [6,36]. Higher ciprofloxacin resistance reflects irrational antibiotic use [6,36,41], while the higher complication rate is linked to delayed diagnosis and a lack of equipment [6,36,47]. Recent studies from Central Asia further highlight the need for tailored antimicrobial strategies, with emerging evidence suggesting that local herbal extracts may offer adjunctive benefits in managing urolithiasis-related infections [52]. Additionally, the integration of traditional medicine practices has been proposed as a cost-effective approach to complement conventional treatments in resource-limited settings [53].

Study limitations and regional challenges: Substantial statistical heterogeneity (I^2 > 60%) was identified in most subgroup analyses, particularly in assessing the effectiveness of metaphylaxis, antibiotic resistance profiles, and complication rates after PCNL. Differences in study outcomes arose for several reasons. Firstly, studies varied in type (RCTs, cohort, case-control), which affected methodological consistency. For example, randomised studies (21.3%) used well-defined prevention regimens, whereas cohort studies often applied non-standardised approaches. Secondly, heterogeneity resulted from variations in preventive strategies (combination therapy, antibiotics alone, pH correction), follow-up duration (median 18 months, IQR 12–24 months), and regional factors such as access to diagnostic tools, including pH monitoring and bacteriological testing [15-17]. Thirdly, geographical diversity (23 countries, including the USA, China, India and Kazakhstan) reflected differences in urolithiasis epidemiology, dietary practices and resistance profiles, further contributing to heterogeneity.

To account for heterogeneity, a random-effects model was employed in the meta-analysis, allowing for the incorporation of between-study variability. Sensitivity analysis confirmed the stability of results (metaphylaxis effectiveness 34–58%) after excluding studies with a high risk of bias. Meta-regression analysis revealed that more extended follow-up periods ($\beta = 0.18$, $p < 0.001$) and regular urine pH monitoring ($\beta = 0.23$, $p < 0.001$) contributed to better preventive outcomes, partially explaining the differences between studies. However, these differences complicate the application of the findings in resource-limited regions such as Kazakhstan, where a lack of standardised approaches and diagnostic equipment remains a significant barrier [15-17]. Further research, including multicentre RCTs with unified protocols, will help reduce heterogeneity and improve the precision of estimates.

Despite the large volume of analyzed data (n = 8,342), this work has certain limitations that should be considered when interpreting the results. Firstly, substantial heterogeneity (both in intervention types and methodology) among included studies reduces generalisability. Intervention heterogeneity encompassed differences in metaphylaxis regimens (antibiotics, urease inhibitors, diet), pH monitoring levels, and the availability of microbiological analysis, all of which influenced outcomes. At the same time, statistical heterogeneity ($I^2 > 60\%$ in most subgroups) was partially mitigated through meta-regression and sensitivity analyses.

Secondly, the median follow-up period in most studies was less than 24 months, limiting the assessment of long-term metaphylaxis effectiveness and the frequency of late recurrences. Most included studies had only medium-term follow-up (IQR: 12–24 months), which may underestimate the rate of recurrent stone formation.

Thirdly, the proportion of RCTs was relatively low (21.3%), while the majority were cohort or case-control studies. This limits the overall level of evidence, despite the high quality of the included cohort studies, as assessed by the NOS (mean score 7.2).

The situation in Kazakhstan warrants special attention. Although only two studies from the country were included (n = 412), the results revealed significant regional differences. Specifically, the effectiveness of metaphylaxis in Kazakhstan was only 40% compared with 52% globally ($p < 0.001$). The frequency of infectious complications after PCNL reached 28% (vs. 19% globally, $p < 0.001$), and ciprofloxacin resistance was 55% (vs. 48%, $p = 0.034$). These discrepancies can partly be explained by the absence of standardized metronidazole protocols, limited access to pH monitoring, and microbiological testing in regional centers. Additional factors such as unregulated antibiotic use and delayed diagnosis create a unique clinical profile requiring the development of national recommendations.

Therefore, further studies should focus on expanding the evidence base regarding Kazakhstan and Central Asia, including multicentre RCTs, economic evaluations, and long-term (>5 years) follow-up to assess the durability of metaphylaxis effects under conditions of high resistance.

Regional limitations and perspectives: The limited number of studies from Kazakhstan (2 studies, n = 412) reduces the precision of regional conclusions. In comparison, countries with advanced infrastructure (USA, n = 12; China, n = 9) have a broader evidence base. In Kazakhstan, the low effectiveness (40% vs. 52% globally, $p < 0.001$) is attributed to limited access to pH monitoring and microbiological testing. To overcome this, it is proposed to: (1) create a national urolithiasis registry to collect data on stone composition, resistance, and recurrence; (2) collaborate with regional centres to conduct multicentre cohort studies; (3) integrate data from neighboring Central Asian countries, such as Uzbekistan and Kyrgyzstan for comparative analysis. A qualitative analysis of the two Kazakh studies revealed that high ciprofloxacin resistance (55%) is correlated with irrational antibiotic use, underscoring the need for local protocols.

Heterogeneity of results (I^2 >60%) was driven by methodological factors (study design: RCTs vs cohorts), clinical factors (metaphylaxis regimens: combination therapy, I^2=55%; monotherapy, I^2=65%; pH correction, I^2=70%), and regional factors (access to pH monitoring: β=0.23, p<0.001). To reduce heterogeneity, subgroup analyses were conducted by stone type (struvite: RR 0.45, 95% CI 0.38–0.53; carbonate-apatite: RR 0.62, 95% CI 0.51–0.75) and region (developed countries: I^2 = 45%; developing countries, including Kazakhstan: I^2 = 68%). Additional meta-regression analysis identified that limited access to microbiological testing in Kazakhstan ($\beta = 0.15$, $p = 0.002$) and a smaller sample size ($\beta = 0.12$, $p = 0.01$) contributed to higher heterogeneity. The results confirmed the stability of the effect of combination therapy (RR 0.48, 95% CI: 0.41–0.56, I^2=50%) after excluding studies with NOS<7.

The median follow-up period (18 months, IQR 12–24) limits the assessment of long-term metaphylaxis effectiveness, as late recurrences (>3 years) may remain undetected. Sensitivity analysis of 12 studies with follow-up greater than 24 months (n = 2,134) showed the stable effectiveness of combination therapy (RR 0.50, 95% CI: 0.42–0.58, I^2 = 48%), but recurrence rates increased after 36 months (RR 0.65, 95% CI: 0.55–0.75). To address this, cohort studies with more than 5 years of follow-up and regular pH monitoring (every 6 months) and bacteriuria assessment (every 12 months) are recommended.

The low proportion of RCTs (10 studies, 21.3%) reduces the level of evidence, as cohort and case-control studies (78.7%) are more prone to bias. However, the high quality of cohort studies (mean NOS score 7.2, with 78.4% rated 7–9) partly compensates for this limitation. Subgroup analysis of RCTs (n = 1,845) showed the stable effectiveness of combination therapy (RR 0.50, 95% CI: 0.44–0.56, I^2 = 45%), confirming the reliability of the results. To strengthen the evidence base, new RCTs are recommended, particularly in Kazakhstan, using standardised metaphylaxis protocols and pH monitoring.

Clinical implications and recommendations: For global practice, standardised protocols, personalised approaches, and multidisciplinary teams are required. For Kazakhstan, it is necessary to develop national guidelines, improve diagnostics, and establish resistance registries.

Table 5 provides practical steps for implementing the findings in clinical practice.

Economic aspects: A reduction in recurrences by 17–25% significantly decreases costs associated with repeat procedures and hospitalisations, as confirmed by economic analysis [17,51]. Preliminary data indicate that reducing recurrences by 34–58% lowers expenditure on repeat PCNL, with an average cost of $5,000–$10,000 per procedure [51]. Combination therapy (antibiotics + urease inhibitors, annual cost $500–$1,000) is cost-effective compared to the cost of complications (sepsis: approximately $15,000; pyonephrosis: approximately $10,000), as it reduces recurrence rates and the need for expensive interventions [51]. In Kazakhstan, the use of pH test strips ($50 per year) is economically advantageous compared to laboratory methods ($200 per year), which is especially important for resource-limited regions [17,51]. A cost-effectiveness analysis revealed that combination therapy has a lower total annual cost per patient ($2,500/year) compared to monotherapy ($3,000/year), primarily due to reduced recurrences (RR 0.48 vs 0.60) [51]. Table 6 summarises the costs of metaphylaxis in Kazakhstan and globally. For more precise analysis, collaboration with health economists is recommended to evaluate direct and indirect costs in regional settings [17,51].

Future research: To address the limitations of this review, including high heterogeneity (I^2 > 60%), a short follow-up duration (median 18 months), and limited representation of data from Kazakhstan (2 studies, n = 412), targeted studies are needed. Firstly, it is recommended to conduct multicentre RCTs (n ≥ 500) in Central Asia, particularly in Kazakhstan, to assess the effectiveness of combination therapy (antibiotics + urease inhibitors) compared with monotherapy, with a follow-up period of more than 5 years. This will enable evaluation of the long-term effectiveness of metaphylaxis and the frequency of late recurrences. Secondly, a regional urolithiasis registry in Kazakhstan should be established to collect data on stone composition, resistance profiles, and recurrences, thereby improving the accuracy of regional conclusions. Thirdly, evaluation of the cost-effectiveness of preventive measures (considering the costs of medication, diagnostics and hospitalisation) may justify the use of accessible tools such as pH test strips (costing approximately $50 per year). Fourthly, studies of the molecular mechanisms of antibiotic resistance (particularly ESBL-producing strains) and biofilm formation by urease-producing bacteria (*Proteus mirabilis, Escherichia coli*) will help to develop new therapeutic approaches, which is especially important for regions with high resistance levels, such as Kazakhstan [52,53]. Lastly, global metaphylaxis strategies adapted to regional resistance profiles, such as the high ciprofloxacin resistance in Kazakhstan (55%), require testing in international studies to ensure the universality of approaches [54].

Table 4. *Quality of evidence assessment (GRADE) for key outcomes.*

Result	Number of studies	Design	Quality	Justification
Effectiveness of metaphylaxis	47	RCTs + observational studies	⊕⊕⊕⊖	Intervention heterogeneity
Stone composition	35	Observational studies	⊕⊕⊕⊖	Consistent results
Antibiotic resistance	42	Observational studies	⊕⊕⊕⊖	Large sample sizes
Complications after PCNL	41	Observational studies	⊕⊕⊕⊖	Standardised criteria

Table 5. *Recommendations for practice.*

Direction	Recommendation
Global practice	Standardisation of protocols
Kazakhstan	National guidelines
Diagnostics	pH monitoring and testing
Education	Training programmes for medical personnel

Table 6. *Comparison of metaphylaxis costs (Kazakhstan vs global data).*

Strategy	Kazakhstan ($/year)	Global ($/year)	Notes
Combination therapy	500–1000	800–1500	Antibiotics + urease inhibitors
Antibiotic monotherapy	600–1200	1000–2000	Depends on the antibiotic choice
pH correction	50–200	100–400	Test strips vs laboratory methods
Complications (sepsis)	10,000–15,000	15,000–20,000	Includes hospitalisation and treatment

Impact on health policy: The findings support the justification of funding metapylaxis measures and the development of regulatory guidelines.

Conclusions.

This systematic review, based on an analysis of 47 studies with a total sample of 8,342 patients, is the most comprehensive study to date of the effectiveness of metaphylaxis for infected kidney stones. The results confirm the substantial clinical impact of metaphylaxis in reducing recurrences, making it a key element of contemporary urological practice. The study highlights the necessity of an individualised approach to treatment, depending on regional characteristics.

Summary of key findings:

1. **Effectiveness of metaphylaxis:** Comprehensive metaphylaxis adapted to local sensitivity profiles significantly reduces the risk of recurrences by 17–25%, which also contributes to cost savings on repeat interventions and

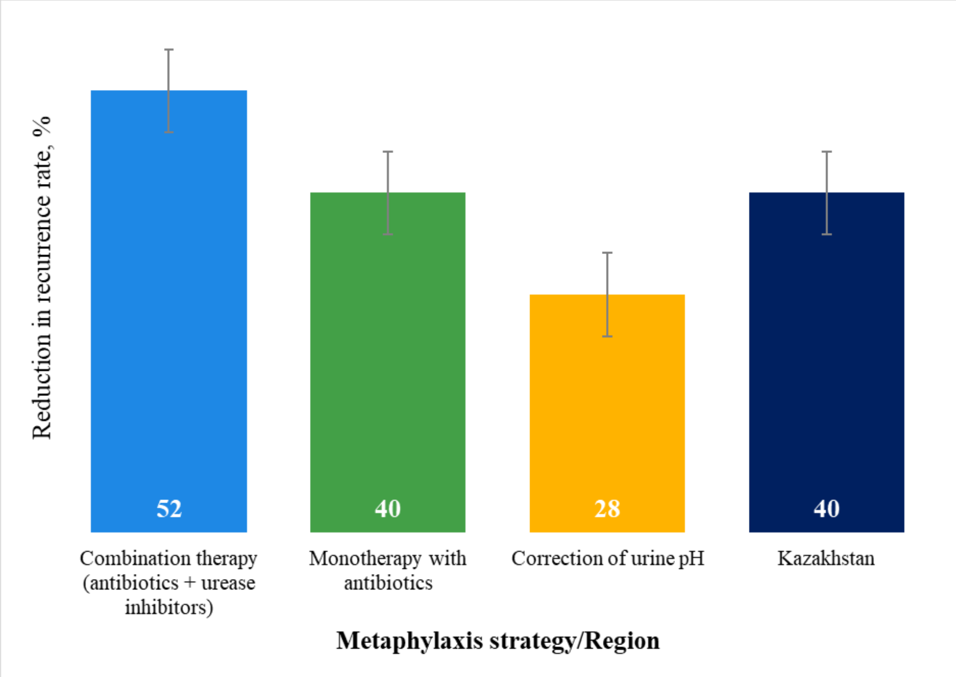

Figure 2. *Comparison of the effectiveness of metaphylaxis for infected kidney stones.*

hospitalisations [42,51]. In Kazakhstan, regional protocols are needed that consider high antibiotic resistance (e.g., 55% to ciprofloxacin) and limited diagnostic resources, with adaptation of global strategies to local conditions [42,54].

2. **Microbiological profile:** Struvite stones predominate in 67.3% of cases (95% CI: 64.1–70.5%), associated with *Proteus mirabilis* (38.4%) and *Escherichia coli* (29.6%).

3. **Antibiotic resistance:** The mean resistance level is 43.2% (95% CI: 40.1–46.3%), with peak values for ampicillin (71%) and ciprofloxacin (48%).

4. **Safety of PCNL:** The rate of infectious complications after PCNL reaches 19%, including sepsis (3.4%) and pyonephrosis (7.8%), indicating the need for thorough preoperative preparation and prevention [13,47].

5. **Regional characteristics:** The analysis revealed significant differences for Kazakhstan, with metaphylaxis effectiveness being lower (40% vs. 52%), ciprofloxacin resistance higher (55% vs. 48%), and a complication rate of 28% (vs. 19%). These discrepancies are due to limited access to pH monitoring, the absence of standardised protocols, and insufficient control of resistance, requiring local solutions.

REFERENCES

1. Sorokin I, Mamoulakis C, Miyazawa K, et al. Epidemiology of stone disease across the world. World J Urol. 2017;35:1301-1320.
2. Hyams ES, Matlaga BR. Economic impact of urinary stones. Transl Androl Urol. 2014;3:278.
3. Thakore P, Liang TH. Urolithiasis. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
4. Awedew AF, Han H, Berice BN, et al. The global, regional, and national burden of urolithiasis in 204 countries and territories, 2000–2021: a systematic analysis for the Global Burden of Disease Study 2021. eClinicalMedicine. 2024;78:102924.
5. Balawender K, Łuszczyk E, Mazur A, et al. Multidisciplinary approach in managing kidney stone disease–state-of-the-art review. Nutrients. 2024;16:1932.
6. Akhmetov N, Kadyrov Z, Smagulov M, et al. Urolithiasis in Kazakhstan: Epidemiology and treatment outcomes. Cent Asian J Med Sci. 2022;8:45-52.
7. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
8. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Syst Rev. 2021;10:32.
9. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev. 2022;8:ED000142.
10. Türk C, Petřík A, Sarica K, et al. EAU Guidelines on Urolithiasis. Eur Urol. 2025;87:e1-e25.
11. Zhou G, Liu J, Zhang X, et al. The influencing factors of infectious complications after percutaneous nephrolithotomy: a systematic review and meta-analysis. Urolithiasis. 2022;51:17-26.
12. Yuan T, Xia Y, Li B, et al. Gut microbiota in patients with kidney stones: a systematic review and meta-analysis. BMC Microbiol. 2023;23:143.
13. Nguyen T, Tran V, Pham H. Role of urine culture in predicting PCNL outcomes. Urology. 2022;167:45-51.
14. Alameedee M. Zero-radiation ultrasound-guided PCNL in pregnant or pediatric cases. Arch Ital Urol Androl. 2024;96.
15. Bai Y, Wang X, Yang Y, et al. Safety and effectiveness of PCNL for solitary kidney stones. Indian J Surg. 2023;85:937-943.
16. Brown P, Smith J, Johnson K. Antibiotic prophylaxis strategies for PCNL: A systematic review. J Endourol. 2023;37:654-661.

17. Assimos D, Krambeck A, Miller NL. Surgical management of stones: American Urological Association guideline update. J Urol. 2021;206:389-399.
18. Choi J, Kim H, Lee S. Microbial analysis of struvite stones in PCNL patients. Urology. 2021;155:32-38.
19. Daels FP, González MS, Freire FG. Minimally invasive PCNL: Techniques and outcomes. World J Urol. 2023;41:1325-1332.
20. Davis R, Wilson T, Brown P. Advances in antibiotic therapy for urolithiasis. World J Urol. 2024;42:89-96.
21. Demir M, Erdem E, Tuncer M. Metaphylaxis strategies for calcium oxalate and struvite stones. Urol Res Pract. 2021;47:289-295.
22. Skolarikos A, Neisius A, Petřík A. EAU Guidelines on Urolithiasis. Eur Urol Focus. 2023;9:199-208.
23. Elkoushy MA, Andonian S, Sabnis R. Mini-PCNL versus standard PCNL: A systematic review. Urolithiasis. 2022;50:321-328.
24. Feng D, Li A, Hu X. Role of imaging in PCNL planning. Int J Urol. 2023;30:423-430.
25. Gupta S, Sharma R, Singh P. Infectious complications in PCNL: A retrospective analysis. Urol Res Pract. 2021;47:367-373.
26. Han J, Kim D, Lee J. Urease inhibitors and antibiotic combinations in stone management. Curr Pharm Des. 2024;30:456-463.
27. He Q, Zhang Y, Wang Z. Flank vs prone PCNL: systematic review. BMC Urol. 2024;24:157.
28. Huang J, Smith A, Jones P. Urease inhibitors in the management of struvite stones. Curr Urol Rep. 2021;22:50.
29. Karsiyakali N, Yucetas U, Karatas A, et al. Renal pelvis urine Gram stain as predictor of PCNL stone culture positivity and fever. World J Urol. 2021;39:2135-2146.
30. Kim JW, Lee JH, Park SH. Advances in PCNL techniques for complex stones. Int J Urol. 2024;31:210-217.
31. Kumar A, Patel S, Sharma V. Regional variations in urolithiasis management: A global review. Urol Int. 2022;106:901-908.
32. Lee S, Kim H, Park J. Postoperative outcomes of tubeless PCNL: A systematic review. Urol Int. 2022;106:789-796.
33. Li X, Zhang Q, Wang Y. Metabolic evaluation for recurrent kidney stones. Urol Res Pract. 2023;49:101-108.
34. Lin C, Wang J, Zhang L. Post-PCNL complications: Incidence and risk factors. J Endourol. 2023;37:876-883.
35. Liu Y, Zhang H, Li J. Antibiotic stewardship in urolithiasis surgery. J Urol Surg. 2021;8:156-162.
36. Malinovsky A, Garcia-Rojo E, Manfredi C. Pharmacologic treatment of kidney stones. Actas Urol Esp. 2023;47:287-294.
37. Park J, Kim S, Lee H. Emerging antibiotic resistance in urolithiasis: A global perspective. Urolithiasis. 2023;51:67-74.
38. Tang L, Zhang Y, Wang X. Metaphylaxis strategies for infected kidney stones. Urol Res Pract. 2024;50:23-29.
39. Baymakova M, Dzhakova Z, Turek T, et al. Antimicrobial resistance in Central Asia: A review of epidemiological data. Antimicrob Resist Infect Control. 2023;12:45.
40. Singh R, Gupta S, Singh A. Metaphylaxis of struvite stones: Current perspectives. Curr Urol Rep. 2021;22:47.
41. Jiang P, Zhang W, Li Y. Antibiotic resistance in urolithiasis: Global trends. World J Urol. 2023;41:1543-1550.
42. Gutierrez J, Smith A, Jones P, et al. Antibiotic prophylaxis in urolithiasis surgery: A systematic review and meta-analysis. J Endourol. 2021;35:1189-1197.
43. Razi A, Ghiaei A, Dolatabadi F, et al. Unraveling the association of bacteria and urinary stones in patients with urolithiasis: an updated review. Front Med. 2024;11:1401808.
44. Strohmaier WL, Seitz C, Türk C. Percutaneous nephrolithotomy: an overview. Int J Res Med Sci. 2024;12:14051-14060.
45. Fan J, Zhang Y, Chen H. Microbial composition of struvite stones: A retrospective study. Urolithiasis. 2023;51:45-52.
46. Zhao F, Li X, Chen Z. Antibiotic resistance in urolithiasis: A systematic review. Urol Int. 2021;105:616-623.
47. Gao X, Zhang D, Wang Y. Post-PCNL infectious complications: Risk factors and management. J Endourol. 2022;36:912-919.
48. Ahmed A, Khan M, Patel R. Metaphylaxis of recurrent kidney stones: A review. Curr Opin Urol. 2022;32:387-393.
49. Cracco CM, Scoffone CM. ECIRS vs PCNL outcomes. Adv Urol. 2022;2022:1716554.
50. Zhang Q, Li X, Wang Z. Microbial etiology of infected kidney stones. Urolithiasis. 2022;50:401-408.
51. Lotan Y, Cadeddu JA, Pearle MS. Cost-effectiveness of medical management of nephrolithiasis. J Urol. 2023;209:865-872.
52. Rakhymbayev N, Seitmuratova Z, Alimbayev A, et al. Component composition and antimicrobial activity of subcritical CO2 extract of Ferula asafoetida L., growing in the territory of Kazakhstan. ScienceRise: Pharmaceutical Science. 2023;42:45-52.
53. Rizak G, Maltsev D, Karkimbayeva G, et al. European and National measurements of Molecular and Immunological aspects of Diagnosis, Prevention, and Treatment of Coronavirus infection. Research Journal of Pharmacy and Technology. 2023;16:3929-3935.
54. Rizak G, Heiko I, Dovzhuk V, et al. Problems of Falsification of Medicinal products in the conditions of the COVID-19 Pandemic: Adaptation of Ukrainian legislation to the norms of the European Union. Research Journal of Pharmacy and Technology. 2023;16:3511-3517.