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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 ფჩხილებში 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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COMPARATIVE EXPERIMENTAL STUDY OF MORPHOLOGICAL CHANGES IN THE KIDNEY IN ACUTE OBSTRUCTIVE PYELONEPHRITIS MODEL: INFLUENCE OF INFECTION ROUTE

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Abstract.

Background: The objective of this study is to conduct a comparative morphological analysis of the kidneys in the context of various infection pathways in models of acute obstructive pyelonephritis.

Methods: The study investigated the structural condition of rabbit kidneys (n=40) in relation to the pathogenesis of acute pyelonephritis. The animals were randomly assigned to four groups: two experimental and two control groups. Experimental Groups I and II underwent urethral ligation to induce obstructive pyelonephritis. In Group I, a bacterial strain was introduced into the gastrointestinal tract to examine intestinal translocation, while in Group II, it was introduced into the urinary bladder to study ascending infection. Control Groups III and IV received a similar introduction of the infectious agent without urethral obstruction. On the third day, morphological examination was conducted using optical microscopy and a computerized microscope capable of digital microphotography.

Results: In Group I, inflammatory changes were detected in 60% of cases, while in Group II, they were found in 70% of cases. No morphological changes were observed in the control groups.

Conclusion: The nature of morphological changes in the kidneys in the model of acute obstructive pyelonephritis did not show statistically significant differences when comparing between the experimental groups. This indicates the involvement of enterorenal bacterial translocation in the development of inflammatory processes in the kidneys in the presence of obstruction.

Key words. Urinary tract obstruction, acute pyelonephritis, intestinal translocation, *E. coli*.

Introduction.

Urinary tract infections are considered to be one of the most prevalent bacterial infections, affecting 150 million people worldwide each year [1]. Among acute infectious-inflammatory kidney diseases, acute pyelonephritis (AP) dominates, being detected in all age groups and comprising approximately 14% of kidney diseases [2]. According to the authors' research, obstructive pyelonephritis is a complication of urological diseases in 89.3% of patients. Women in the 20-50 age group have a significantly higher prevalence of urinary tract infections compared to men, with a 50-fold increase [3]. There are researchers who support the hypothesis that bacteria are more frequently introduced into the kidneys through reflux from the lower urinary tract. Based on this hypothesis, the rectum, perineum, and urethra are considered potential reservoirs of uropathogenic bacteria. In men, the prostate gland can serve as a source of such bacteria, while in women, it can be the vagina. This assumption is associated with the development of pyelonephritis and is considered in the context of potential mechanisms of infection transmission in the urinary system [4,5]. In modern literature, there has been a rise in the number of publications where authors express the viewpoint on the substantial role of bacterial translocation from the intestine in the pathogenesis of various pathological conditions of the urinary system [6,7]. In the study conducted by Magruder et al., it was observed that increased colonization of the gut by Enterobacteriaceae bacteria is correlated with an elevated risk of developing bacteriuria and subsequent urinary tract infections in patients undergoing kidney transplantation. These findings suggest a potential association between the composition of the gut microbiota and adverse complications following kidney transplantation [8]. The study conducted by Forde et al. (2019) examined the dynamics of the Escherichia coli ST131 population in an elderly woman with recurrent urinary tract infections over a five-year period. The findings provide compelling evidence for the existence of an intestinal reservoir for recurrent urinary tract infections [9]. However, the phenomenon of bacterial translocation in the development of acute obstructive pyelonephritis is currently insufficiently studied. Researchers are interested in conducting experimental studies aimed at investigating the role and identifying the pathogenic mechanisms associated with the development of this condition [10]. Currently, there are several different models of acute pyelonephritis that are used in research studies. In the study by L. Harrison et al. (1973), an experimental model of acute ascending pyelonephritis was conducted in dogs. The study also investigated the association between urinary tract infection and kidney changes through transvesical inoculation of *E. coli* [11]. P. Larsson et al. (1980) created a model of acute ascending pyelonephritis in rats by introducing bacteria through the urethra into their bladder. The study showed that strains of *E. coli* and Proteus mirabilis 03H1 were the most capable of inducing pyelonephritis in rats [12]. In a study conducted by S. Tancheva et al. (2011), models of acute hematogenous pyelonephritis in rats were developed by inoculating a mixed bacterial suspension consisting of S. aureus and *E. coli*. By ligating the ureter, infection was successfully achieved without obstruction, leading to the development of

pyelonephritis. As a result of the combined infection with the aforementioned bacteria, pathological changes in renal tubules were successfully induced in rats [13]. In the study by S. Zeidan et al. (2012), the contribution of partial unilateral ureteral obstruction and bacterial virulence was examined in a model of ascending urinary tract infection in mice. The results showed that bacterial virulence plays a significant role in the persistence of *E. coli* in the kidneys, while partial ureteral obstruction does not lead to infection induction. However, the combination of obstruction and virulent infection affects kidney growth, enhances inflammation, and results in fibrotic changes [14].

Existing methods for modeling acute obstructive pyelonephritis (AOP) are limited in their application due to the introduction of the infectious agent either into the bloodstream or directly into the urinary tract. To study the role of intestinal microbiota translocation in the development of this disease, complete asepsis and minimization of exogenous contamination are required. Therefore, our own models of acute obstructive pyelonephritis have been developed, taking into account these factors and aligning with the research objectives.

Materials and Methods.

The study design obtained approval from the Bioethics Committee of the Karaganda Medical University (No. 7 dated 22.02.2022, assigned number No. 28). All animals were kept under identical conditions, including a temperature of 20-23°C, humidity of 70-75%, lighting with a 12-hour light-dark cycle, and a standard diet. Prior to the experiment, animals underwent quarantine and acclimatization in the vivarium of the Karaganda Medical University for at least 14 days, following sanitary rules. The portions of the diet for laboratory animals were uniform. To conduct the experiment, two models of acute obstructive pyelonephritis were created by obstructing the urethra to study intestinal translocation and ascending *E. coli* infection. The study was conducted on 40 sexually mature non-pedigree male rabbits, aged 3 to 4 months, with a weight of 3.0±0.5 kg. The animals were divided into 4 groups, each consisting of 10 animals.

I Group (n=10) - experimental group where a model of acute obstructive pyelonephritis was induced to study intestinal translocation of *E.coli* by obstructing the urethra. The model was created by inserting a gastric tube through the mouth into the stomach, followed by the administration of a capsule with the infectious agent into the gastric lumen. Urethral obstruction was achieved by suturing the external urethral orifice.

II Group (n=10) - experimental group where a model of acute obstructive pyelonephritis was induced to study ascending *E. coli* infection by obstructing the urethra. The model was created by catheterizing the bladder and introducing a bacterial suspension into it. Urethral obstruction was achieved by suturing the external urethral orifice.

III Group - control group where bacterial strain administration was conducted similarly to Group I but without urethral obstruction.

IV Group - control group where bacterial strain administration was conducted similarly to Group II but without urethral obstruction.

In the experiment, a reference marker strain of *E. coli* No. 49579 obtained from a patient with urological infection was used. This strain was resistant to cefepime, ciprofloxacin, and tetracycline. For the experiment, a 0.5 McFarland suspension was prepared from a 24-hour culture of *E. coli* strain No. 49579 grown on meat-peptone agar at 37°C [15].

In Groups I and Sham III, the strain was administered into the gastrointestinal tract using enteric-soluble capsules (gelatin capsules, size 2). Each capsule contained meat-peptone agar containing a 0.5 McFarland bacterial suspension of *E. coli* strain No. 49579.

Additionally, each animal received the analgesic ketotop in the thigh muscle area at a dose of 100 mg/mL twice a day, calculated based on body weight (1 mg/kg). All animals were euthanized on the third day under general anesthesia, and material for morphological studies was collected.

Microbiological study of the microflora of kidney tissue and urine:

Urine and kidney tissue above the obstruction were used for microbiological testing. Biological samples were collected on the third day after the experiment [16].

Kidney tissue and urine for microbiological examination were collected directly during surgery in sterile 2 ml tubes with trypticase soy broth. Microbial cultures were collected on blood agar containing 5% sheep blood, and pure cultures were isolated using standard methods. Microorganisms in the sample were quantified by counting the number of colonies grown on the plate. Microbial strains obtained during the study were considered clinically significant if they contained $>10^5$ CFU/ml.

Identification of microorganisms:

Species identification of the isolated microorganisms was performed by matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) using a Microflex LT system and MALDI Biotyper Compass 4.1.80 software (Bruker Daltonics, Germany). Recommended Score values ≥ 2.2 were used as a criterion for reliable species identification [17]. The isolated and identified microorganisms were frozen at -70°C in trypticase soy broth with the addition of 30% glycerol before subspecies typing.

Subspecies typing of microorganisms using MALDI-TOF MS:

Strains that had been deep frozen were reconstituted on nutrient agar (37°C, 18 hours). Samples were then spotted on an air-dried MBT Biotarget 96 target plate with 1 ml of a saturated cyano-4-hydroxycinnamic acid (HCCA) matrix solution in 50% acetonitrile and 2.5% trifluoroacetic acid. Mass spectra were acquired on a Microflex LT mass spectrometer (Bruker Daltonics) using default parameters (linear positive detection, laser frequency 60 Hz, ion source voltages 2.0 and 1.8 kV, objective voltage 6 kV) over the m/z range of 2000–20000. Six spectra were acquired for the strain according to the master spectra protocol (MSP). External calibration of the mass spectra was performed using the Bruker Bacterial Test with ethanol/formic acid extraction according to the manufacturer's recommendations (Bruker Daltonix, Bremen, Germany) [18].

The data files (obtained bacterial spectra) were transferred to FlexAnalysis software (version 2.4; Bruker) for automatic peak

extraction. Peak lists containing masses and intensities were exported as Excel files [19].

Phenotypic confirmation of the marker strain in the experiment:

To phenotypic confirm the marker strain in the experiment, antibiotic susceptibility testing was chosen. During the experiment, the animals were exposed to an *E. coli* strain resistant to cefepime, ciprofloxacin, and tetracycline. Therefore, when isolating *E. coli*, susceptibility testing to these antibacterial agents was performed first.

Determination of susceptibility, as well as interpretation to antimicrobial drugs: to cefepime, ciprofloxacin and tetracycline, loads were carried out by the disk diffusion method on Mueller-Hinton agar in accordance with EUCAST recommendations [20]. To prepare the inoculum, we directly suspended the colonies in sterile isotonic solution to a density of 0.5 according to the McFarland turbidity standard. The cultures were incubated at 37°C for 24 hours.

Morphological studies.

The morphological studies were conducted in the Pathomorphology Laboratory of the Karaganda Medical University. For histological analysis, kidney specimens were obtained by cutting the organ in the middle part, encompassing all layers and the renal hilum. The collected material was fixed in a 10% neutral formalin solution, then subjected to the standard protocol for histological examination and embedded in a paraffin block. Subsequently, the prepared paraffin sections, with a thickness of 5-6 microns, were stained with hematoxylin and eosin. The histological material was examined using a computerized microscope with a digital camera "Leica DFC320" and a microscope "Leica DM1000" from Leica Microsystems, at magnifications of 100, 200, and 400 times.

Statistical analysis.

The statistical analysis was conducted using the software programs "Statistica 8.1 (Statsoft)" and "StatTech v. 2.8.8". The exact Fisher's test was applied to evaluate the statistical significance between groups for qualitative parameters. Differences were considered statistically significant when the p-value was less than 0.05.

Results.

Comparison of microbiological test results:

According to the table provided, when analyzing the number of lg CFU (Colony Forming Unit) *E. coli* in urine after the experiment between the experimental and control groups, we found significant statistical differences between the groups on day 3 ($p \leq 0.05$). The level of lg CFU *E. coli* in urine on day 3 in the intact rabbit groups and the control group did not change throughout the experiment, showing zero values ($p \geq 0.05$) (Table 1).

According to the study results, *E. coli* was detected in the urine and kidney tissue of all animals in the experimental groups. When comparing the number of CFU of *E. coli* in urine on the third day after the experiment between Groups I and II, no statistically significant differences were found. Similarly, when comparing the number of CFU of *E. coli* in kidney tissue on the third day after the experiment between Groups I and II, no statistically significant differences were found (Table 2).

Thus, a comparative analysis of the CFU level of the marker strain of the experimental groups in the AOP model with urethral blockage did not show statistically significant differences and was higher than 105, which is of clinical significance for the development of pyelonephritis.

Results of identification, subspecies typing and phenotypic typing of microorganisms isolated from urine and kidney tissue of animals:

To evaluate the effectiveness of the method for introducing a marker strain into the gastrointestinal tract using enteric-coated capsules, identification, subspecies typing, and phenotypic typing of microorganisms were performed. The study utilized collections of *E. coli* isolates recovered from urine (n=20) and kidney tissue (n=20) during the study.

All 40 isolates included in the study were identified as *E. coli* by MALDI-TOF MS with scores >2.0 (categorized as highly probable species identification) when analyzed by Biotyper software.

Table 1. *Comparative analysis of lg (logarithm) CFU E.coli in urine on the 3rd day after the experiment between the experimental and control groups.*

Groups	**lg CFU *E.coli* in urine after the experiment (CFU/ml)**			**P**
	Me	**IQR**	**n**	
I	7,00	7,00-8,00	10	0,0002
III	0	0	10	
II	7,00	7,00-8,00	10	0,00004
IV	0	0	10	
Note: Me-median, IQR-interquartile range, p-significance level				

Table 2. *Comparative analysis of lg CFU E.coli in urine and kidney tissue on day 3 between experimental groups.*

Groups	**lg CFU *E.coli* in urine after the experiment (CFU/ml)**			**P**	**lg CFU *E. coli* in kidney tissue after the experiment (CFU/ml)**			**P**
	Me	**IQR**	**n**		**Me**	**IQR**	**n**	
I	7,00	7,00 – 7,75	10	0,483	7,00	7,00 – 7,75	10	0,752
II	7,00	7,00 – 8,00	10		7,00	7,00 – 7,75	10	
Note: Me-median, IQR-interquartile range, p-significance level								

MALDI Biotyper is based on comparing the peak pattern of an unknown MALDI-TOF spectrum with the peak pattern of a known strain. For each strain, a summary spectrum of approximately 50 peaks was compiled from the mass spectra of bacterial cells. All peaks in the summary spectrum in the range of 2000–20000 m/z were included in the analysis.

In Figure 1, comparing 20 isolates recovered from urine after modeling OOP with urethral blockage, using the "pre-experiment isolates/post-experiment isolates" criterion, two isolates had matching ribosomal protein peaks.

As seen in Figure 2, comparing 20 isolates recovered from kidney tissue after modelling AOP with urethral blockage, using the "pre-experiment isolates/post-experiment isolates" criterion, two isolates had matching ribosomal protein peaks. *E. coli* strains recovered after the experiment were compared with the strains used to infect the animals. *E. coli* isolates recovered from kidney tissue after the experiment had the same susceptibility profile as the marker strain.

Comparison of morphological characteristics:

The main qualitative characteristics used for histological evaluation were as follows:

- Inflammatory infiltration.
- Edema of the renal pelvis and calyces.
- Edema of the ureteral stroma.
- Infiltration in the cortical layer of the kidneys.
- Infiltration in the medullary layer of the kidneys.
- Narrowing of the tubular lumen.
- Vascular congestion.

In Group I, out of 10 observations, 6 animals showed stromal edema and scattered lymphocytic infiltration in the renal pelvis and calyces after the model creation (Figure 3A). The infiltration was predominantly observed in perivascular zones, accompanied by interstitial edema and vascular congestion (Figure 3B).

In Group II, 7 animals had areas of the ureter where the lumen was free of contents, but the wall exhibited interstitial edema and an inflammatory reaction characterized by scattered lymphocytic and leukocytic infiltration, mainly perivascular (Figure 3C). These animals also showed moderate lymphocytic and leukocytic infiltration in the stroma of the renal pelvis and calyces, impaired blood circulation manifested by vascular congestion in the ureter wall, and focal erythrodiapedesis (Figure 3D).

In the control groups, histological examination of the material showed no pathological changes in the structure of renal tissue in all animals (Figure 3E,3F).

In the morphological analysis, it was found that 60% of animals in Group I (experimental group) exhibited inflammatory infiltration in the kidney, edema of the renal pelvis and calyces, and stromal edema of the ureter. Vascular congestion in the kidney was also observed in these animals. These results were statistically significantly different from Group III (control group), where no histological changes were detected in any of the animals. In Group I, inflammatory infiltration in the kidney and edema of the renal pelvis and ureter were noted, but no changes were observed in the medullary and cortical layers of the kidney. Purulent changes were not detected in the examined macroscopic preparations of this group (Table 3).

In the comparative assessment of the pathomorphological changes, including inflammatory infiltration in the kidney, edema of the renal pelvis, stromal edema of the ureter, and vascular congestion in the kidney, it was found that 70% of animals in Group III exhibited these pathological alterations. In contrast, animals in the control group showed no structural changes or inflammatory processes. These differences between the groups were significant and statistically significant (Table 3).

Table 3. *Frequency of development of morphological changes.*

Morphological characteristic	**Groups**								**P**
	I		**III**		**II**		**IV**		
	N=10		**N=10**		**N=10**		**N=10**		
	yes	**no**	**yes**	**no**	**yes**	**no**	**yes**	**no**	
Inflammatory infiltration in the kidney	60%	40%	0%	100%	70%	30%	0%	100%	*0.011 #0,003 ^1,000
Edema of the pelvicalyceal system	60%	40%	0%	100%	70%	30%	0%	100%	*0.011 #0,003 ^1,000
Swelling of the stroma of the ureter	60%	40%	0%	100%	70%	30%	0%	100%	*0.011 #0,003 ^1,000
Infiltration in the cortex kidney layer	0%	100%	0%	100%	0%	100%	0%	100%	-
Infiltration in the medulla of kidney	0%	100%	0%	100%	0%	100%	0%	100%	-
Narrowing of the lumen tubules	0%	100%	0%	100%	0%	100%	0%	100%	-
Vascular plethora	60%	40%	0%	100%	70%	30%	0%	100%	*0.011 #0,003 ^1,000
P - Fisher's exact test (* - comparison of groups I and III, # - comparison of groups II and IV, ^- comparison of groups I and II)									

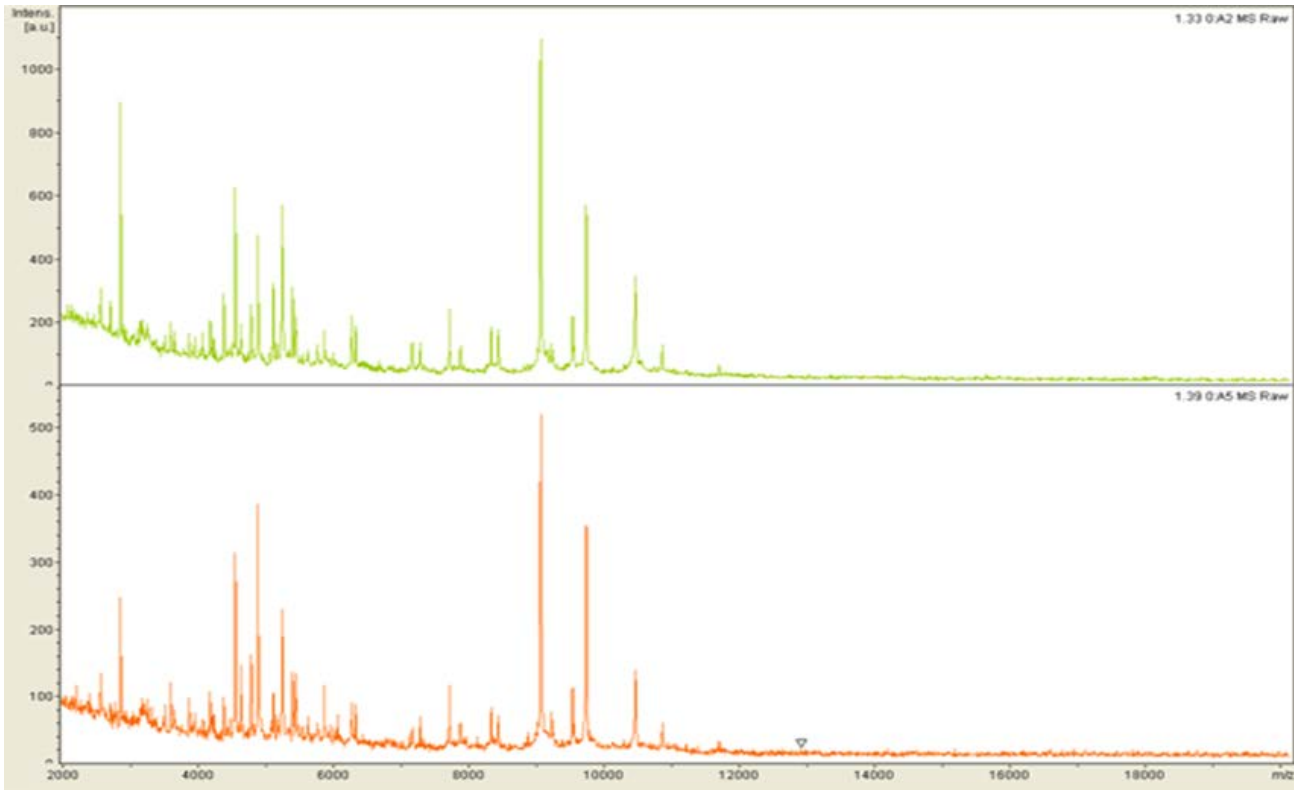

Figure 1. *Mass spectra of E. coli isolated from urine from the category "isolates before the experiment/isolates after the experiment".*

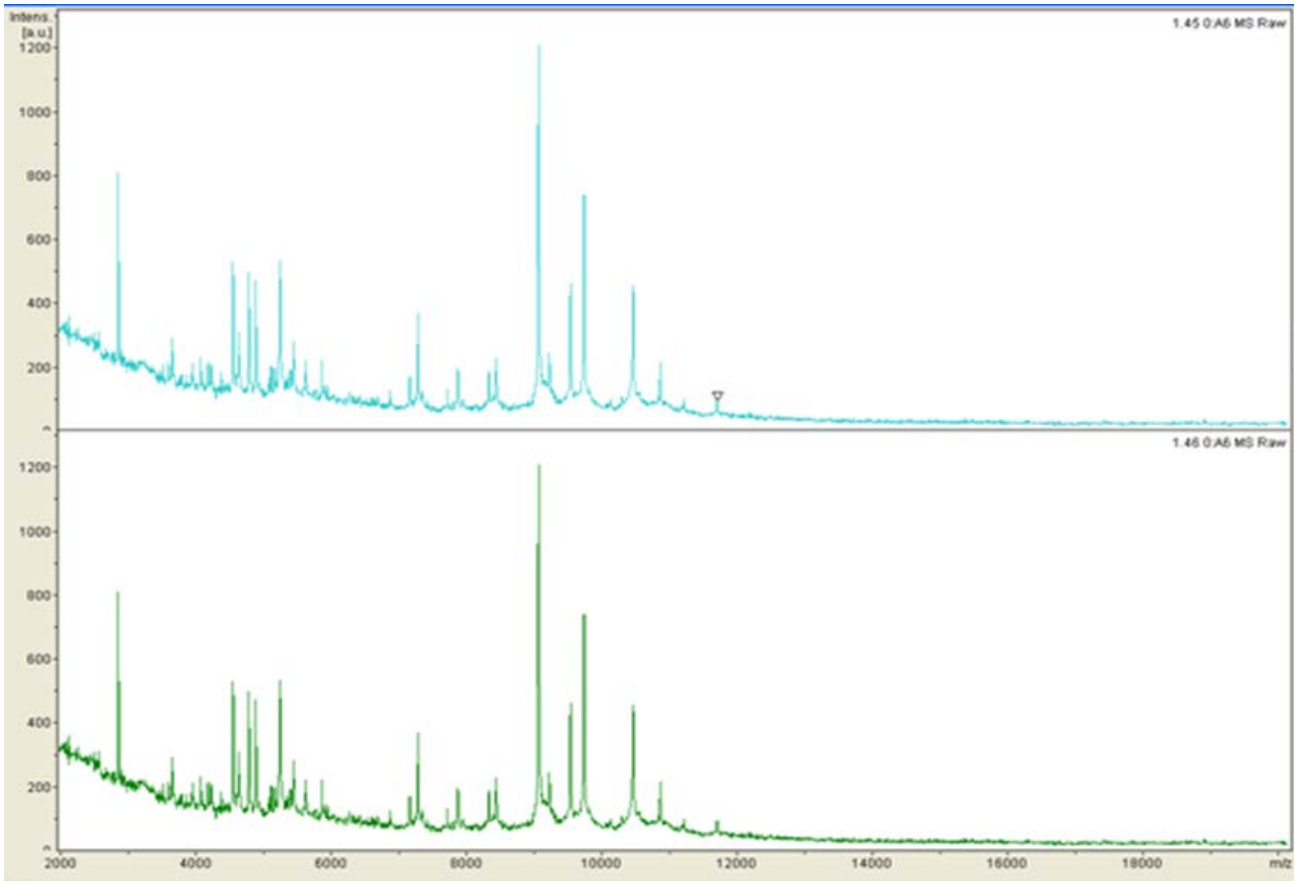

Figure 2. *Mass spectra of E. coli isolated from kidney tissue from the category "isolates before the experiment/isolates after the experiment".*

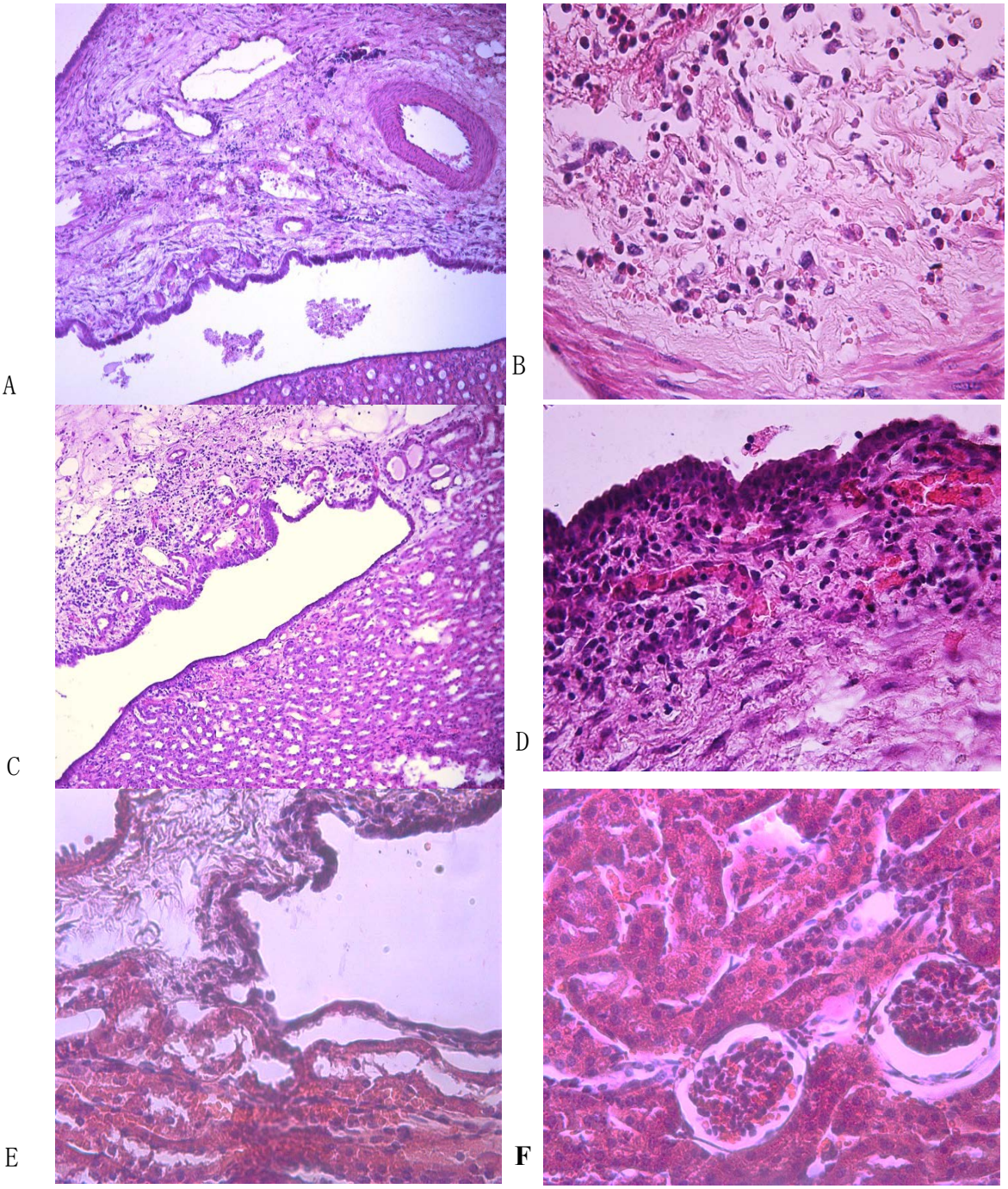

Figure 3. *Group I. Renal pelvis and calyces showing stromal edema and scattered lymphocytic infiltration. Staining: hematoxylin and eosin. Magnification: 200x (A). Group I. Stromal area of the renal pelvis showing stromal edema and vascular congestion. Staining: hematoxylin and eosin. Magnification: 400x (B). Group II. Renal pelvis and calyces with moderate lymphoid infiltration. Staining: hematoxylin and eosin. Magnification: 100x (C). Group II. Vascular congestion and lymphocytic and leukocytic infiltration in the ureteral wall. Staining: hematoxylin and eosin. Magnification: 400x (D). Group III. Blood vessels in the renal pelvis and calyces appear normal. Staining: hematoxylin and eosin. Magnification: 200x (E). Group IV. Overall histological structure is preserved, with evenly distributed renal corpuscles in the cortical layer and a columnar epithelium in the tubules. Staining: hematoxylin and eosin. Magnification: 200x (F).*

Discussion.

This study was a pilot project and had certain limitations and drawbacks. One of the main limitations was the limited sample size. The sample size for this segment of the study was determined based on the formula proposed by Charan J et al. [21].

Another limitation of this study was the limited observation period. The choice of a model with complete urethral occlusion was dictated by the need to reproduce the state of acute complete obstruction—a key factor in the pathogenesis of obstructive pyelonephritis. To minimize animal suffering, the experimental duration was deliberately limited to 72 hours. According to our pilot data, this prevents spontaneous death from bladder rupture (observed on day 4) and is sufficient for the development of characteristic pathological signs of acute renal infection.

All procedures were performed under anesthesia with daily monitoring of the animals' condition and were approved by the ethics committee.

The primary goal of our study was to model and compare two clinically significant conditions: obstructive and non-obstructive pyelonephritis. Therefore, the experimental design focused on groups with bacterial inoculation, which explains the absence of an "obstruction-only" control group. We recognize that such a group could have helped to more clearly distinguish the effects of the infectious and mechanical (obstructive) components.

In our previous study, a comparative analysis of two mechanisms of obstructive pyelonephritis development was also conducted, taking into account the nature of the pathomorphological changes in the kidneys and ureters by creating a model of obstructive pyelonephritis at the level of the ureter. The histological changes observed in the kidneys and ureters in the experimental groups with the ascending infection model were found to be similar to the findings of other researchers. The results of our previous study, where a model of obstructive pyelonephritis was created at the level of the ureter, determined that intestinal translocation plays a role in the development of obstructive pyelonephritis. On the third day, the morphological picture of the kidney and ureter in the ascending infection group was more pronounced than in the enterorenal translocation group. However, on the fifth day, marked inflammatory changes in the kidney and ureter tissue were present in both groups [22]. The study by Zeidan S et al. demonstrated that the introduction of both highly virulent and low-virulent strains of *E. coli* leads to severe kidney damage with fibrosis, replacement of medullary and cortical substance, and the development of ascending pyelonephritis with diffuse fibrosis. These results indicate significant changes in the kidneys in obstructive pyelonephritis, regardless of the virulence level of the *E. coli* strain [23]. Skowron B et al. developed an experimental model of acute renal failure caused by Escherichia coli-induced pyelonephritis. The results showed that the introduction of *E. coli* at specific concentrations leads to different forms of pyelonephritis and acute renal failure. Histopathological analysis of kidney samples revealed the presence of chronic pyelonephritis and tubulointerstitial nephritis with varying degrees of inflammation. In the study by Li et al. an acute pyelonephritis model was created in rats by simply introducing *E. coli* into the bladder without performing laparotomy. Microscopic examination of kidney samples obtained from the infected group at 3 days revealed a significant number of neutrophils and lymphocytes located beneath the mucous membrane of the renal pelvis and interstitial area. In the infected group at 7 days, a large number of lymphocytes and some eosinophils were also observed beneath the mucous membrane of the renal pelvis. At the same time, no apparent changes were detected in the glomeruli and renal tubules in both groups [24].

Conclusion.

Our study aimed to compare the role of ascending infection and intestinal translocation of *E. coli* in the development of acute obstructive pyelonephritis. The pathogenesis of obstructive pyelonephritis is a relevant issue in both clinical urology and urological research. Thus, our study further confirmed the role of ascending infection in the development of obstructive pyelonephritis. However, we did not encounter any studies demonstrating the impact of intestinal microbial translocation on the pathomorphological changes in acute pyelonephritis. Based on the results of our study, it can be concluded that obstruction acts as a trigger for the intestinal translocation of microorganisms into the urinary tract.

Author Contributions.

Conceptualization and methodology, M.T.; data curation Yu.P., Ye.Zh. and K.B.; writing-original draft preparation, Ye.Sh.; writing-review and editing, M.T. and Ye.T.; supervision, Ye.T. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest.

The authors declare no conflicts of interest.

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