

Results of dynamic monitoring of the spectrum of bacterial causes of acute urinary tract infections in children

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

The aim of the study: to explore in dynamics the structure of pathogens in children of Zaporizhzhia region with acute urinary tract infections and the possible changes in their antibiotic susceptibility.

Materials and methods. We analysed results of urine culture in 439 children aged 4 to 18 years with acute urinary tract infection (293 patients in 2014–2016 and 146 patients in 2018–2020). Determination of bacterial species and susceptibility to antibiotics was performed on a bacteriological analyzer VITEK 2 COMPACT (bioMerieux, France) using AES software: Global CLSI-based + Phenotypic (2014, 2018) in accordance with CLSI and EUCAST tables. The coefficient of antibiotic resistance was additionally calculated for each isolate.

Results. According to the analysis of bacteriological monitoring, it was found that in 2018–2020 compared to 2014–2016 among the causative agents of acute urinary tract infections in children, the role of gram-negative bacteria had raised due to increasing the proportion of *Escherichia coli* and *Proteus mirabilis*. Gram-positive microflora has been represented by bacteria of the genus *Enterococcus*, in 2018–2020 in most samples was isolated *Enterococcus faecium* (28.1 %), in 2014–2016 among the representatives *Enterococcus faecalis* prevailed (38.9 %).

The analysis of antibiotic resistance showed that in 2018–2020 the number of resistant strains of *E. coli* to amikacin increased 6.8 times to 2014–2016 ($P < 0.01$) and there was a decrease in the sensitivity of *Enterococcus* to aminopenicillins from 91.4 % to 41.3 % ($P < 0.01$). Among bacteria of the genus *Enterococcus* the average values of the coefficient of resistance to antibiotics in 2018–2020 increased 3.75 times compared to 2014–2016 due to a 2.3-fold increase in the frequency of multidrug-resistant strains ($P < 0.05$).

Conclusions. The obtained data are convincing evidence of the need for mandatory bacteriological examination of urine before antibacterial therapy to increase the effectiveness of therapeutic measures, prevention of the emergence and spread of antibiotic resistance. An increase in resistance of *E. coli* to amikacin and *Enterococcus spp.* to ampicillin does not allow the use of these drugs as empirical therapy of acute urinary tract infections in children.

Key words:

children, urinary tract infections, antibiotic resistance.

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Результати динамічного моніторингу спектра бактеріальних збудників гострих інфекцій сечовивідної системи у дітей

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Мета роботи – дослідити в динаміці структуру збудників гострих інфекцій сечовивідної системи у дітей Запорізької області та можливу зміну їхньої чутливості до антибіотиків.

Матеріали та методи. Здійснили аналіз результатів бактеріологічних засівів сечі 439 дітей віком від 4 до 18 років, які хворі на гостру інфекцію сечовивідної системи (293 пацієнти за період 2014–2016 рр. та 146 пацієнтів за 2018–2020 рр.). Визначення видів та чутливості бактерій до антибіотиків здійснили на бактеріологічному аналізаторі VITEK 2 COMPACT (bioMerieux, Франція) з використанням програмного забезпечення AES: Global CLSI-based + Phenotypic (2014, 2018) відповідно до таблиць SLSI та EUCAST. Для кожного ізоляту додатково розраховували коефіцієнт резистентності до антибіотиків.

Результати. Встановлено, що в 2018–2020 рр. порівняно з періодом 2014–2016 рр. серед збудників гострих інфекцій сечовивідної системи у дітей зросла роль грамнегативних бактерій внаслідок збільшення питомої ваги *Escherichia coli* та *Proteus mirabilis*. Грампозитивна мікрофлора представлена бактеріями роду *Enterococcus*, серед них у 2018–2020 рр. переважав *Enterococcus faecium* (28,1 %), а в 2014–2016 рр. в більшості проб виділяли *Enterococcus faecalis* (38,9 %).

У 2018–2020 рр. порівняно з 2014–2016 рр. збільшилась в 6,8 раза кількість резистентних штамів *Escherichia coli* до амікацину ($p < 0,01$) та відбулось зниження кількості культур ентерококів, чутливих до амінопеніцилінів, з 91,4 % до 41,3 % ($p < 0,01$). У 2018–2020 рр. коефіцієнт резистентності бактерій роду *Enterococcus* до антибіотиків збільшився в 3,75 раза щодо показника 2014–2016 рр. внаслідок збільшення в 2,3 раза частоти виділення мультирезистентних штамів ($p < 0,05$).

Висновки. Результати свідчать про необхідність обов'язкового бактеріологічного дослідження сечі перед початком антибактеріальної терапії гострих інфекцій сечовивідної системи у дітей для підвищення ефективності терапевтичних заходів і профілактики виникнення, зростання антибіотикорезистентності. Збільшення резистентності *E. coli* до амікацину та *Enterococcus spp.* до ампіциліну не дає змоги використовувати ці препарати як емпіричну терапію при цій патології.

Ключові слова:

діти, інфекції сечовивідної системи, антибіотико-резистентність.

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Urinary tract infections are the second most common infectious disease after respiratory pathology in medical practice, including children, affecting up to 150 million people worldwide every year [1,2] and is currently the second most common indication for antibiotic prescription [3]. According to these facts, frequent use of antibiotics in both the hospital and the outpatient settings, is causing the rise in antibiotic resistance worldwide, which increases the risk of treatment failures [1].

One of the leading reasons for the formation of antibiotic resistance and its progressive increase is mainly the irrational use of these drugs [4]. Given that, the choice of antibiotic to obtain the results of bacteriological examination of urine is mostly empirical, especially in outpatient treatment settings, indicators of susceptibility of pathogens to antibacterial drugs are important for the effective therapy of urinary tract infections. Importantly, if the level of resistance of any antibacterial drug in the region is more than 10 %, this is the reason for limiting its use as initial therapy [5], therefore, physicians need to know the main uropathogens they encounter in the treatment of urinary tract infections in children, and their sensitivity according to their territorial distribution.

Aim

The aim of the study was to explore in dynamics the structure of pathogens in children with acute urinary tract infections of Zaporizhzhia region and the possible changes in their antibiotic susceptibility.

Materials and methods

To analyze the structure of pathogens of acute urinary tract infections and the dynamics of their sensitivity to antibiotics, a study of urine cultures of 439 children with acute urinary tract infections who were hospitalized at the Zaporizhzhia Regional Children's Clinical Hospital in 2014–2016 and 2018–2020 was provided. During the period 2014 to 2016 293 patients and in 2018–2020 – 146 patients were examined.

The study material was the middle portion of naturally voided morning urine obtained after thorough toilet of the external genitalia. The material was delivered to the local laboratory in sterile, hermetically sealed containers.

Inclusion criteria: children aged 4 to 18 years (mean age was 10.1 ± 1.2 years in 2014–2016 and 10.4 ± 1.1 years in 2018–2020); the presence of the clinical picture of acute urinary tract infection; detection of the pathogen in the titers $> 10^5$ CFU/ml.

In all patients the diagnosis was confirmed by anamnesis, clinical-laboratory, X-ray, microbiological and ultrasound examination of the urinary system according to the protocol of the Ministry of Health of Ukraine (Order of the Ministry of Health of Ukraine No. 627 of 03.11.2008). The microbiological study was performed in the bacteriological laboratory of Zaporizhzhia Regional Children's Clinical Hospital. Uropathogens were cultured on ready-to-use Columbia blood agar (bioMérieux, France), selective chocolate agar (bioMérieux, France). Determination of species and susceptibility to antibiotics of gram-positive and gram-negative bacteria

was performed on a bacteriological analyzer VITEK 2 COMPACT (bioMérieux, France) using AES software: Global CLSI-based + Phenotypic (2014, 2018). Antibiotic susceptibility was considered in accordance with CLSI and EUCAST tables (Version 4.0–6.0; 8.0–10.0). According to the recommendations of EUCAST [6,7], to determine the sensitivity of *Escherichia coli*, ceftazidime was used as a marker antibiotic for the third-generation cephalosporins, and cefepime for the fourth generation. To characterize microorganisms, the generally accepted indicators “sensitive”, “moderately sensitive” and “resistant” were used.

The coefficient of antibiotic resistance was calculated for each isolate by the formula: $K = R / N$, where K is the antibiotic resistance coefficient, R is the number of antibiotics to which the studied isolate was resistant, N is the total number of antibiotics tested for this isolate. This indicator allows us to judge the relative integral resistance of strains of microorganisms to antibacterial drugs used in the study. The minimum value of the coefficient, which means the lack of resistance of strains of the studied microorganisms, is “0”, the maximum, which indicates the resistance of the pathogen to all drugs accepted in the study – “1”.

Mathematical analysis and statistical data processing were performed on a PC using the licensed software package Statistica for Windows 13.0 serial No. JPBZ804I382130ARCN10-J with the calculation of the arithmetic mean (M), standard deviation (σ) and mean error (m). Student's t-test as well as Fisher's angular transformation were used to assess differences in the compared groups. Differences were considered significant at $P < 0.05$.

All the conducted research complied with the ethical standards of the Institutional and National Research Committee and the Helsinki Declaration of 1964 and its subsequent amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. The complete set of data on children, their parents and doctors confirming the results of this study was not publicly available due to limited initial ethical approvals.

Results

According to the analysis of bacteriological monitoring, it was found that in 2018–2020 compared to 2014–2016 among the causative agents of acute urinary tract infections in children, the role of gram-negative bacteria had raised due to increasing the proportion of *Escherichia coli* and *Proteus mirabilis* (Table 1).

Gram-positive microflora in both periods of observation has traditionally been represented by bacteria of the genus *Enterococcus*. However, in 2014–2016 among the representatives of this genus of bacteria *Enterococcus faecalis* prevailed (38.9 %), in 2018–2020 in most samples was isolated *Enterococcus faecium* (28.1 %).

Depending on the nosology, it was found that in 2018–2020 *E. coli* was significantly more often the etiological causative agent of unspecified urinary tract infections and acute pyelonephritis compared to the period 2014–2016 (Table 2).

It should be noted that *P. mirabilis* in 2018–2020 was mainly isolated among patients with acute cystitis (26.7%), while in the previous analyzed period this agent was isolated only in 2 (1.3%) children with acute pyelonephritis and in no case with acute cystitis.

Bacteria of the *Enterococcus* genus in 2018–2020 compared to the period 2014–2016 were 1.5 times less likely to cause unspecified urinary tract infections, 4.9 times less common in acute cystitis and tended to decrease in acute pyelonephritis. But it should be emphasized once again that in 2018–2020, in contrast to the period 2014–2016, the development of enterococcal urinary tract infections was dominated by *E. faecium*, while *E. faecalis* was sown in isolated cases.

Given that the structure of the causative agents of acute urinary tract infections was dominated by strains of uropathogenic *E. coli* and bacteria of the *Enterococcus* genus, we analyzed the dynamics of the sensitivity of these microorganisms to antibiotics (Tables 3, 4).

The analysis of antibiotic resistance showed that in 2018–2020 the number of resistant strains of *E. coli* to amikacin increased 6.8 times to 2014–2016 ($P < 0.01$). At the same time, the number of susceptible strains to cefepime, meropenem, ceftazidime and ciprofloxacin significantly increased (Table 3). In 2018–2020 all isolates of *E. coli* were sensitive to tigecycline, while in 2014–2016 only 9.9% of *E. coli* strains were resistant or moderately sensitive to this antibiotic.

The analysis of the dynamic changes in antibiotic susceptibility of *Enterococcus spp.* strains in the period 2014–2016 demonstrated higher sensitivity to penicillins, vancomycin, nitrofurantoin, linezolid and tigecycline (Table 4).

However, in 2018–2020 there was a sharp decrease in the susceptibility of the genus *Enterococcus* bacteria to aminopenicillins from 91.4% to 41.3% due to 6.8 times increase of resistant strains ($P < 0.01$). It was noted that in 2018–2020, 6.5% of enterococcal strains were resistant to this antibiotic, which was the evidence for the emergence of antibiotic-resistant strains. In 2018–2020 bacteria of the genus *Enterococcus* were highly sensitive to nitrofurantoin, linezolid and tigecycline in the whole range of studied antibacterial drugs.

In 2014–2016, there was no guidelines for testing susceptibility of enterococci against imipenem, as it was believed that the susceptibility of enterococci to imipenem can be predicted from the results of penicillin or ampicillin activity, so testing imipenem in clinical laboratories is not necessary [8]. At the same time, the study of the sensitivity of the genus *Enterococcus* bacteria to imipenem in 2018–2020 demonstrated that no strain was sensitive to this antibiotic: 89.1% of enterococcal strains were moderately sensitive to imipenem, and 10.9% of strains were imipenem-resistant.

It should also be noted that the coefficient of resistance to antibiotics of *E. coli* strains did not change during both periods (Table 5), and among bacteria of the genus *Enterococcus* the average values of this coefficient in 2018–2020 increased 3.75 times compared to 2014–2016 due to a 2.3-fold increase in the frequency of multidrug-resistant strains ($P < 0.05$).

Table 1. Etiological structure of pathogens of acute urinary tract infections in children

Group of microorganisms Absolute number of strains	2014–2016, n = 293		2018–2020, n = 146	
	Absolute number of strains	% of the number of all isolated strains	Absolute number of strains	% of the number of all isolated strains
Gram-negative microorganisms				
<i>Escherichia coli</i>	117	39.9	78	53.4**
<i>Enterobacter cloacae</i>	2	0.7	2	1.4
<i>Klebsiella pneumoniae</i>	30	10.2	12	8.2
<i>Proteus mirabilis</i>	2	0.7	8	5.5**
<i>Acinetobacter baumannii</i>	2	0.7	0	0
<i>Pseudomonas aeruginosa</i>	7	2.4	0	0
Total	160	54.6	100	68.5**
Gram-positive microorganisms				
<i>Enterococcus faecalis</i>	114	38.9	5	3.4**
<i>Enterococcus faecium</i>	19	6.5	41	28.1**
Total	133	45.4	46	31.5**

*: $P < 0.05$ compared to 2014–2016; **: $P < 0.01$ compared to 2014–2016.

Table 2. Monitoring the structure of pathogens of acute urinary tract infections depending on the nosology, (%)

Agent	2014–2016, n = 293			2018–2020, n = 146		
	UUTI, n = 104	AC, n = 31	AP, n = 158	UUTI, n = 87	AC, n = 15	AP, n = 44
<i>Escherichia coli</i>	37.5	38.7	41.8	50.6*	46.7	61.4**
<i>Enterobacter cloacae</i>	0.96	0	0.6	2.3	0	0
<i>Klebsiella pneumoniae</i>	7.7	29.0	8.2	8.0	20.0	4.5
<i>Proteus mirabilis</i>	0	0	1.3	3.4	26.7**	2.3
<i>Acinetobacter baumannii</i>	1.9	0	0	0	0	0
<i>Pseudomonas aeruginosa</i>	0	0	4.4	0	0	0
<i>Enterococcus spp.</i>	51.9	32.2	43.6	35.6*	6.6**	31.8
<i>Enterococcus faecalis</i>	38.4	19.3	43.0	3.4**	0	4.5**
<i>Enterococcus faecium</i>	13.5	12.9	0.6	32.2**	6.6	27.3**

*: $P < 0.05$ compared to 2014–2016; **: $P < 0.01$ compared to 2014–2016; UUTI: undefined urinary tract infections; AC: acute cystitis; AP: acute pyelonephritis.

Table 3. The dynamics of sensitivity to antibacterial drugs of *Escherichia coli* strains isolated from children with acute urinary tract infections

Antibiotic	2014–2016, n = 117			2018–2020, n = 78		
	R, %	I, %	S, %	R, %	I, %	S, %
Amykacin	3.2	0	96.8	21.7**	0	78.3**
Cefepime	26.7	16.7	56.6	17.4	0	82.6**
Ceftazidime	37.2	10.1	52.7	13.0**	10.9	76.1**
Meropenem	8.7	13.5	77.8	2.2*	2.2**	95.6**
Ciprofloxacin	13.3	10.5	76.2	8.7	0	91.3**
Nitrofurantoin	1.6	7.1	91.3	2.2	0	97.8
Tigecycline	5.4	4.5	90.1	0	0	100*

*: $P < 0.05$ compared to 2014–2016; **: $P < 0.01$ compared to 2014–2016; R: resistant strains; I: moderately sensitive strains; S: sensitive strains.

Table 4. Dynamics of sensitivity of the genus *Enterococcus* bacteria isolated from children with acute urinary tract infection to antibacterial drugs

Antibiotic	2014–2016			2018–2020		
	R, %	I, %	S, %	R, %	I, %	S, %
Ampicillin	8.6	0	91.4	58.7**	0	41.3*
Imipenem	X	X	X	10.9	89.1	0.0
Vancomycin	0	0	100	6.5	0	93.5*
Nitrofurantoin	3.1	3.1	93.8	0	0	100
Linezolid	0	0.9	99.1	2.1	2.1	95.8
Tigecycline	0	1.2	98.8	0	0	100

*: $P < 0.01$ compared to 2014–2016; R: resistant strains; I: moderately sensitive strains; S: sensitive strains; X: testing was not performed.

Table 5. Isolation frequency of multidrug-resistant strains of *Escherichia coli* and *Enterococcus spp.* and the coefficient of resistance to antibiotics

Etiological factor	2014–2016		2018–2020	
	Frequency of isolation	Coefficient of resistance	Frequency of isolation	Coefficient of resistance
<i>Escherichia coli</i>	14.4 %	0.12 ± 0.01	15.4 %	0.11 ± 0.02
<i>Enterococcus spp.</i>	5.6 %	0.04 ± 0.007	13.0 %*	0.15 ± 0.02*

*: P < 0.05 compared to 2014–2016.

Discussion

The obtained results has demonstrated that in 2018–2020, as well as in 2014–2016, the most common uropathogen involved in the development of acute urinary tract infections in children was *E. coli*. Results are relatively similar to most other comparative studies on the etiological structure of urinary tract infections [1,4]. This prevalence of the pathogen connected to the fact that *E. coli* has several types of adhesives that improves sticking of the pathogen to the uroepithelium, despite the flushing effect of urine flow [9].

Based on our data, sensitivity of *E. coli* in the dynamics of the observation improved to the most of antibacterial drugs used in the treatment of urinary tract infections in children. At the same time, there was a high level of resistance of this microorganism in 2018–2020 to amikacin (21.7 %), cefepime (17.4 %) and ceftazidime (13.0 % of resistant and 10.9 % of moderately sensitive strains), which is probably due to the frequent use of these antibiotics as drugs for initial therapy. The obtained results indicate the irrationality of the use of these groups of antibiotics for empirical therapy of patients with acute urinary tract infections due to the level of *E. coli* resistance to the antibacterial drugs listed above that is more than 10 %. Interestingly, the resistance is 8.7 % of *E. coli* strains isolated from children's urine to ciprofloxacin, a drug contraindicated before the age of 12 due to the risk of musculoskeletal disorders and used as a second- and third-line drug for the treatment of complicated urinary tract infections. At the same time, high sensitivity to meropenem (95.6 %), nitrofurantoin (97.8 %) and tigecycline (100.0 %) remained.

The most important mechanism of *E. coli* resistance to cephalosporins is associated with production of extended spectrum β -lactamases, which led to the development of partial resistance of *E. coli* to III–IV generation cephalosporins [10]. The resistance of enterobacteria to this group antibiotics can be caused by mutations or presence of mobile DNA elements such as plasmids, transposons and integrons [11]. Another mechanism of antibiotic resistance is the ability of *E. coli* to form a biofilm that protects the pathogen from the host's immune system [12].

E. coli resistance to aminoglycosides is thought to be related to several mechanisms: genomic mutations that alter the respiratory chain or activate outflow pumps and changes in ribosome binding due to decreased permeability and inactivation of enzymes [4]. A recent experimental study showed that the *E. coli* AAC (6')-Ib-cr resistance gene can also significantly reduce the bactericidal activity of amikacin in vitro [13].

The main role in the development of resistance to quinolones and fluoroquinolones in *E. coli* is played

by mutations in the area that determines resistance to quinolones (QRDR), which change the target of the drug, reduce the concentration of antibiotics in bacterial cells due to efflux pumps by modifying inflows and outflows; and the acquisition of plasmid-mediated resistance genes (PMQRs), which produce a protein that protects quinolone targets from inhibition [14,15]. In addition, a high frequency of resistance to fluoroquinolones was found among isolates of *E. coli* producing extended-spectrum β -lactamases, indicating cluster transfer of resistance genes [15].

As well as *E. coli* is the leading pathogen of urinary tract infections in both outpatients and inpatients, a significant proportion of enterococci in the structure of pathogens of acute urinary tract infections also attracts attention [16]. Despite their low virulence, these microorganisms belong to the group ESCAPE, which are important as pathogens of nosocomial infections [17,18].

Compared to other reports in Northern and Eastern Europe [19], where the second most common uropathogen was *E. faecalis*, our study found a change in the ratio of *E. faecalis* / *E. faecium* as an etiological factor in acute urinary tract infections in children in favor of *E. faecium*. The obtained data coincide with the results of other studies, which show the growing etiological role of *E. faecium* in the occurrence of enterococcal infection [20]. The predominance of this species among gram-positive microflora in urinary tract infections, first of all, can be explained by its natural antibiotic resistance to cephalosporins and aminoglycosides – drugs most commonly used in the treatment of this pathology [20]. At the same time, due to the high plasticity of the genome and the ability to form a biofilm, it can also acquire many other resistances, including resistance to vancomycin [16]. Vancomycin resistant *E. faecium* was categorized as high priority pathogens for which new and effective treatments are needed [21]. In many countries around the world, an increase in the number of infections caused by vancomycin-resistant enterococci is reported [22,23]. Enterococci become resistant to vancomycin by acquiring genes through plasmid or transposon that enable bacteria to bypass antibiotic susceptible critical steps in cell wall formation [24]. The resistance genes can be passed on to various Enterococci species and even to other genera, such as Staphylococci, through conjugation [25]. Various factors that increase the risk of infection with vancomycin-resistant enterococci in a medical intensive care unit include prolonged hospitalisation, younger age, use of ceftriaxone and vancomycin [26]. Hospital workers can also transmit Vancomycin resistant *E. faecium* because it can persist on fingers for about 30 minutes even after hands washing [24]. Moreover, according to the 2014 ESPGHAN consensus, probiotics containing the *E. faecium* SF68 strain are classified as negatively recommended for the use in children due to the fact that this isolate is a possible recipient of vancomycin resistance genes [27].

It is noteworthy that most modern isolates of *E. faecium* are highly resistant to ampicillin [20]. We got similar results indicated that ampicillin-resistant strains of *Enterococcus* genus increased from 8.6 % in 2014–2016 to 58.7 % in 2018–2020.

Although imipenem is thought to be clinically effective against enterococcal infections, including those caused

by *E. faecium*, and ampicillin-sensitive strains of *Enterococcus* genus are presumably susceptible to imipenem [9,28–30], studies have reported that ampicillin susceptibility testing cannot be used to predict susceptibility to imipenem due to increased resistance of *Enterococcus* spp. to β -lactam antibiotics [31,32]. This conclusion is fully consistent with results of our study, which showed that most enterococcal isolates (89.1 %) were moderately sensitive, 10.9 % of isolates were resistant and in no case enterococcal strains were sensitive to imipenem, which limits the use of it, as well as ampicillin, in the treatment of acute urinary tract infections in children. *Enterococcal* resistance to imipenem and ampicillin has been shown to be associated with major mechanisms of antibiotic resistance, such as β -lactamase production and penicillin-binding protein overproduction (PBP4 or PBP5) [33,34]. Another problem in the treatment of urinary tract infections caused by different species of enterococci is the proliferation of multidrug-resistant strains, which greatly complicates therapy and, unfortunately, is a manifestation of the global trend of increasing antibiotic resistance [16].

Thus, the monitoring of pathogens and analysis of their sensitivity to antibiotics revealed certain trends and the most effective antibacterial drugs for the treatment of acute urinary tract infections in children before determining the antibiotic susceptibility.

Conclusions

1. In children with acute urinary tract infection, along with *E. coli* and other gram-negative microorganisms with high frequency and gram-positive microflora, mainly of the genus *Enterococcus* which must be taken into account, especially in the ineffectiveness of standard initial antibacterial therapy.

2. The obtained data on the characteristics of the spectrum of bacterial pathogens of the urinary system are convincing evidence of the need for mandatory bacteriological examination of urine before antibacterial therapy to increase the effectiveness of therapeutic measures, prevention the emergence and spread of antibiotic resistance.

3. The results of monitoring the susceptibility of uropathogens to antibacterial drugs indicate an increase in resistance of *E. coli* to amikacin and *Enterococcus* spp. to ampicillin, which does not allow the use of these drugs as empirical therapy of acute urinary tract infections in children.

4. The results presented in this paper suggest that third-generation cephalosporins have retained the ability to act as the drug of choice, but when a level of resistance of more than 15 % is reached, this issue should be reconsidered.

Prospects for further research. Investigation of the spectrum of pathogens and their susceptibility to antibiotics in chronic urinary tract infections in children, and further monitoring of pathogens of acute urinary tract infections in children with assessment of their antibiotic susceptibility to prevent an increase in antibiotic resistance of microorganisms and rational choice of etiological therapy.

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