

# Management of antibacterial therapy of infectious and inflammatory diseases of the urinary tract in children and regional peculiarities during the COVID-19 pandemic

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## ABSTRACT

Urinary tract infections (UTIs) remain an urgent issue in clinical pediatrics. Empirical selection of antibacterial therapy becomes more complicated, and antibacterial drug indication is not always clinically substantiated. This study aimed to compare the antibacterial susceptibility pattern of the main group of urinary tract infectious agents from 2009–2016 with intermediate results from 2020–2021, during the COVID-19 pandemic, among children in the Chernivtsi region. Urine samples were collected from 3089 children (0–17 years old) treated at the health care institutions in the Chernivtsi region (2009–2016). The clinical-laboratory examination of 177 children (0–17 years old) was carried out from 2020 to 2021. The children received specialized medical care at the Department of Nephrology. Preliminary data of regional monitoring (2020–2021) are not considerably different from the previous regional susceptibility of antibiotics: to penicillin ( $p < 0.01$ ), II-III generation cephalosporin ( $p < 0.01$ ); an increased resistance to levofloxacin ( $\chi^2 = 4,338$ ;  $p < 0.01$ ), tetracycline –  $\chi^2 = 7,277$ ;  $p < 0.01$ ; doxycycline –  $\chi^2 = 5,309$ ;  $p < 0.01$ ) and imipenem –  $\chi^2 = 5,594$ ;  $p < 0.01$ ). The data obtained did not explain an increased resistance to fluoroquinolones completely (ofloxacin, pefloxacin, ciprofloxacin), except for levofloxacin ( $\chi^2 = 4,338$ ;  $p < 0.01$ ). A reliable difference of susceptibility of tetracycline group was registered (tetracycline –  $\chi^2 = 7,277$ ;  $p < 0.01$ ; doxycycline –  $\chi^2 = 5,309$ ;  $p < 0.01$ ). Furthermore, there was a regional increase in some UTI-pathogen strains resistant to carbapenems (imipenem –  $\chi^2 = 5,594$ ;  $p < 0.01$ ). The use of antibiotics from the group of penicillins and II-III generation cephalosporins as the starting antibacterial therapy for STIs during the COVID-19 pandemic should be justified. A regional increase (2020–2021) of some uropathogenic strains resistant to carbapenems administered to treat severe bacterial infections requires their exclusively designated purpose in everyday pediatric practical work.

**KEYWORDS:** urinary tract infections, COVID-19, antibiotic resistance, children.

INTRODUCTION

Antibiotic resistance to the main agents of infectious diseases is one of the greatest problems in modern medicine [1–3]. Antibiotics are widely used in modern medicine since these increase life expectancy, especially in a significantly vulnerable group of older people who have been disproportionately affected by the current COVID-19 pandemic. Antibiotic resistance both during and after these events is well recognized [4–6].

The use of antibacterial therapy is not always clinically justified according to antibacterial sensitivity. Urinary tract infections (UTIs) remain an urgent issue in clinical pediatric sections. Empirical selection of antibacterial therapy becomes more complicated, and administration of an antibacterial drug is not always clinically substantiated [7–16].

MATERIAL AND METHODS

This study aimed to compare the susceptibility of antibacterial drugs to the main groups of urinary tract infectious agents from 2009–2016 with intermediate results from 2020–2021 among children in the Chernivtsi region during the COVID-19 pandemic. We studied the etiological structure of uropathogens – UTI pathogens among children in the Chernivtsi region from 2009–2016 and 2020–2021. Urine samples were collected from 3089 children (0–17 years old) in the Chernivtsi region (2009–2016). Clinical-laboratory examination of 137 children (0–17 years old) who received specialized medical care at the Department of Nephrology during 2020–2021 was performed. There were 102 (74.45%) children with infectious-inflammatory urinary tract diseases (the diagnosis was made according to ICD-10: No.10-11.1) as follows: kidney infection including No.10 acute tubulointerstitial nephritis – 52 patients; No.11 chronic tubulointerstitial nephritis – 21 patients; No.11.1 chronic obstructive pyelonephritis – 8 patients; No.30.0 acute cystitis – 10 patients; No.30.1 chronic cystitis – 11 patients) and 35 (25.55%) children with non-infectious diseases of the urinary tract (according to ICD-10: N00 acute nephrotic syndrome – 6 patients; No.03 chronic nephrotic syndrome – 5 patients; No.04 nephrotic syndrome – 10 patients; No.15; other renal tubulointerstitial diseases – 3 patients; No.18 chronic renal failure – 6 patients; No.39.2 orthostatic proteinuria, not specified – 2 patients; R30 pain associated with urination – 1 patient; R30.1 tenesmus of the urinary bladder – 1 patient; R32 enuresis, not specified – 1 patient).

RESULTS

Preliminary intermediate data of the regional monitoring (2020–2021) of antibiotic susceptibility to UTI-pathogens and

*Enterobacteriales* family in particular as leading etiological agents among children in the Chernivtsi region during the COVID-19 pandemic did not considerably differ from previous screening (2009–2016), namely to penicillin ( $p < 0.01$ ), and II-III generation cephalosporin ( $p < 0.01$ ) [17, 18].

The data obtained from 2020 to 2021 did not reveal increased resistance to fluoroquinolones completely (ofloxacin, pefloxacin, ciprofloxacin), except levofloxacin ( $\chi^2 = 4,537$ ;  $p < 0.01$ ). A reliable difference of sensitivity to the tetracycline group was registered (tetracycline –  $\chi^2 = 7,307$ ;  $p < 0.01$ ; doxycycline –  $\chi^2 = 5,369$ ;  $p < 0.01$ ). A regional increase of some UTI-pathogen strains resistant to carbapenems (imipenem –  $\chi^2 = 5,613$ ;  $p < 0.01$ ) was also registered.

Preliminary intermediate results from the clinical-laboratory examination of 137 children (0–17 years) in 2020–2021, who received specialized medical care at the Department of Nephrology, found a reliable difference in the etiological structure of the microbiota in the urine of children with infectious-inflammatory diseases of the urinary tract: *gram-positive cocci* –  $n = 21$  (21.0%),  $p = 0.042$ ; *enterobacteria* –  $n = 26$  (25.0%),  $p = 0.012$ ; *resident microbiota* –  $n = 17$  (17.0%),  $p = 0.000$  compared with isolation of UTI-pathogens in case of non-infectious disease of the urinary tract in children: *gram-positive cocci* –  $n = 5$  (14%); *enterobacteria* –  $n = 2$  (6.0%); *resident microbiota* –  $n = 26$  (74.0%) (Table 1).

DISCUSSION

Antibiotic resistance is an urgent problem, and it has become relevant during the coronavirus infection pandemic. A rational approach to the choice of antibacterial therapy during the COVID-19 pandemic improves the clinical picture, reduces the cost of treatment for each patient, and helps maintain the sensitivity of pathogens in the long term [19].

The intermediate results of regional monitoring (2020–2021) of antibiotic resistance among children in the Chernivtsi region raise certain concerns about the increase of some uropathogenic strains resistant to carbapenems (imipenem –  $\chi^2 = 5,613$ ;  $p < 0.01$ ). This is relevant given the growing resistance to carbapenems during the COVID-19 pandemic [20, 21].

Carbapenems are used to treat severe bacterial infections caused by gram-negative causative agents resistant to antibacterial therapy. Nowadays, the treatment of gram-negative infections, including those with multiple pharmacological resistance, should be based on information about regional antibiotic susceptibility and the local epidemiological picture. The presence of carbapenems in the doctor's arsenal is an important support in the context of pandemic multidrug resistance as it requires investigation of specific algorithms and improvement tactics to administer antibacterial drugs. Therefore, major factors to consider in administering carbapenems are cooperation between doctors and

Table 1. The etiological spectrum of UTI-pathogens in children with diseases of the urinary tract examined during 2020–2021.

Structure of the etiological spectrum of UTI-pathogens isolated	Infectious-inflammatory diseases of the urinary tract (n=102)		Non-infectious-inflammatory diseases of the urinary tract (n=35)		p
	abs., n	%	abs., n	%	
Lack of growth	38	37%	5	14%	0.012
Gram-positive cocci	21	21%	2	6%	0.042
Enterobacteria	26	25%	2	6%	0.012
Resident microbiota	17	17%	26	74%	0.000

microbiologists, finding the focus of infection before empirical therapy indication, and considering the synergic effects of antibiotics for a combined therapy [22, 23].

## CONCLUSIONS

Administration of potentially pathogenic therapy (*e.g.*, antibiotics from the group of penicillins and II-III generation cephalosporins as starting antibacterial therapy in children) should be carefully managed due to recent increases in regional antibiotic resistance of uropathogens. Bacterial strains resistant to carbapenems used to treat severe infections during the COVID-19 pandemic also require strict risk-benefit consideration in everyday pediatric clinical practice. Dynamic monitoring and surveillance of regional antimicrobial resistance should be enforced and used to inform clinical practice and contain the phenomenon.

## ACKNOWLEDGMENTS

### Conflict of Interest

The authors declare no conflict of interest.

### Ethical approval

The study was approved by the Institutional Review Board of BSMU (No.5 from 17.02.2022).

### Consent to participate

Written informed consent was obtained from the participants.

### Authorship

VVB contributed to conceptualizing, the methodology, writing the original draft and data analysis. IDS contributed to conceptualizing, methodology and writing the original draft. OSG contributed to data collection, data curation and editing the manuscript. OHB, OIP, LMH, OVM, OYV, MMH, MIV, SVY, MDH, TSB, LVR contributed to data collection and curation. NIV and MIS contributed to editing the manuscript.

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