

Multidrug-Resistant Microorganisms Associated with Urinary Tract Infections Following Orthopaedic Patients: A Laboratory-Based Analysis of 5239 Patients

Grzegorz Ziółkowski

Sosnowiec Medical College, Sosnowiec, Poland

Iwona Pawłowska

St. Barbara Specialized Regional Hospital No.5, Division of Microbiology and Epidemiology, Sosnowiec, Poland

Michał Stasiowski

1. Clinical Department of Anaesthesiology and Intensive Therapy, Faculty of Medical Science in Zabrze, Medical University of Silesia, Katowice, Poland. 2. Department of Anaesthesiology and Intensive Therapy, St. Barbara Memorial Regional Hospital, Sosnowiec, Poland

Estera Jachowicz (✉ estera.jachowicz@doctoral.uj.edu.pl)

Uniwersytet Jagiellonski w Krakowie Collegium Medicum <https://orcid.org/0000-0002-1067-9964>

Tomasz Bielecki

Medical University of Silesia, Katowice, Poland

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Abstract

Background: The risk of healthcare associated infections (HAI) in surgical wards remains closely related to the type of surgery and procedures performed on patients. They also condition the risk of various, apart from the most common, surgical site infections, forms of clinical infections, especially urinary tract infections (UTIs). Their occurrence in orthopedic patients is most often – in about 70%-80%, associated with the use of the bladder catheter in the perioperative period. The aim of this study was the epidemiological and microbiological analysis of UTIs following orthopedic patients, especially MDR in 2013-2015.

Methods: The study was conducted in 38-bed Department of Orthopedic-Traumatic Surgery in Sosnowiec, Poland. 5 239 patients surgery included in the study, the urinary catheter utilization rate was 30.7 %. Laboratory based study using the UTI definition of the HAI-Net program, MDR was defined as resistant to at least one antibiotic from 2< antibiotics groups. The results were analyzed using the statistical package PQStat ver. 1.6.0.428 using the chi-square test (χ^2) or Fisher's exact test.

Results The UTI incidence was 3.2% (168 cases), CA-UTI incidence density was 9.6/1 000 catheter-days. The highest risk of UTI was found in patients aged 75 years and older. Gram-negative flora prevailed among microorganisms: 76.1%. Predominantly isolated *Enterobacterales* were: *Escherichia coli*, *Klebsiella pneumoniae*. Isolated microorganisms were fully sensitive to carbapenems. Gram-negative bacilli showed the lowest sensitivity to extended substrate spectrum penicillins and fluoroquinolones: 37-64%, trimethoprim-sulfamethoxazole: 50%; MDR prevalence: 24.4%.

Conclusions The presented data indicate that UTI incidence is a significant problem in studied population, as well as antimicrobial resistance, especially to quinolones and extended spectrum cephalosporins, as first-line therapy remains a major challenge. To reduce the problem of high UTI incidence and MDR prevalence, the priority should be the reduction of UTI risk – which exceeded the expected values.

Background

The risk of healthcare associated infections (HAI) in surgical wards remains closely related to the type of surgery and procedures performed on patients. They also condition the risk of various, apart from the most common, surgical site infections, forms of clinical infections, especially urinary tract infections (UTIs). Their occurrence in orthopedic patients is most often – in about 70%-80%, associated with the use of the bladder catheter (CA-UTI, catheter-associated urinary tract infections) in the perioperative period [15]. Each element of the bladder catheterization procedure involves the risk of introducing microorganisms from the microbiota of the urethral mucosa. Therefore, effective CA-UTI prophylaxis associated with proper decontamination of skin and mucous membranes during the procedure of introducing the catheter into the bladder is of great importance [20, 18, 25].

Both UTI and CA-UTI are caused by both Gram-negative and Gram-positive bacteria, as well as by some fungi, viruses and protozoa, but Gram-negative bacilli dominate, including *Escherichia coli*, responsible for about 80% cases of all UTIs and other Gram-negative bacilli, including multi-drug resistant strains, such as *Proteus mirabilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterobacter spp.*, as well as enterococci and staphylococci [18, 10].

The analysis of etiological factors and their sensitivity to antibiotics and risk factors for the development of UTIs, as well as constant monitoring of the occurrence of UTI is the basis for surveillance of HAIs and implementation of rational methods of HAIs control and prevention [25], also in the orthopedic department.

The aim of this study was the epidemiological and microbiological analysis of UTIs in patients undergoing surgery in the orthopedic department together with a description of the drug sensitivity of the etiological factors of UTIs. In addition, the use of catheterization procedures was analyzed for patients both in the perioperative period and for catheterization for other reasons. The authors' experiences have already been partially discussed, however, they only concerned surgical site infections without taking into account the different types of HAIs [21].

Materials And Methods

The study of the incidence of urinary tract infections was carried out in the years 2013–2015 in a 38-bed Clinical Department of Orthopedic, Trauma, Oncological and Reconstructive Surgery of the Provincial Specialist St. Barbara Hospital No. 5 in Sosnowiec. A total of 5 239 patients were operated on in the studied period (51 170, patient-days, pds). Each of the operated patients had a catheter in the perioperative period, both insertion and removal took place within the ward, outside the operating theater. At the study time, the hospital did not use a closed bladder drainage system, the catheter was usually used for 48 hours in the perioperative period.

Retrospective analysis of urinary tract infections (UTI) was conducted on the basis of prospective microbiological surveillance – a laboratory based study in cooperation with the Hospital Infections Control Team using the definition of the HAI-Net program implemented by ECDC [7]. The decision about the collecting the sampling and culture was made each time by the treating physician, based on clinical symptoms. Symptomatic UTI – without an asymptomatic bacteriuria – was diagnosed and classified as symptomatic infections: microbiologically confirmed or without microbiological confirmation based on the uniform definitions issued by the ECDC, a catheter-associated UTI (CA-UTI) was defined as a symptomatic UTI in which the positive culture was taken when an indwelling urinary catheter had been in place for more than 48 hours [7].

Only unique isolates were selected for microbiological analysis, excluding subsequent cultures from the same patient and UTI case. Antibiotic susceptibility testing was performed using the Phoenix 100 automated system (Becton Dickinson, Warsaw, Poland). Combo panels NMIC/ID and PMIC/ID were used to identify and determine sensitivity.

Antibiotic susceptibility tests were interpreted in accordance with the EUCAST recommendations valid for the relevant calendar year, i.e. version 3.1 (2013), then 4.0 (2014) and 5.0 (2015) [9]. Intermediately sensitive isolates for a given antibiotic were classified as resistant [8]. The extended spectrum beta-lactamases (ESBL) were detected by double disc synergy test (DDST) using 30 µg ceftazidime and 30 µg cefotaxime placed at a distance of 2 cm (between centers) from the disc with amoxicillin with clavulanic acid 20/10 µg. To increase the sensitivity of the test, discs with aztreonam 30 µg and cefepime 30 µg were added [3].

Bacteria belonged to the multidrug-resistant (MDR) category, i.e. resistant to at least one antibiotic from three or more groups of antibacterial drugs and extensively drug resistant (XDR), i.e. antibiotic-sensitive to one or two groups of drugs only.

The epidemiological analysis of data took into consideration the following indicators [7]: UTI incidence rate, calculated using the following formula: $(N \text{ of UTI} \times 100) / N \text{ of operations}$; CA-UTI rate: $N \text{ of CA-UTI} \times 1000 / N \text{ of urinary catheter days}$ and urinary catheter utilization rate: $N \text{ of urinary catheter days} / N \text{ of patient-days}$.

In the statistical analysis, the number and percentage of individual variants was used. The results were analyzed using the statistical package PQStat ver. 1.6.0.428 using the chi-square test (χ^2) or Fisher's exact test. Analyses of changes in individual multi-drug resistant strains were analyzed by estimating Tau-Kendall's rank correlation coefficients. $p = 0.05$ was considered significant.

The use of data was approved by the Bioethical Committee of Sosnowiec Medical College in Sosnowiec (No. PW/WSM/36/17). All data entered into the electronic database and analyzed in this study were previously anonymised.

Results

168 UTI cases were diagnosed, including 151 CA-UTI cases, the urinary catheter utilization rate was 30.7%. The UTI incidence rate was 3.2%, and CA-UTI incidence density was 9.6 per 1 000 catheter-days. 209 strains of various pathogenic species considered to be UTI etiological factors were analyzed. In 5 cases of UTI, the etiological factor was not isolated. Gram-negative microorganisms (76.1%) dominated among isolated microorganisms, among them *Enterobacteriaceae* from the *Enterobacterales* ord family. nov.: *Escherichia coli*, *Klebsiella pneumoniae* and from the *Morganellaceae* family: *Proteus mirabilis*, as well as non-fermenting rods - *Pseudomonas aeruginosa*. *Enterococcus faecalis* dominated among Gram-positive flora. In 16 patients (7.7% of all UTIs), yeast infection was confirmed (Table I) and 6 (37.5%) cases involved women.

Isolated microorganisms showed full sensitivity to carbapenems, linezolid and glycopeptides over the study period. Gram-negative bacilli showed the lowest sensitivity to penicillins with extended spectrum and quinolones: 37–64% and trimethoprim-sulfamethoxazole: 50%. The lowest total sensitivity was shown by *K. pneumoniae* strains, which showed high resistance, in addition to the above-mentioned ones

also to the third generation cephalosporins (cefotaxime and ceftazidime), penicillins in combination with beta-lactamase inhibitors and aminoglycosides (Table II). The prevalence of drug-resistant microorganisms was 24.4% and remained at a similar level during the study period ($\tau = -0.3333$, $p = 0.6015$). MDR strains were isolated on average on day 19 after admission to hospital. The rarely isolated non-fermenting *Acinetobacter baumannii* and second in terms of isolation frequency *Klebsiella pneumoniae* had the highest prevalence of MDR, respectively 77.8% and 65.6% (Table III).

Discussion

UTIs are the second most common postoperative complication of patients treated in orthopedic wards, more common than deep venous thrombosis, pneumonia or renal failure [11, 1]. The risk of major postoperative complications such as surgical site infections (SSIs) after orthopedic surgery is estimated from 1.4% to over 20%. In the studied center, SSI incidence rate was 6.6%, about 6 times higher as compared with European HAI-Net [21].

Unfortunately, the presented data indicate that in the studied department, the epidemiology of the UTI is also a significant problem, e.g. according to the data of the American NHSN program regarding the departments of orthopedics and traumatology, CA-UTI incidence density was more than three times lower [5]. In the European ECDC infection surveillance program, the CA-UTI incidence rate was 4.1 per 1000 patient-days, hence it was more than twice lower than in the examined ward – in spite that it concerns intensive care units [6].

The data obtained in this study are also significantly higher than in another comparable hospital in Poland [13].

Unfortunately, the problem may have been the bladder catheterization procedure used in this ward, which has never been validated, hence the conclusion about the need for systematic surveillance regarding UTIs identification, but also infection prevention and control, especially for indwelling catheters, i.e. insertion and hygiene [25, 24]. An example would be the intervention described by Takker *et al.* in the surveillance of patients undergoing total hip and knee replacement and hip fracture treatment, where morbidity was reduced from 2.1–1.1%. The intervention involved the implementation of catheter surveillance principles, including qualification for catheterization, which resulted in a reduction in the number of procedures from 55.2–19.8% [25]. Our presented data indicate a significantly higher proportion of catheterized patients, which is probably the result of overusing this procedure, not only in intraoperative but also in postoperative period.

In case of orthopedic patients, it has been shown that the proper use of perioperative antibiotic prophylaxis in accordance with local decision-making standards improves the patient's prognosis in terms of SSIs and additionally also in the prevention of CA-UTIs [11]. Indwelling catheters can increase postoperative urinary tract infection and may not be required in total joint arthroplasty [15]. Based on the current evidence, the urinary catheterization during total joint arthroplasty increased the postoperative CA-UTIs, and it may not be routinely required for patients undergoing such procedures.

On the other hand, however, postoperative complication is urinary retention, especially common after anorectal and hernia surgery and after orthopedic surgery [4, 2], hence withdrawal of routine perioperative catheter use may prove difficult in practice, especially in the elderly patient population, because the risk increases with the patient's age.

In addition to the catheterization procedure itself, many other factors contribute to the development of UTI, including patient-dependent unmodifiable factors, with age that is a particularly strong predictor of UTI. This is confirmed by other authors [1, 14] as well as by presented results, which indicate a significant, more than 3-fold higher risk of infection in patients aged 75 years and older. One of the conditions may be a generally weaker immune response in older patients, but also a weaker physical condition or limited mobility. Consideration should be given to HAI surveillance by introducing special HAI exposure alert among various other elements of HAI – including UTIs prevention and control in orthopedic departments, using the generally accepted scale for geriatric patients, e.g. the Bathel scale, used to assess patients' mobility. Such a stratified description of patients would facilitate the implementation of special surveillance of persons exposed to HAIs.

Typical microbial virulence factors are important in CA-UTI pathomechanism, especially formation of abundant biofilm and urease responsible for increasing urine pH and accompanying precipitation of urinary stones. These features are present in the *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Morganella morganii*, *Proteus mirabilis* and some *Providencia* spp. infections. Also some strains of *Staphylococcus aureus* and coagulase-negative staphylococci [18, 22]. Thus, the dominance of *Enterobacterales* Gram-negative bacteria [11, 19, 23] in presented study is not a cause for concern.

However, the described low drug sensitivity is a big problem. Especially resistance to quinolones and extended spectrum cephalosporins remains a major challenge, because these antibiotics are widely used as first-line therapy in the treatment of UTIs. Particular consideration should be given to penicillins sensitive to beta-lactamases (due to the high proportion of ESBL + strains) and fluoroquinolones, which significantly limits the available therapeutic options. CTX-M ESBLs are becoming more common worldwide, especially CTX-M-15, often associated with the uropathogenic *E. coli* clone. In addition plasmids, that are often carrying ESBL genes also carry determinants of fluoroquinolone resistance [17]. Therefore, the use of both ciprofloxacin - a drug common in empirical therapy of UTIs, as well as eagerly used empirically in Poland, for bladder infections - trimethoprim / sulfamethoxazole, carry the risk of therapeutic failure.

The matter gets complicated by the high prevalence of MDR strains, especially non-fermenting *Acinetobacter baumannii* and *Klebsiella pneumoniae*, which account for about 1/4 of all UTIs [12, 16]. The studied department, unfortunately, represents a very typical ward. According to data from Mazzariol *et al.* [16] from 2014 in EU / EEA countries the percentage of ESBL (+) *K. pneumoniae* resistant strains in UTIs was even over 70% (Romania, Grece), and ESBL (+) *E. coli* over 40% (Bulgaria). In Poland, above ESBL (+) strains constituted 65% of *K. pneumoniae* strains and 11% of *E. coli*. In the countries of Northern Europe (Finland, Iceland), the prevalence of this type of resistant strains is significantly lower [16].

Unfortunately, in the studied unit the high prevalence of MDR microorganisms was observed not only in UTIs, but also in surgical site infections: 22.6%, and also mainly concerned the Gram-negative bacilli: *Acinetobacter baumannii* and *Klebsiella pneumoniae* [21].

The limitation of our study was retrospective rather than prospective UTI analysis and limited ability to compare our results with various local antibiotic sensitivity patterns in the UTI orthopedic patient population, due to the lack of comparative data – non-SSI infections in patients after orthopedic surgery are poorly described.

Conclusions

Gram-negative microorganisms (76.1%) dominated among isolated microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*. *Enterococcus faecalis* dominated among Gram-positive flora. Isolated microorganisms showed full sensitivity to carbapenems, linezolid and glycopeptides. Gram-negative bacilli showed the lowest sensitivity to penicillins with extended spectrum and quinolones and trimethoprim-sulfamethoxazole. The lowest total sensitivity was shown by *K. pneumoniae* strains, which showed high resistance, in addition to the above-mentioned ones also to the third generation cephalosporins (cefotaxime and ceftazidime), penicillins in combination with beta-lactamase inhibitors and aminoglycosides. In order to reduce the problem of drug resistance and the occurrence of MDR in the studied ward, the reduction of UTI risk should be of paramount importance – the incidence significantly exceeds expectations, it is necessary to implement and adhere to the principles of infection prevention and control with systematic validation of procedure measures, especially in catheterized patients. The key element of CA-UTI surveillance should be regular feedback of unit-specific CA-UTI rates to clinical care staff. It is also necessary to implement continuous surveillance of drug sensitivity and antibiotic therapy, including empirical therapy, as this element can be a serious problem in the studied ward. It would be appropriate to discuss the legitimacy of catheterization after certain procedures and overusing it, not only in the intraoperative but also postoperative period.

Abbreviations

HAI- healthcare associated infections

UTI urinary tract infections

CA-UTI catheter-associated UTI

ESBL- spectrum beta-lactamases

DDST- double disc synergy test

MDR- multidrug-resistant

XDR- extensively drug resistant

Declarations

Ethics approval and consent to participate

The use of data was approved by the Bioethical Committee of Sosnowiec Medical College in Sosnowiec (No. PW/WSM/36/17). All data entered into the electronic database and analyzed in this study were previously anonymised.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated or analysed during this study are available and can be accessed from Iwona Pawłowska (e-mail: ivi5@op.pl) on reasonable inquiry.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Conceptualization, GZ, IP and TB; Methodology, GZ, IP; Software, IP; Formal Analysis, GZ, IP, EJ, MS; Investigation, IP, MS, TB; Resources MS, TB; Data Curation, IP; Writing—Original Draft Preparation: GZ, IP, TB, EJ; Writing, Review and Editing GZ, EJ, MS; Supervision, TB; Project Administration GZ; Review and revision of the manuscript: EJ; Acquisition of Funds for publication TB. All Authors give final approval of the version to be published.

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Tables

Table I. The most frequently isolated etiological factors in urinary tract infections in the Clinical Department of Orthopedic-Traumatic, Oncological and Reconstructive Surgery in 2013-2015.

Pathogen	n [%]	ranking
Gram-positive (16.3% of all microorganisms)		
<i>Enterococcus faecalis</i>	20 (9.6)	5
<i>Staphylococcus aureus</i>	2 (1.0)	11
<i>Enterococcus faecium</i>	1 (0.5)	12
Others	11 (5.3)	7
Gram-negative (76.1% of all microorganisms)		
<i>Escherichia coli</i>	61 (29.2)	1
<i>Klebsiella pneumoniae</i>	32 (15.3)	2
<i>Proteus mirabilis</i>	25 (12.0)	3
<i>Pseudomonas aeruginosa</i>	21 (10.0)	4
<i>Acinetobacter baumannii</i>	9 (4.3)	8
<i>Enterobacter cloacae</i>	3 (1.4)	10
Others	8 (3.8)	9
<i>Candida spp.</i>	16 (7.7)	6
total	209 (100)	

n - number of isolates; UTI - urinary tract infections

Table II. Drug susceptibility of the most common etiological factors of UTIs in the Clinical Department of Orthopedic, Traumatic, Oncological and Reconstructive Surgery in 2013-2015.

Antibiotics	<i>Escherichia coli</i> n=61	<i>Klebsiella pneumoniae</i> n=32	<i>Proteus mirabilis</i> (n=25)	<i>Pseudomonas aeruginosa</i> n=21
Beta-lactam antibacterials: penicillins, with extended spectrum, beta lactamase resistant penicillins, combinations of penicillins incl. beta-lactamase inhibitors				
ampicillin	26%	0%	37%	NT
piperacillin	28%	0%	35%	75%
amoxicillin+clavulanate	82%	35%	91%	NT
piperacillin+tazobactam	70%	31%	92%	85%
ticarcillin+clavulanate	NT	NT	NT	90
Other beta-lactam antibacterials: second/third-generation cephalosporins, carbapenems				
cefuroxime	84%	25%	78%	NT
ceftazidime	94%	38%	93%	85%
cefotaxime	96%	38%	94%	NT
cefepime	92%	31%	97%	100%
imipenem	100%	100%	33%	77%
meropenem	100%	100%	100%	77%
ertapenem	100%	100%	100%	NT
Aminoglycoside antibacterials				
gentamicin	87%	25%	67%	88%
tobramycin	73%	36%	60%	91%
amikacin	88%	50%	67%	92%
netilmicin	89%	40%	60%	82%
Quinolone antibacterials				
ciprofloxacin	64%	42%	57%	37%
levofloxacin	64%	38%	43%	50%
Other antibacterials				
nitrofurantoin	96%	NT	NT	NT
fosfomycin	100%	80%	NT	98%
trimethoprim-sulfamethoxazole	55%	42%	50%	NT

n- total isolates, NT: not tested.

Table III. Multidrug-resistant microorganisms isolated from urinary tract infections in the Clinical Department of Orthopedic, Traumatic, Oncological and Reconstructive Surgery in 2013-2015.

Pathogen	No. of isolates	MDR n [%]	Occurrence Trend
<i>Acinetobacter baumannii</i> XDR	9	7 (77.8)	Tau=-0.3333 p=0.6015
<i>Klebsiella pneumoniae</i> MDR, incl. ESBL	32	21 (65.6)	Tau=0.3333 p=0.6015
<i>Pseudomonas aeruginosa</i> MDR, XDR	21	5 (23.8)	Tau=0.3333 p=0.6015
<i>Proteus mirabilis</i> MDR, incl. ESBL	25	4 (16.0)	Tau=0.8165 p=0.2008
<i>Escherichia coli</i> MDR, incl. ESBL	61	8 (13.1)	Tau=-0.3333 p=0.6015
Others	61	6 (9.8)	Tau=-0.3333 p=0.6015
Total	209	51 (24.4)	Tau=-0.3333 p=0.6015

ESBL - extended-spectrum beta-lactamases; MDR – multidrug-resistant; XDR – extensively drug resistant