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Antimicrobial Resistance among Urology Patients with Documented Bacteriuria and Predictors of Urosepsis: A Single-Center, Retrospective Surveillance Study

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Authors' contributions

This work was carried out in collaboration among all authors. Author MRMM is the main author who designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors PN and RZ are the supervisors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: We aimed to identify predictors of microbiologically-proven urosepsis in Urology. Further to that, we intend to determine the microbiological diversity and incidence of antibiotic resistance among consecutive urological patients undergoing treatment in Urology department.
Study Design: This was a cross-sectional retrospective study performed in Hospital Sultanah Bahiyah, Malaysia. A database of positive urine cultures from the Urology department between 1 January 2019 and 31 January 2020 were analysed.
Methodology: All adult patients with positive urine culture were included in this study. Urine cultures were performed for patients symptomatic for urinary tract infections or asymptomatic patients planned for urological procedures. A total of 348 subjects were included for analysis. Patients' demographics and variables of interest were collected via digital clinical notes.
Results and Conclusion: 348 subjects were included. Among Urology patients with proven bacteriuria, incidence of urosepsis was 12.1%. Stepwise multivariate logistic regression revealed that younger patients, the presence of multidrug resistant organism (MDRO) isolates, pre-existing

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chronic kidney disease (CKD), and the presence of underlying malignancies were all predictors of Urosepsis (all $p<0.05$). From the total, 94% of uropathogens were Gram negative organisms with the 3 common organisms being *E.coli* (24%) followed by *K. pneumoniae* (11.8%), and *P. aeruginosa* (15.2%). *P. aeruginosa* (26.2%) were commonest in urosepsis. Antimicrobial resistance (AMR) including MDRO, is alarmingly high and concerning. In urosepsis, AMR rate was more than 10 percent for all commonly used antibiotics including carbapenems. To improve guideline development, empirical combination antibiotics therapy should be studied employing urosepsis predictors. Judicious use of antibiotics with adherence to antibiotic stewardship and infection control to curb emergence of AMR is important.

Keywords: Urology; Urosepsis; antimicrobial resistance; MDRO; Malaysia.

1. INTRODUCTION

Sepsis and septic shock are prevalent life-threatening conditions linked with a high mortality rate and significant costs to the healthcare system. Urosepsis in adults accounts for approximately 25% of all sepsis cases following a complicated urinary tract infection [1]. In different patient groups, urosepsis may result in mortality rates ranging from 25% to 60% [2,3]. Prompt treatment, including early administration of appropriate intravenous antibiotic, is crucial for achieving the best possible outcomes. However, with the rising threat of global antimicrobial resistance (AMR), inadequate empirical antibiotic coverage has been identified as a critical challenge in urosepsis [3-6]. Furthermore, geographical variations in microbial spectrum and antimicrobial resistance (AMR) patterns, which have been extensively documented, add to the complexity of clinical decision making and antibiotic guideline development [7,8,9].

Patients with urological conditions are at-risk population for antimicrobial resistance and UTI including urosepsis. We undertook this study to identify predictors of microbiologically-proven urosepsis in Urology. Further to that, we intended to determine the microbiological diversity and incidence of antibiotic resistance among consecutive urological patients undergoing treatment in our facility.

2. MATERIALS AND METHODS

2.1 Study Design

This retrospective cross-sectional study was conducted at the Urology Unit of Hospital Sultanah Bahiyah Alor Setar, Malaysia from 1 January 2019 to 31 January 2020. All adult patients with a positive urine culture were included in this study. Urine culture was performed for patients symptomatic for urinary tract infections or asymptomatic patients planned for urological procedure.

The specimens were collected either via mid-stream urine or via a urinary catheter. Specimens were collected and analyzed within a single microbiology laboratory in Hospital Sultanah Bahiyah. The interpretive criteria for susceptibility or resistance, as well as the screening for Extended spectrum beta lactamase (ESBL) and carbapenemase-producing bacteria, were carried out in accordance with the Clinical Laboratory Standards Institute (CLSI) Performing Standards for Antimicrobial Susceptibility testing guideline [10]. When the CLSI did not provide clear interpretation zones, the researchers utilized the European Committee for Antimicrobial Susceptibility Testing (EUCAST) criteria [11]

We collected demographic data of all the patients who fulfilled the inclusion criterion, such as age, gender, and comorbidities including diabetes mellitus, chronic kidney disease (CKD), underlying malignancy and history of hospitalization within six months. With regards to urological risk factors- we collected data such as the presence of urinary lithiasis, indwelling urinary catheters (in the lower or upper urinary tract), duration of the indwelling catheters, the presence of a neurogenic bladder and the presence of multidrug-resistant organism (MDRO) bacteriuria.

2.2 Definitions

Urosepsis was identified, as reported by the treating physician in patients' clinical notes. MDRO was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories. We use the ECDC and CDC definitions, which include Enterobacteriaceae producing extended-spectrum beta-lactamase (ESBL) or those resistant to carbapenems, Enterococcus spp.

resistant to vancomycin, and Methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa resistant to more than three classes of antimicrobial agents [12].

For statistical analysis we included organisms with intermediate sensitivity into antimicrobial-resistant organism group.

2.3 Statistical Analysis

Data was gathered in an electronic form from patient records. Categorical data were displayed as percentages and frequencies; quantitative data were reported as mean and standard deviation (SD) unless stated otherwise. A logistic regression was done. The univariate analyses were done using Chi-square tests or Fisher's exact test for categorical variables and an independent t-test for continuous variables to determine risk factors for urosepsis. The variables with $p < 0.25$ in the univariate analysis were included in a multivariate logistic regression analysis to determine independent risk factors for urosepsis. Frequencies and odds ratio (OR) with 95% confidence interval (95% CI) were reported. A value of $p < 0.05$ in the multivariate regression was considered statistically significant. We utilized the Statistical Package for Social Sciences version 23.0 (SPSS Inc., Chicago, IL., USA) for data collection and analysis.

3. RESULTS AND DISCUSSION

3.1 Results

A total of 348 urinary bacterial isolates from Urology patients treated at our hospital during a 13-month period were analysed retrospectively. Of these patients, 219 (62.9%) were male and 129 (37.1%) were female. Mean age was 61.1 (SD:15.9) years. Inpatients and outpatients comprised for 245 (70.4%) and 103 (29.6%) patients, respectively.

3.1.1 Uropathogen spectrum

We observed that Gram-negative organisms predominate (94.0%) and Gram-positive organisms constituted the remaining 6.0%. The most common isolates were *Escherichia coli*, found in 132 (24%) of positive urine cultures, followed by 69 (19.8%) *Klebsiella pneumoniae*, 53 (15.2%) *Pseudomonas Aeruginosa*, 23 (6.6%), *Proteus spp*., 14 (4.0%) *Citrobacter spp.* and the rest were not common- as described in Table 1.

3.1.2 Anti-Microbial Resistance (AMR) profile

The overall Anti-Microbial Resistance (AMR) patterns of the uropathogens identified are summarized in Fig. 1. We found that resistant pathogens isolated from Urology patients was 80.7% resistance rate to at least one antibiotic. Ampicillin had the highest resistance at 78.5%. High resistance rates were observed to most commonly used antibiotics, such as- aminopenicillin + beta-lactamase inhibitors (44.6%), cefuroxime (42.2%), ciprofloxacin (32.2%), trimethoprim + sulfamethoxazole (43.7%), nitrofurantoin (30.3%), amikacin (20.0%), tazosin (19.2%) and gentamycin (18.9%). Resistance to third and fourth generation cephalosporins were equally high with cefotaxime (35.3%), cefepime (28.0%) and ceftazidime (27.3%). Among carbapenem antibiotics, ertapenem resistance was the lowest (4.7%) followed by meropenem (9.5%) and imipenem (11.7%). Among the tested isolates- our study revealed no resistance against vancomycin and polymyxin B antibiotics.

Table 1. Frequency and percentages of isolated uropathogens (N=348)

	Organism	Frequency	(%)
Gram Positive n=21 (6.0%)	*Staphylococcus aureus*	6	1.7
	Enterococcus spp	6	1.7
	BSB	5	1.4
	Staphylococcus CONS	4	1.1
Gram Negative n=327 (94.0%)	*Escherichia coli*	132	37.9
	Klebsiella pneumoniae	69	19.8
	Pseudomonas aeruginosa	53	15.2
	Proteus spp.	23	6.6
	Citrobacter spp	14	4.0
	Acinetobacter baumannii	7	2.0
	Other GNB	29	8.3
	Total	**348**	**100.0**

BSB = Group B streptococcus, GNB = Gram negative bacilli, CONS = coagulase-negative

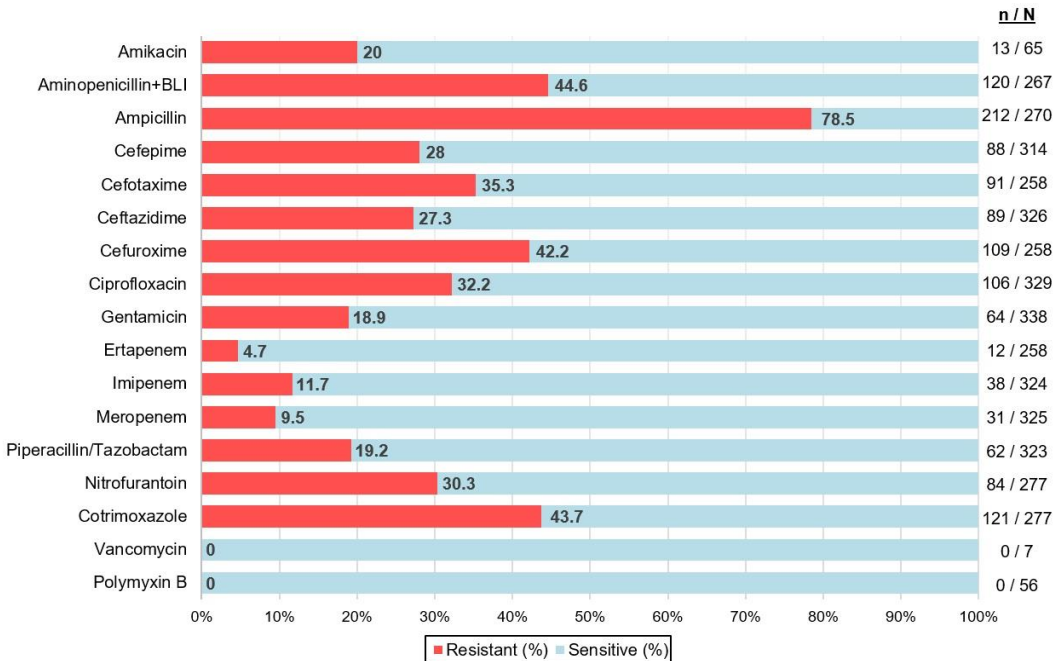

Fig. 1. Antimicrobial Resistance Pattern in Urology Department Hospital Sultanah Bahiyah (%)
BLI = Beta lactamase inhibitor

Table 2. Antimicrobial resistance patterns of common uropathogens and urosepsis

Antimicrobials	**Organism**						**Urosepsis**	
	E. coli		***K. pneumoniae***		***P. aeruginosa***			
	N = 132		N = 69		N = 53		N = 42	
	n	(%)	n	(%)	n	(%)	n	(%)
Ampicillin	97	73.5	64	92.8	NT	-	24	57.1
Ceftazidime	36	27.3	28	40.6	14	26.4	21	50.0
Ciprofloxacin	52	39.4	18	26.1	11	20.8	21	50.0
Aminopenicillin + BLI	47	35.6	33	47.8	NT	-	18	42.9
Cefepime	39	29.5	26	37.7	13	24.5	18	42.9
Cefuroxime	52	39.4	32	46.4	NT	-	18	42.9
Cefotaxime	45	34.1	28	40.6	NT	-	17	40.4
Gentamicin	23	17.4	9	13.0	12	22.6	16	38.1
Piperacillin/Tazobactam	12	9.1	21	30.4	11	20.8	15	35.7
Cotrimoxazole	63	47.7	27	39.1	NT	-	15	35.7
Nitrofurantoin	11	8.3	34	49.3	NT	-	14	33.3
Imipenem	3	2.3	5	7.2	13	24.5	11	26.2
Meropenem	2	1.5	5	7.2	13	24.5	10	23.8
Amikacin	NT	-	NT	-	9	17.0	8	19.0
ESBL-producers	41	31.1	19	27.5	0	0.0	13	30.9
3rd Generation Cephalosporins Resistant	45	34.1	28	40.6	14	26.4	24	57.1
Carbapenem Resistant	4	3.0	6	8.7	13	24.5	11	26.2

BLI = Beta lactamase inhibitor, ESBL = Extended spectrum beta lactamase, NT = not tested

Table 3. Summary of antimicrobial resistance profile of isolated uropathogens

N_{total} = 348	**Any AMR**	**MDRO**	**ESBL-producer**	**Carbapenem Resistance**	**Fluoroquinolone Resistance**	**3rd Generation Cephalosporins Resistance**
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Escherichia coli (n=132)	120 (90.9)	79 (59.8)	41 (31.1)	4 (3.0)	52 (39.4)	45 (34.1)
Klebsiella pneumoniae (n=69)	66 (95.7)	38 (55.1)	19 (27.5)	6 (8.7)	18 (26.1	28 (40.6)
Pseudomonas aeruginosa (n=53)	15 (28.3)	14 (26.4)	0	13 (24.5)	11 (20.8)	14 (26.4)
Proteus spp. (n=23)	21 (91.3)	11 (47.8)	1 (4.3)	4 (17.4)	8 (34.8)	6 (26.1)
Acinetobacter baumannii (n=7)	5 (71.4)	5 (71.4)	0	4 (57.1)	4 (57.1)	5 (71.4)
Citrobacter spp. (n=14)	14 (100.0)	7 (50.0)	0)	1 (7.1)	2 (14.3)	6 (42.9)
other GNB (n=29)	26 (89.7)	13 (44.8)	0	11 (37.9)	8/25 (32.0)	6/28 (21.4)
Staphylococcus aureus (n=6)	4 (66.7)	0	0	0	NT	NT
CoNS (n=4)	3 (75.0)	2 (50.0)	0	0	NT	NT
BSB (n=5)	4 (80.0)	0	0	0	NT	NT
Enterococcus spp. (n=6)	3 (50.0)	0	0	0	3 (50.0)	NT
Total (N=348)	**281 (80.7)**	**169 (48.6)**	**61 (17.5)**	**43 (12.4)**	**106 (32.2)***	**110 (33.7)****

BSB = Group B Streptococcus, CoNS = Coagulase-negative Staphyloccus, GNB = Gram negative bacilli
**N=329 **N=326*

Table 2 describes AMR patterns of the three commonest isolates, namely *Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa* as well AMR pattern of uropathogens isolated from patients diagnosed with urosepsis. Table 3 summarizes AMR patterns of isolated uropathogens. Multidrug resistant organisms (MDRO) were found in 48.6% of our study population. MDR rate was the highest among *Acinetobacter baumannii* with 71.4% (5), followed by *Escherichia coli* at 59.8% (79/132) and *Klebsiella pneumoniae* at 55.1% (38/69). *Pseudomonas aeruginosa* had and MDR rate of 26.4% (14/53). Gram-positive organisms, on the other hand, had an MDR rate of 9.5% (2/21). ESBL-producers accounted for 17.5% (61/348) of all patients, and the incidence of uropathogens resistant to third-generation cephalosporins were 33.7% (110/326) and overall carbapenem-resistance of 12.4% (43/348).

3.1.3 Microbial profile and predictors of Urosepsis

In our urology-patients cohort, individuals with documented bacteriuria had a urosepsis rate of 12.1%. Uropathogens found in patients with urosepsis were listed in the following order, from most common to least common: *Pseudomonas aeruginosa* (26.2%), *Escherichia coli* (23.8%), *Klebsiella pneumoniae* (19.0%), *Acinetobacter baumannii* (4.8%), *Enterobacter spp.* (4.8%), *Citrobacter spp.* (4.8%), *Proteus spp.* (2.4%), *Staphylococcus aureus* (2.4%), Group B *Streptococcus* (2.4%), coagulase-negative *Staphylococci* (2.4%) and others (7.2%). This bacterial spectrum did not differ statistically from those isolated from non-septic patients ($p = 0.20$) (Fig. 2).

Among patients diagnosed with urosepsis, Carbapenems had the lowest overall resistance (26.2%), while the remaining antibiotics had resistance ranging from 30.9% to 57.1% as described in Table 2. From the total, 30.9% of urosepsis causative pathogens were ESBL producers. MDR rate for uropathogens in this group of patients were 71.4% (n = 30).

Based on the findings of the univariate analysis, the following factors were chosen for inclusion in the multivariate analysis of independent risk factors associated with urosepsis: age, location of urine specimen collection, location of indwelling urinary catheter, recent hospitalisation, MDRO isolates, neurogenic bladder, chronic kidney disease, and malignancy. Patients diagnosed with urosepsis were found to be significantly younger than those who were not (54.6 (SD:19) years versus 62.1 (SD:15) years; $p = 0.001$). Additionally, we discovered that inpatient urine samples (adjusted OR (AOR) = 3.28, $p = 0.039$), MDRO isolates (AOR = 3.26, $p = 0.003$), pre-existing chronic kidney disease (AOR = 4.00, $p = 0.005$), and presence of underlying malignancy (AOR = 3.41, $p = 0.005$) were all independent predictors of urosepsis. Details are listed in Table 4.

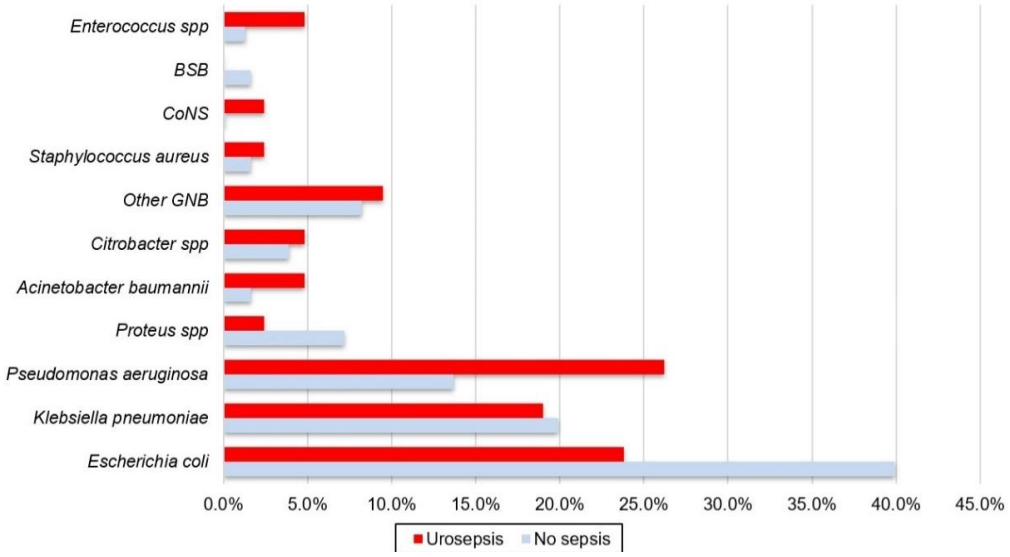

Fig. 2. Microbial spectrum of urosepsis vs. non-septic patients

BSB = Group B Streptococcus, CoNS = Coagulase-negative Staphyloccus, GNB = Gram negative bacilli

Table 4. Univariate and multivariate analysis of Urosepsis predictors

			Univariate analysis			Multivariate analysis		
Variables	**Urosepsis**	**No urosepsis**	**OR**	**95% CI**	***P*-value**	**Adjusted OR**	**95% CI**	***P*-value**
Age	54.6 (19)	62.1 (15)	0.97	0.95-0.99	***0.004****	0.95	0.93-0.97	***0.001****
Mean (SD)								
	N (%)	**N (%)**						
Gender								
Male	27 (12.3)	192 (87.7)	1.07	0.55-2.09	0.846			
Female	15 (11.6)	114 (88.4)	Reference					
Sample types								
Inpatient sample	38 (15.5)	207 (84.5)	4.54	1.58-13.09	***0.002****	3.28	1.06-10.12	***0.039****
Outpatient sample	4 (3.9)	99 (96.1)	Reference			Reference		
Indwelling Catheter								
None	21 (11.2)	167 (88.8)	Reference					
In Upper tract	17 (17.7)	79 (82.3)	1.88	0.93-3.81	0.077	1.20	0.53-2.72	0.655
In Lower tract	4 (6.2)	60 (93.8)	0.58	0.19-1.78	0.338			
Catheter > 6 month	7 (10.0)	63 (90.0)	0.76	0.32-1.79	0.527			
None	35 (12.8)	239 (87.2)	Reference					
Admission last 6 month	28 (17.0)	137 (83.0)	2.42	1.23-4.79	***0.009****	1.32	0.58-2.99	0.509
None	14 (7.8)	166 (92.2)	Reference			Reference		
MDRO	30 (17.7)	139 (82.3)	3.00	1.48-6.09	***0.002****	3.26	1.51-7.08	***0.003****
Non MDRO	12 (6.7)	167 (93.3)	Reference			Reference		
Stone	19 (12.1)	138 (87.9)	1.00	0.53-1.92	0.986			
No stone	23 (12.0)	168 (88.0)	Reference					
Neurogenic bladder	1 (2.8)	35 (97.2)	0.19	0.03-1.42	0.071	0.14	0.01-1.49	0.105
Non neurogenic bladder	41 (13.1)	271 (86.9)	Reference			Reference		
Diabetes	12 (11.1)	96 (88.9)	0.88	0.43-1.78	0.713			
No diabetes	30 (12.5)	210 (87.5)	Reference					
Chronic kidney disease	9 (27.3)	24 (72.7)	3.20	1.37-7.47	***0.005****	4.00	1.51-10.61	***0.005****

			Univariate analysis			Multivariate analysis		
Variables	**Urosepsis**	**No urosepsis**	**OR**	**95% CI**	***P*-value**	**Adjusted OR**	**95% CI**	***P*-value**
no CKD	33 (10.5)	282 (89.5)	Reference			Reference		
Malignancy	13 (23.6)	42 (76.4)	2.82	1.36-5.85	***0.004****	3.41	1.44-8.06	***0.005****
No malignancy	29 (9.9)	264 (90.1)	Reference			Reference		

*Bold **values** with ***** denote statistical significance at the P < 0.05 level. OR=Odds ratio, CI=Confidence interval, SD=standard deviation, MDRO=multidrug-resistant organism, CKD=chronic kidney disease*

3.2 Discussion

In septic patients, Kumar et al. (2006) reported a 7.6% decrease in survival for every hour of delay in administering proper antibiotic therapy [6]. Prompt treatment, including early administration of intravenous antibiotic, is crucial for achieving the best possible outcomes in management of urosepsis [3-6]. Generally, initial antimicrobial treatment should be empirical with a broad antimicrobial spectrum to cover all potential causing bacteria, and should be modified based on culture results [3,13]. In urosepsis, inadequate antibiotic coverage has been reported as a major concern [4,13]. Given that resistance rates for empiric treatment of severe infections should not exceed 10 percent, our treatment options for urosepsis are limited [14]. Therefore, research establishing antibiotic susceptibility patterns is necessary everywhere, even between different regions or localities, to aid in the formulation of appropriate empirical therapy guidelines for UTI and urosepsis.

European Section of Infection in Urology (ESIU) found in a global multinational point prevalence of infections in Urology (GPIU) study that Urology patients had a urosepsis prevalence of 1.5% and accounted for 25% of all hospital-acquired UTI (HAUTI) [14]. Bjerklund et al. [15], reported 12% of Urology patients with HAUTI were diagnosed with urosepsis [15]. Comparable results were obtained in our study, where we discovered that 12.1% of urology patients with confirmed bacteriuria had urosepsis.

Clinicians may observe different bacterial spectrums in treating Urology patients in comparison to general population with uncomplicated UTI. Consistent with previously published international studies, we observed Gram-negative organisms' predominance, accounting for 94% of all uropathogens. *Escherichia coli* (37.9%) followed by *Klebsiella pneumoniae* (15.2%) and *Pseudomonas aeruginosa* (6.6%) were the commonest in our Urology patient cohort [9,16,17]. According to a recent GPIU report, the leading cause of HAUTI in European urology departments is Gram-negative organisms with the following ranks: *Escherichia coli* > *Klebsiella pneumoniae* > *Pseudomonas aeruginosa* > others [16]. In contrast, studies reviewing causative uropathogens in uncomplicated community acquired UTI showed a slight variation in microbial spectrum. *Pseudomonas aeruginosa* were less common in this population, with an incidence of 0% and 1.3% in Malaysia and Europe respectively, albeit Gram-negative enterobacteriales and *Escherichia coli* predominance. [9,18].

In the present study, the majority of causative pathogens of urosepsis were still gram-negative organisms, but there had been a slight variation where we observed *Pseudomonas aeruginosa* being the most prevalent followed by *Escherichia coli, Klebsiella pneumoniae*, and the remainder, as illustrated in Figure 2. We also observed higher incidence of *Acinetobacter baumannii* and Gram-positive organisms cultured among urosepsis patients. However, this observation was not statistically significant (P = 0.196). Comparatively, when GPIU data from multiple urology departments in Europe between 2006 to 2017 was evaluated by Tandogdu et al. [16], *Escherichia coli* remained the most prevalent causative pathogen in urosepsis, but similar to our findings, the percentage of *Pseudomonas aeruginosa* was higher compared to non-septic patients [16].

In our center, an alarming 80.7% of urinary bacteria obtained from Urology patients were resistant to at least one antibiotic. AMR rates for routinely used antibiotics, excluding carbapenems, vancomycin, and polymyxin B, range from 18.9% (Gentamicin) to 78.5% (Ampicillin), are well above the ten percent threshold advised for empirical antibiotics for severe infections. Among the three most common uropathogens, with the exception of resistance to ciprofloxacin, cotrimoxazole, and gentamicin, *Klebsiella pneumoniae* has a higher AMR rate than *Escherichia coli* in general. This aligns with the GPIU statistics compiled by Medina et al. On the other hand, contrary to the Asian GPIU data, our investigation revealed a lower rate of resistance to ciprofloxacin (20.8% vs 97%) and tazocin (20.8% vs 61%) among *Pseudomonas aeruginosa*. In addition to this, lower quinolone resistance was also observed in *Klebsiella pneumoniae* (26.1% vs 73%) and *Escherichia coli* (39.4% vs 57%) [9].

We also observed a concerningly higher incidence of MDRO (71.4%) with adjusted OR = 3.26, among patients with urosepsis. Further to that, monotherapy antimicrobial coverage for urosepsis in this study exceeded the recommended ten percent for all antibiotic classes, including carbapenems. This warrants further research into combination antibiotics to treat septic Urology patients. To address this

issue Tandogdu et al. [16] investigated different antibiotic regimens, including combination therapy, using the Bayesian weighted incidence syndromic antibiogram (WISCA) and Bayesian factor considering different HAUTI diagnoses, including urosepsis, to improve empirical antibiotic selection. Although condition-specific surveillance was found to be helpful, the authors admit that geographical variation of microbial spectrum and AMR as well as the short-term (two-year) data used in their study limit its generalizability. Consequently, validation in local surveillance studies is needed [16].

Recognizing these challenges, early detection of those at risk of urosepsis is absolutely essential as it may aid in individualized treatment recommendations and consequently improve overall outcomes. In general, Urology patients are at risk population to develop UTI and urosepsis. Urological conditions such as urolithiasis, benign prostate enlargement, urethral stricture, neurogenic bladder and congenital anomalies are all common underlying risk factors for the development of urosepsis compared to the general population [2,3,19] Additionally, those undergoing urological procedures are more vulnerable especially if they have positive urine cultures [3,19,20].

Advanced age has been associated with higher risk of urosepsis [3,20]. In our study, however, we discovered that among Urology patients with documented bacteriuria, patients diagnosed with urosepsis were significantly younger than those who were not (54.6 ± 19 years versus 62.1 ± 15 years; P = 0.001). We found that male and female gender shared similar risk for developing urosepsis. Peach et al. (2016) conducted a systematic review and found that there are conflicting findings on the effect of age and gender on the risk of urosepsis [21].

Approximately 67-70% of hospitalized Urology patients have a urinary catheter and 70-80% of healthcare-related UTIs are attributable to urinary catheters. Additionally, UTIs associated with urinary catheter use are associated with increased morbidity, mortality, and costs [9,22]. The challenge is even more apparent in the management of patients with long term urinary catheters as they are associated with biofilm formation and multidrug-resistant organisms [2]. Chugh et al. 2021 reported that among patients undergoing URS prolonged preoperative stent placement particularly more than 30 days were associated with higher risk of urosepsis [23]. Our study revealed no difference in urosepsis risk for patients with urinary catheters, regardless of type and dwell time. Peach et al. (2016) observed inconsistent results regarding catheter use as a risk factor for urosepsis in their systematic review. The authors attributed their findings to the inconsistent definition of catheter-associated urinary tract infection (CAUTI) and the potential use of antibiotics among patients with indwelling catheter [21].

Urosepsis has also been linked to a number of other co-morbid conditions, including diabetes, chronic renal disease, ischemic heart disease, and immune deficiencies [3,19]. In our study, prevalence of diabetes was 31%. The incidence of urosepsis in this population was not different between diabetics and non-diabetics. Similar to previous researches, we discovered that patients with chronic renal disease are more likely to develop urosepsis [2,3]. In addition to that, we report that underlying malignancy is a risk factor of urosepsis. This may be the result of an abnormal urinary outflow brought upon by tumour compression or immunosuppression caused by chemotherapy.

This study was exposed to several limitations. the study's retrospective design could lead to potential biases and present a problem with possibility of inadequate data. Our study was conducted in a single institution, which may have resulted in institutional bias. Multicenter and prospective research would be extremely beneficial in the future as it would aid in the generalizability of the study findings. Future researches may also benefit from including past colonisation and recent urological intervention as risk factors for urosepsis.

4. CONCLUSION

In Urology patients with proven bacteriuria, the incidence of urosepsis was 12.1%. Younger patients (mean = 54.6 vs 62.1 years), the presence of MDRO isolates, pre-existing CKD, and the presence of underlying malignancy are all predictors of urosepsis. Overall, the most common organism was *Escherichia coli*. *Pseudomonas aeruginosa*, on the other hand, was more commonly found in cases of urosepsis. Antimicrobial resistance, including multidrug resistance organisms, is alarmingly high among urology patients with documented bacteriuria. To improve guideline development, empirical combination antibiotics therapy should be studied employing urosepsis predictors. Continuous

surveillance, judicious antibiotic use, and adherence to antibiotic stewardship are critical to containing this global threat.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This research was approved by Malaysian Medical Research and Ethics Committee (approval no. *NMRR-21-1849-61315*). Ethical guidelines specified in the Declaration of Helsinki, 2013 and the Malaysian Good Clinical Practice Guideline were followed when conducting this study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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