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Assessment of Microbial Diversity Pattern of Sensitivity and Antimicrobial Susceptibility in Patients Admitted with Urosepsis

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Author`s Contribution

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ABSTRACT

Objectives: To determine the spectrum of bacteria causing urosepsis and antibiotic sensitivity patterns among admitted patients with a clear diagnosis of urosepsis.

Methodology: A cross-sectional study was conducted in General Medicine OPDs at the Hayatabad Medical Complex, Peshawar from January 2022 to December 2022. Data was collected prospectively. We included a total of 800 patients with a confirmed diagnosis of urosepsis, the diagnosis was confirmed using >5 pus cells per HPF as a cut-off value. Samples were sent for culture sensitivity testing in the microbiology lab and after identification of the causative bacteria, the sensitivities to a spectrum of antibiotics were assessed.

Results: Out of the 800 enrolled patients, samples of 664 patients grew colonies, mostly comprised of Gram-negative ones. The gender distribution showed (54.70%) females as compared to (45.30%) males, with an age range of 18 -70 years. The species grown primarily is E. Coli 57.5%, Providencia Sp. 9.3%, Enterococcus faecium 7.5%, Enterobacter 7.5%, Klebsiella 2.4%, and a mixed growth pattern in 9.0% of samples. The sensitivity percentage for E. coli against Meropenem was 99.5%, Imipenem 99.6%, Colistin 99.9%, Polymyxin-B 99.9%, Fosfomycin 96.4%, Amikacin 96.7%, Gentamicin 97.4%, Nitrofurantoin 91.5%, Ceftriaxone 34.4%, Ciprofloxacin 31.5%, Piperacillin/Tazobactam 10.2%, Cefepime 39.1%, Co-Amoxiclav 19.0%, Ceftazidime 37.4% and Cefoperazone /Sulbactam 26.5%.

Conclusion: The spectrum of bacteria sensitivity showed high sensitivity towards Meropenem, Imipenem, Colistin, Polymyxin-B, Amikacin, and Gentamicin; medium sensitivity to Fosfomycin and Nitrofurantoin; and low sensitivity against Ceftriaxone, Ciprofloxacin, Piperacillin/Tazobactam, Cefepime, Co-Amoxiclav, Ceftazidime, and Cefoperazone /Sulbactam among patients with urosepsis.

Keywords: Antimicrobial sensitivity, Spectrum, Bacteria, Culture Sensitivity, Urosepsis.

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Introduction

Antibiotics serve as invaluable drugs targeting microorganisms like bacteria by either inhibiting their growth or reducing their activity, effectively minimizing infections. However, a global trend of misusing and overusing antibiotics has led to the emergence of antibiotic resistance, a concerning issue highlighted during World Health Day organized by the WHO in 2011.[1] The theme Fighting Antimicrobial Resistance: Dormancy Today, No Treatment Tomorrow' underscored the dangers associated with antibiotic misuse and emphasized the urgent need for innovative strategies to combat bacterial resistance.[2] Presently, numerous scientists focus on curbing antibiotic misuse and educating the public on the importance of proper prescription practices.[3]

This escalating health challenge arises from both the unwarranted use of antimicrobials in human health and insufficient resources to combat the spread of infections (World Health Day 2011).[4]

Sepsis and Septic Shock are highly serious conditions with significant mortality rates,[5] often among the leading causes of death in ICU patients after cardiovascular diseases.[6] Urosepsis, originating from urogenital tract infections, constitutes a notable portion of these cases, accounting for 9% to 31% of the total sepsis burden based on geographical factors.[7]

Antibiotics are very useful drugs that act on microorganisms like bacteria they inhibit the bacteria or reduce the growth of bacteria thus it is used to minimize infections. However, there is a growing trend of misuse and overuse of antibiotics worldwide, resulting in antibiotic resistance.[1] World Health Day was organized by WHO in 2011, and labeled as fighting antimicrobial resistance: dormancy today, no treatment tomorrow.[2] This highlighted the danger and growing concern of misuse of antibiotics and pressed on the need to improve new ways to stop bacterial resistance. Nowadays, a large number of scientists are working and focusing on stopping the misuse of antibiotics and highlighting the need the knowledge, and the importance of prescription use of antibiotics use by the public.[3] This emerging health problem is due to both the unjustified utilization of antimicrobials for human health and the fewer resources to stop the prevalence of infection. (World Health Day 2011).[4]

Sepsis and Septic Shock are conditions with very serious outcomes5. The mortality of sepsis and septic shock is high enough that is a serious amongst serious cause of mortality in intensive care unit (ICU) patients after cardiovascular disease.[6] A significant portion of these cases and associated mortality stems from Urosepsis, which can be defined as Sepsis originating from infection of the urogenital tract. Based on geographical location, urosepsis accounts for 9% to 31% of the total sepsis burden.[7]

The antimicrobial resistance pattern has not been assessed among patients admitted with urosepsis. Complications associated with bacterial spectrum, nosocomial, and acquired urinary tract infections are considered representative of urosepsis. Implementing preventive treatment for urosepsis is a practical approach to prevent multi-drug resistance, playing a crucial role.[8] Gram-negative sepsis causing UTIs in admitted patients and those in outpatient departments are predominantly attributed to Enterobacteriaceae and Escherichia coli, accounting for approximately 75–90% of these infections.[8]

One of the primary causes of antibiotic resistance (ABR) is the improper prescribing of antibiotics over several years. Administering an antibiotic once daily or using a particular antibiotic for an extended duration over a year poses a risk of bacterial resistance.[9] Non-compliance of patients has also been found to contribute to antibiotic resistance (ABR). In many cases, inadequate use of antibiotics can result in treatment failure.[9] While antimicrobial drugs are crucial for managing microbial infections, the latest drugs available in the market have not kept pace with the growing need for improved infection management (World Health Organization 2012).[10]

In 2014 a program was launched by the government with a name called antimicrobial stewardship program for betterment of the prescribing attitude of doctors. It primarily consists of direction, commitment, and responsibility, and leading experts execute policies for best antimicrobial use and interceding to minimize microbial resistance. The strategy reinforces the implementation of facility-specific treatment guidelines. The Centers for Disease Control and Prevention (CDC) have recommended guidelines to enhance antimicrobial prescriptions in hospitals (Centers for Disease Control and Prevention 2013; Centers for Disease Control and Prevention 2014).[11] The World Health Organization (WHO) has also proposed a curriculum for medical undergraduates on the prudent prescription of antimicrobials (World Health Organization 2012).[12]

Antimicrobial resistance is a critical situation with increased cost of treatment, high rates of hospitalization, and poor patient outcomes.[12] In developing countries, the expense of medications is an important issue for medical healthcare experts and patients. Research indicates that antibiotic costs comprise nearly 50% of a hospital's overall drug budget. There has been widespread misuse of antimicrobial drugs in recent years, with nearly 50% of prescribed antibiotics found to be poorly chosen. In such cases, the improper use of anti-infective drugs can result in microbial resistance to commonly used antimicrobials. Consequently, this resistance can drive the need for newer, more expensive antibiotics to combat the growing crisis of microbial resistance.[1,5,7]

The study aims to determine the distribution of different bacterial species, their resistance patterns to commonly used antibiotics, and the correlation between patient demographics, comorbidities, microbial diversity, and susceptibility. This information is valuable for selecting the most appropriate combination of antibiotics for treatment, thereby minimizing complications. Such studies support physicians in prescription writing, reducing the likelihood of treatment failures. Understanding trends in antibiotic resistance in uropathic isolates is crucial for delivering clinically appropriate and economically viable treatment.[13]

Methodology

A cross-sectional study was conducted over a total duration of six months, from January 2022 to December 2022, in the General Medicine unit at Hayatabad Medical Complex, Peshawar. Data were collected using a convenience non-probability sampling technique from 800 patient records within the 18-70 age group who were enrolled in the study. Diagnosis was confirmed using a cutoff of >5 pus cells per high power field (HPF).[3]

The data was compiled in an Excel sheet. Patients receiving outpatient treatment for UTI or having a history of antibiotic use within the previous fourteen days were excluded, as were patients whose Urine C/S showed no growth. All variables were recorded in a questionnaire format after obtaining informed consent from the patients' records. Aseptic collection of fresh midstream urine samples was conducted in sterile containers for assessment. Subsequently, the samples were sent to the pathology department's microbiology lab for bacterial identification. Culture sensitivity analysis was performed to assess the spectrum of antibiotics. The data underwent comparative analysis, contrasting the results of grown colonies, percentages of growth, and sensitivity patterns for each antibacterial agent. The final count of positive cultures was 664.

Results

Out of a total of 800 patients, the growth was observed among 664 samples that were cultured for the growth. The growth pattern yielded a variety of bacteria which mostly comprised of Gram-negative ones. (Figure 1).

The remaining 44 cultures showed a growth pattern on a variety of bacteria but were insignificant in number. These comprised Proteus Mirabilis, Proteus Vulgaris, Pseudomonas aeruginosa, Citrobacter Species, Acinetobacter, Serratia species., Staphylococcus Aureus Species, Staphylococcus saprophyticus, Streptococcus Species, Burkholderia cepacia. The sensitivity details were assessed for almost all bacteria among the patients with urinary tract infections.

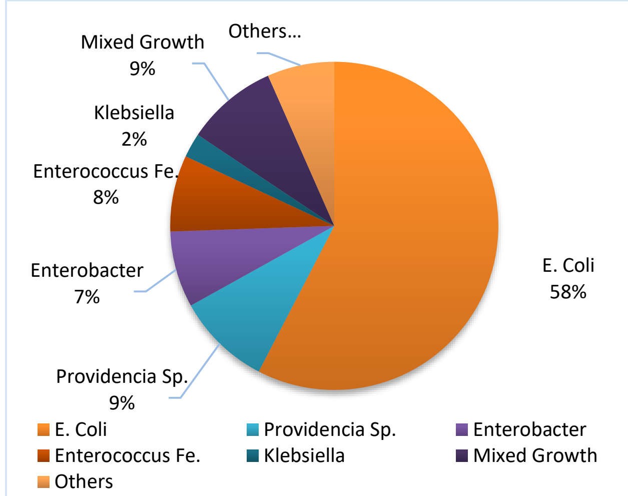

Figure 1. Bacterial Culture-pattern of growth.

In our testing, the drugs with the greatest sensitivities for E. Coli were Meropenem (99.5%), Imipenem (99.6%), Colistin (99.9%), Polymyxin-B (99.9%), Fosfomycin (96.4%), Amikacin (96.7%), Gentamicin (97.4%) as shown in table I.

Table I: Antimicrobial Sensitivity Patterns of Urinary E. coli (n=382)

Antibiotic	Sensitivity %
Colistin	99.9%
Polymixin-B	99.9%
Imipenem	99.6%
Meropenem	99.5%
Gentamicin	97.4%
Amikacin	96.7%
Fosfomycin	96.4%
Nitrofurantoin	91.5%
Cefepime	39.1%
Ceftazidime	37.4%
Ceftriaxone	34.4%
Ciprofloxacin	31.5%
Cefoperazone/Sulbactam	26.5%
Co-Amoxiclav	19%
Piperacillin/tazobactam	10.2%

The sensitivity analysis of urinary Providencia highlighted high sensitivities to Meropenem (99.9%), Imipenem (96.4%), Colistin (99.4%), Polymyxin-B (98.5%), Fosfomycin (97.2%), Amikacin (100%), and Gentamicin (100%). Notably, Piperacillin demonstrated a low sensitivity of 12.5% in urinary Providencia patients (Table II) for detailed sensitivity percentages.

Table II: Antimicrobial Sensitivity Patterns of Urinary Providencia (n=62)

Antibiotics	Sensitivity %
Amikacin	100%
Gentamicin	100%
Meropenem	99.9%
Colistin	99.4%

Polymixin-B	98.5%
Fosfomycin	97.2%
Imipenem	96.4%
Nitrofurantoin	95.8%
Cefoperazone/Sulbactam	38.3%
Cefepime	34.1%
Ciprofloxacin	33.6%
Ceftriaxone	33.4%
Ceftazidime	31.4%
Co-Amoxiclav	16.4%
Piperacillin/ Tazobactam	12.5%

The antimicrobial sensitivity patterns for urinary Enterobacter cases are outlined in Table III.

Table III: Antimicrobial Sensitivity Patterns of Urinary Enterobacter (n=50)

Antibiotics	Sensitivity in %
Gentamicin	100%
Amikacin	99.9%
Colistin	99.9%
Fosfomycin	99.7%
Polymixin-B	99.3%
Meropenem	99.1%
Imipenem	97.1%
Nitrofurantoin	94.5%
Cefoperazone/Sulbactam	40.0%
Cefepime	39.7%
Ceftriaxone	31.2%
Ceftazidime	29.6%
Ciprofloxacin	29.5%
Piperacillin/ Tazobactam	18.9%
Co-Amoxiclav	13.5%

The sensitivity pattern for urinary Enterococcus faecium cases revealed high sensitivity to Meropenem (99.8%), Fosfomycin (99.8%), and other antibiotics. Specific percentages for additional antibiotics are mention in Table IV.

Urinary Pseudomonas aeruginosa's antimicrobial sensitivity profile revealed varying sensitivities. Meropenem (99.3%), Imipenem (99.3%), Colistin (99.9%), Polymyxin-B (99.4%), and several others were tested. The results showed a remarkable sensitivity pattern against pseudomonas aeruginosa species. Complete sensitivity percentages can be seen on Table V.

Table IV: Antimicrobial Sensitivity Patterns of Urinary Enterococcus Faecium (n=50)

Antibiotics	Sensitivity %
Fosfomycin	99.8%
Meropenem	99.8%
Colistin	99.8%
Polymixin-B	99.8%
Imipenem	99.1%
Gentamicin	98.7%
Amikacin	98.7%
Nitrofurantoin	96.4%
Ciprofloxacin	40.1%
Cefoperazone/Sulbactam	39.4%
Ceftazidime	36.4%
Ceftriaxone	34.5%
Cefepime	32.1%
Co-Amoxiclav	22.5%
Piperacillin/ Tazobactam	19.5%

Table V: Antimicrobial Sensitivity Patterns of Urinary Pseudomonas aeruginosa (n=16)

Antibiotics	Sensitivity pattern %
Polymixin-B	99.4%
Imipenem	99.3%
Meropenem	99.3%
Colistin	98.8%
Gentamicin	97.2%
Amikacin	96.4%
Fosfomycin	94.7%
Nitrofurantoin	91.3%
Ciprofloxacin	26.4%
Ceftazidime	24.7%
Cefoperazone/Sulbactam	22.1%
Ceftriaxone	22.1%
Cefepime	20.2%
Piperacillin/ tazobactam	16.5%
Co-Amoxiclav	11.1%

Discussion

Urosepsis is a prevalent clinical condition. Our study revealed a higher incidence of urosepsis among females. In our study cohort, 363 (54.70%) females were diagnosed with urosepsis compared to 301 (45.30%) males admitted to the hospital. This indicates a greater susceptibility among females towards the disease, a trend similar to findings in a Spanish study.[14] These results align with existing research indicating a higher prevalence of these infections in women, often attributed to anatomical and physiological factors.7 It's estimated that one in every three women will require antimicrobial therapy for a UTI, and 50% of women will experience a UTI at some point in their lives.[8]

In our study, the culture growth exhibited various species, with E. coli shaving higher growth percentage of 57.5%. Other species identified included Providencia sp. at 9.3%, Enterococcus faecium at 7.5%, Enterobacter at 7.5%, Klebsiella at 2.4%, and a mixed growth pattern observed in 9.0% of samples. A study with a similar pattern reported a significantly higher percentage (80.95%) of bacterial strains being K. pneumoniae, indicating the presence of extended spectrum beta-lactamases.[15]

Previous reports highlight E. coli and Pneumonia as the most common bacterial strains among the Enterobacteria family, serving as major pathogenic agents in drug resistance, with resistance rates nearing 80% in samples.[16]

Our study also correlates with findings of the study conducted previously showing, the total burden of urosepsis and sensitivity pattern of gram negative bacteria's[17] the Gram-negative bacteria was the main etiological factor of urosepsis, with the distribution as follows: Escherichia coli 50%, Proteus spp. 15%, Enterobacter and Klebsiella 15% and Pseudomonas aeruginosa 5%, while Gram-positive bacteria represent only 15%.[10] Therefore, our main focus has been primarily on E. Coli, but for a deeper dive into the epidemiology, which would then allow us to make more inclusive recommendations, we did consider all the bacterial spectrum.[5,6]

The susceptibility pattern of our study was assessed and compared to the study conducted regionally showing that there are significant regional differences in the in vitro susceptibility of E. coli urine isolates to the most popular first line antibiotic treatments prescribed for UTI.[11,12] This reinforces the need for a detailed local study to identify the local causative organisms and their respective sensitivities, to be able to counter more effectively even before receiving the culture results. In a local study carried out in Peshawar, Pakistan, the isolated uro-pathogens were more sensitive against amikacin and gentamicin while most of the uro-pathogens showed resistance against tobramycin and ciprofloxacin.[13] While in another study using Amikacin or Cefoperazone/Sulbactam as the initial treatment with empirical therapies and broad-spectrum antibiotics were prescribed as choice while awaiting culture results was recommended.[18]

Our study showed , a steep decline in the sensitivities pattern, In our testing the drugs with the greatest sensitivities observed was Meropenem showing the sensitivity of (99.5%), followed by Imipenem (99.6%), Colistin (99.9%), Polymyxin-B (99.9%), Fosfomycin (96.4%), Amikacin (96.7%), Gentamicin (97.4%), Nitrofurantoin (91.5%), similar results showing the highest sensitivity for meropenem was observed in a previous study supporting our findings.[19] This phenomenon could be partly, attributed to the development of beta-lactamases, enzymes that degrade penicillin's and cephalosporins by hydrolyzing their b-lactam nucleus; especially, the presence of extended-spectrum beta-lactamase (ESBL) in these strains.[19-20]

In our study the low sensitivity pattern was observed in Ceftriaxone showing sensitivity (34.4%), followed by Ciprofloxacin (31.5%), Piperacillin/ Tazobactam (10.2%), Cefepime (39.1%), Co Amoxiclav (19.0%), Ceftazidime (37.4%) and Cefoperazone /Sulbactam (26.5%), the Antimicrobial resistance is a growing problem and a cause of great concern throughout the world. Antimicrobial resistance is a major public health issue in Pakistan.[21] However the resistant pattern varies from patient to patients providing the limited window for the potential antibiotics, a similar study conducted on the resistance showed with a steady increase in the level of resistance to commonly used antibiotics over the period of time, increase by 20% of patients to 28.4% of patients towards commonly used antibiotics.[22] This higher resistance rate appears to be the result of many factors, one of which is the public's high and uncontrolled consumption of these antibiotics over the past decade in our region.

Urinary tract infections vary from patient to patient depending on the symptoms, sometimes totally asymptomatic, bacteriuria, and a septic shock. UTI and Urosepsis a very common conditions amongst the general population. A similar study showed meta-analysis of 93 studies done in Pakistan revealed UTIs and Urosepsis having a cumulative burden of 16.1% of all the reported clinical diagnoses.[15] Pakistan is a country where most of its occupants are from a low socioeconomic status thus throwing a substantial health care burden.[23]

Antimicrobial resistance is a potential global threat, the antibacterial resistance is growing widely and the spectrum of bacteria is evolving at an alarming rate along with the fact that previously recommended empirical antibiotics are now less sensitive. We recommend starting with Carbapenems and Aminoglycosides in patients with suspicion of Urosepsis while awaiting culture results.

Urinary infections are largely influenced by host factors. The severity of infection depends on the patient, contributing to higher morbidity rates, UTI-related complications, and mortality. These infections are linked to elevated healthcare costs, increased hospitalization rates, resistance patterns, reduced antibiotic sensitivity, and heightened risks of urosepsis progression.[25]

Conclusion

The resistance pattern was observed clearly among the patients with different urinary tract infections specifically urosepsis. The results of the study showed the sensitivity pattern against microbial growth and the most effective antibiotics were meropenem and carbapenem with remarkable differences. The rationale prescribing practice is strongly recommended as per WHO guidelines to avoid the multiple drug resistance. The findings suggest the assessment of multiple trains of gram-negative bacteria's and sensitivity pattern of bacterial strains on a large number of samples to support the evidence based use of bacterial therapies.

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