ORIGINAL ARTICLE

Antimicrobial Susceptibility Patterns of Leading Uropathogens and an Empirical Therapy at a Tertiary Care Hospital, Muzaffarabad

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Abstract

Background: Urinary tract infections (UTI) with non-specific treatment are leading to drug resistance. Cost-effective empirical therapy demands a brief survey of causative agents with their antibiograms. This study will show the bacterial spectrum and their susceptibility toward drugs which will enable us to make an accurate choice of drugs for empirical therapy.

Aim: The aim of this study is to determine the bacterial profile in UTI and demonstrate its pattern of antimicrobial susceptibility.

Method: This cross-sectional study was conducted in the microbiological lab of Sheikh Khalifa Bin Zayed Al-Nahyan Hospital, Muzaffarabad, Azad Jammu and Kashmir (AJK) from Oct 2017 to Oct 2018. Mid-stream urine received in the Department of Microbiology with symptomatic UTI was considered and inoculated onto Cysteine Lactose Electrolyte Deficient (CLED) agar. Bacterial identification with a series of biochemical tests and diffusion disc-based antimicrobial susceptibility test were done according to standard operating procedures.

Results: Out of 552 samples, 113(20.4%) of the specimens were cultured positive with the majority of females with 80(70.7%) of prevalence while the male were 33(29.3%). *E. coli* was most frequent bacteria isolated about 49(43.4%) followed by *S. aureus* 23(20.4%), *Klebsiellapneumonia* 15(13.3%), *Pseudomonas aeruginosa* 9(8%), *Proteus mirabilis* 6(5.3%), *Enterobacter spp.* 5(4.4%), *Citrobacter spp.* 3(2.6%), *Salmonella* 2(1.7%) and *Klebsiellaoxytoca* 1(0.9%). Gram-negative bacteria showed great susceptibility for Tazobactam-piperacillin, Meropenem, Levofloxacin and Nitrofurantoin. Gram-positive were highly sensitive to Nitrofurantoin, Amikacinand Cefixime. Ampicillin showed the highest resistance rate of 87.4%.

Conclusion: As an empirical treatment, Tazobactam-piperacillin and Meropenem are good choices for gram-negative bacteria while Nitrofurantoin showed high efficacy toward gram-positive bacteria.

Keywords: *UTI, sensitivity, resistance, empirical therapy, susceptibility, efficacy.*

INTRODUCTION

Urinary tract infection (UTI) are still ranked as the most common complaint infection [1]. Each year about 150 million people are affected from this disease [2]. Bacteria infiltration is the major factor in which *E. coli* has been ranked at top for causing urinary tract infection [3, 4]. In 90% of cases, uropathogenicity is initiated due to contamination of the urinary tract with normal flora of the genitourinary tract and rectum [5]. The international studies showed that this infectious state is more frequent in females and one in every five experiences UTI in her life [6-8].

This problematic event is augmented by the emergence of antimicrobial drug resistance, a major health care issue with inter-regional variability [9]. In developing countries, lack of education, high poverty rate, and poor hygienic practices are the leading factors initiating resistance, while a number of fake and spurious medicines with doubtful quality are also in the circle [10]. These countries have easy access to drugs without a prescription, whose extensive use increases the rate of resistance among the microbial population [11-13]. It is very strenuous to satisfy patient's health with appropriate empirical therapy. A detailed and brief study is needed to improve the prescription of antibiotics. According to the Infectious Diseases Society of America's recommendation, it is very important for the physician to obtain local data of resistance patterns in order to monitor the changing susceptibility pattern of pathogens [2].

As there is no organized data on microbiological profile of UTI in an adult in Muzaffarabad, this study will contribute in demonstrating the most sensitive antibiotics for gram-positive and gram-negative bacteria which will guide the physician to select effective therapy and evaluate a detailed antibiogram which may help to avoid unnecessary usage of drugs which return in limitation of drug resistance.

MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of Microbiology at Sheikh Khalifa Bin Zayed

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Al-Nahyan Hospital, Muzaffarabad, AJK from Oct 2017 to Oct 2018. A well-mixed and non-centrifuged urine sample in a sterile container was inoculated by a urine strip that can deliver up to 0.2µl of urine on Cysteine Lactose Electrolyte Deficient agar plate (Oxoid Ltd, Basingstoke, UK) within 30 mins of collection and incubation at 37°C for 24hrs. Isolate having a pure growth of $>10^5$ colony forming units (CFU) was considered to be significant. Isolates were identified on the basis of their physical characters such as colony morphology, presence, and pattern of hemolysis and then by a series of biochemical reactions according to standard practice procedures [14, 15]. All gram-negative rods and enterococci were processed for biochemical test API 10. Antimicrobial sensitivity was performed using Kirby-Bauer disc diffusion technique [16] on Mueller-Hinton agar (OXOID Ltd) according to Standard [17, 18].

On the basis of the zone of inhibition of bacterial growth, susceptibility and resistance pattern of drugs were classified as sensitive, intermediate or resistant [18]. Methicillin-resistant *Staphylococcus aureus* (MRSA) was detected using cefoxitin disk and the isolate with the zone of inhibition of ≤21mm was confirmed phenotypically to be MRSA.

The study protocol was approved by an ethical review committee of Azad Jammu and Kashmir Medical College, Muzaffarabad. Data was entered and analyzed by using SPSS version 21 and the studied variables were abridged in the form of percentage and frequency.

RESULTS

A total of 552 clinical urine samples were included in this study in which a high presentation of female 314(57%) was seen than male 238(43%). 113(20.4%) of the specimen showed significant growth of uropathogens. A high prevalence of UTI was observed in females 80(70.7%) while in males it was 33(29.3%). Gram-negative bacteria were a dominating group with a high frequency of 90(79.6%) than gram-positive bacteria 23(20.4%). *E. coli* 49(43.4%) was the most frequent isolate. **Fig. (1)** illustrated the distribution of isolates.

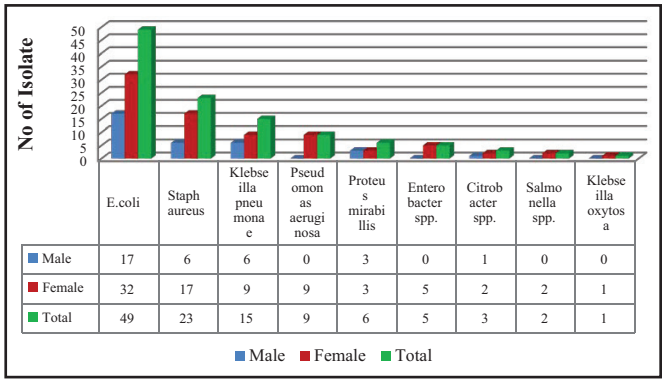

Fig. (1): Distribution of Pathogen.

Table. 1: Antibiogram of Uropathogen toward drugs.

-	*Staph aureus*		*E. coli*		*Pseudomonas aeruginosa*		*Proteus mirabilis*		*Klebsiella pneumoniae*	
	S	R	S	R	S	R	S	R	S	R
Amikacin	83.3	16.7	65.2	21.7	50	50	0	100	100	0
Ampicillin	14.2	85.8	20.6	75.8	28.5	71.4	0	100	0	100
Augmentin	45	55	22	75.6	0	100	33.3	66.6	10	90
Cefradine	50	50	28.5	71.4	ND	ND	0	100	0	100
Cefixime	75	25	16.6	83.3	ND	ND	ND	ND	33.3	66.6
Ciprofloxacin	41.6	50	32.1	67.8	42.8	57.1	20	80	70	20
Cotrimoxazole	30	70	45.5	54.5	0	100	100	0	44.4	55.5
Ceftriaxone	55.5	44.4	38.4	61.5	0	100	0	100	28.5	71.4
Clarithromycin	42.8	57.2	ND	ND	ND	ND	ND	ND	ND	ND
Cefoxitin	66.6	33.3	100	0	100	0	100	0	66.6	33.3
Doxycycline	70	30	ND	ND	ND	ND	ND	ND	ND	ND
Gentamicin	50	50	100	0	100	0	ND	ND	50	50
Erythromycin	ND	ND	100	0	ND	ND	0	100	0	100
Levofloxacin	40	60	53.8	46.1	75	25	ND	ND	75	25
Imipenem	70.1	29.9	87.1	10.2	100	0	60	40	93.3	6.6
Meropenem	65	35	90.4	9.5	66.6	33.3	100	0	100	0
Nitrofurantoin	85.7	14.2	92.3	3.4	80	20	100	0	90	10
Tazobactum Pipracillin	50	50	96	4	86	14	96	4	100	0
Vancomycin	71.4	28.6	ND	ND	ND	ND	ND	ND	ND	ND

S= Sensitive R=Resistant ND=Not Determined

The highest susceptibility of Tazobactam-Piperacillin (99%) was seen in gram-negative bacteria along with Meropenem (81.7%), Levofloxacin (76%), Nitrofurantoin (72.4%) and Imipenem (65%). Nitrofurantoin and Amikacin remained the highest sensitive drugs toward gram-positive bacteria with a sensitivity rate of 85.7% and 83.3% respectively. Table **1** demonstrated the sensitivity and resistance profile.

Out of 23 *S. aureus*, 18 were tested for cefoxitin of which 33.3% found to be MRSA. *S. aureus* exhibits high sensitivity for Nitrofurantoin (85.7%), Amikacin (83.3%), Cefixime (75%) Vancomycin (71.4%), Imipenem (70.1) and Doxycycline (70%) with high resistance toward Ampicillin (85.7%) and Co-trimoxazole (70%).

The highly consumable antibiotics showed less susceptibility against gram-positive and negative bacteria. Ampicillin showed the highest resistance rate of 87.4% **(Fig. 2)**.

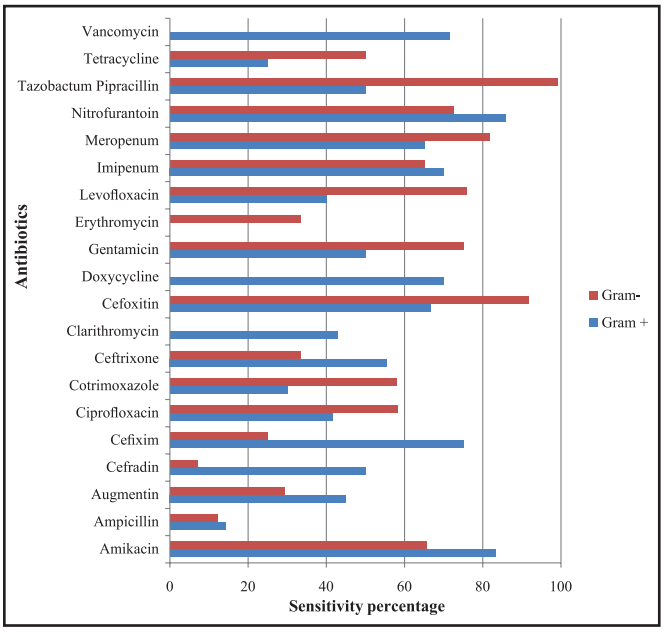

Fig. (2): Sensitivity percentage of antibiotics against Gram-Positive and Gram-Negative Bacteria. In antibiotic susceptibility test, Erythromycin was not determined in gram positive bacteria while Vancomycin, Doxycycline, and Clarithromycin was not determined in gram negative pathogen.

DISCUSSION

While microbial resistance is increasing, it is very important for a physician to have a look at local antibiogram history before the recommendation of empirical treatment. This study will contribute to providing the data for the distribution of UTI causing agents and their susceptibility towards drugs and will be useful in making guidelines for drug recommendation.

In our study, the overall prevalence of UTI was 20.4%, which is highly near to the study conducted in International Medical College and Hospital, Gazipur and PIMS Hospital, Islamabad with the prevalence of 20.2 and 20.7 respectively [19, 20].

There was a high prevalence of UTI in females than male with 80% of the ration. As reported globally, prevalence of UTI in females was recorded higher than males [21]. This study also explored that gram-negative bacteria are a major factor in this complaint. A study conducted by Ahmed *et al*. in Jinnah Hospital, Lahore concluded that gram-negative group is causing 81% of UTI [22].

Our investigation isolated *E. coli* as the most leading UTI causing pathogen with a prevalence of 43.3% which bears a close resemblance in Islamabad 43.2%, while high percentage was reported in Peshawar and Lahore with a ratio of 66% and 76.8% [19, 23, 24]. Our study concluded *S. aureus* as the second most common pathogen of UTIs. In 2013, a research carried out in Mayo Hospital, Lahore also ranked *S. aureus* as the second-leading agent causing UTIs while studies in Nigeria and India reported the same results [11, 25, 26]. Thus, these recent findings confirm *S. aureus* as an important etiologic agent in UTIs. Gram-negative bacteria were highly sensitive to Tazobactam piperacillin, Meropenem and Imipenem, another study showed the same sensitivity pattern in Ethiopia and Lahore [27, 28]. A research conducted in Creek General Hospital, Karachi and tertiary care hospital of Kerala, India rated Nitrofurantoin and Amikacin as highly sensitive drug towards Staph aureus-induced UTI which extends our study [29, 30].

This study revealed that the highly recommended drugs have low efficacy, which is the result of overuse or misuse of drugs. This situation was also seen in Sri Lanka and Ethiopia in which susceptibility Ampicillin, Co-trimoxazole, Ciprofloxacin and Ceftriaxone were recorded low [31, 32]. 85% of UTI cases showed resistance to Ampicillin, that was 76% in a Turkish study [33].

CONCLUSION

This evaluation concluded that females are more vulnerable toward UTI with high portion of gram-negative group while *E. coli* remains on top. This study alarmed about the high resistance of commonly recommended drugs. Gram-negative should be empirically treated with Tazobactam-piperacillin and Meropenem while gram-positive with Nitrofurantoin and Amikacin.

This study recommends that the hospital should adopt policies for regulation of antibiotic usage and antibiotic stewardship to limit increasing resistance. Empirical treatment should be prescribed by reference to the antibiogram of that area. The patient should be properly guided regarding right usage of drugs. There should be a constant evaluation of antibiotic spectrum of commonly used drugs. Hospitals in collaboration with stakeholders should make a committee to evaluate the quality of drugs launched by a pharmaceutical industry.

AVAILABILITY OF DATA AND MATERIALS

The data used to support the findings of this study is available from the corresponding author upon request.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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