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RESEARCH ARTICLE
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ANTI-MICROBIAL RESISTANCE AND SENSITIVITY PATTERNS OF E.COLI, AMONG ADULT PATIENTS WITH URINARY TRACT INFECTIONS AT DHQ HOSPITAL, ORAKZAI DISTRICT, KHYBER PAKHTUNKHWA, PAKISTAN - A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Urinary tract infections (UTI) are among the most common and serious public health problems worldwide, being primarily caused by Escherichia coli. Treatment strategies are being complicated by an increasing incidence of antimicrobial resistance (AMR).

Objectives: The objective of this cross-sectional study was to determine the frequency, Prevalence and antimicrobial resistance patterns among urinary tract infections (UTIs) in adult patients at District Headquarters Hospital Orakzai Khyber Pakhtunkhwa Pakistan.

Methods: During May – June 2023, a total of adult patients with clinical suspicion to UTIs (n= 130) were included. We performed ordinary microbiological urine culture and identification of isolated bacteria. Antibiotic susceptibilities were performed in accordance to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) by Kirby-Bauer disc diffusion method.

Results: The frequency of UTIs was 26.6%, and Ecoli were the responsible pathogens in 92% of positive cultures. The most striking finding: 80% of E. coli isolates made an enzyme called extended-spectrum beta-lactamases (ESBLs). Antibiogram analysis showed that amikacin (85.1 %), fosfomycin(85%), imipenem (92.5%), ertapenem (92.5%), cefoperazon/sulbactam(88%) and piperacilin/tazobactam were highly sensitive against E.coli. On the other hand, high rate of cefepime (81 %), ceftriaxone (88.8%), ceftazidirne(77%) and cefotaxime resistant isolates were noticed.

Conclusions: The changing spectra of antimicrobial resistance highlights the importance of ongoing monitoring for trends in susceptibility. These are important steps to help direct empiric therapy for UTIs.

Keywords: Urinary tract infections, (UTI), Escherichia coli, antimicrobial resistance.

INTRODUCTION

UTI is one of the most common bacterial infections in humans, affecting both different age groups and sex populations whether they are community or hospital acquired [1]. UTIs are one of the major

threats that contribute significantly to enormous impact on healthcare AS WELL as financial burden. Globally nearly 150 million patients are diagnosed with UTIs annually and this causes a substantial public health burden on the economy costing more than $6million USD in both developed and developing countries [2]. UTIs reflect the presence of bacteria in the urine with associated symptoms, irrespective on which anatomic subregion (cystitis / pyelonephritis) is infected [3-4]. At minimum, localized genitourinary symptoms (i.e., cystitis or urethritis), pyuria (as evidence of urinary tract inflammation) and a positive urine culture meeting the definition for an identifiable UTI pathogen are needed to make a diagnosis of symptomatic UTI in patients [5]. Those may be clinically asymptomatic (although many current references distinguish it as a separate entity under the name of "asymptomatic bacteriuria", which for most part does not need to receive antibiotic treatment, and is considered outside of UTIs) or present with distressing signs such as cystitis — pyelonephritis, and urethritis [6,7]. Because of key anatomical differences, females are at a greater risk than males for developing UTIs, especially uncomplicated infections [8],[9]. About 50% of women will have at least one UTI in their lifetime [10]. The majority of men do not experience this illness, and the few who develop it are over 50 years old, presenting a devastating form [11]. Risk factors such as age, history of UTI, multiple sex partners and diabetes are important. There are two categories of UTIs – complicated and uncomplicated. The spectrum of causative
organisms for a complicated infection is much broader than that associated with an uncomplicated UTI, but the major pathogens likely to be responsible for both upper and lower urinary tract infections are similar[12]. UTI can be caused by both Gram negative and positive bacteria. The main reason for both severe and This occurs in uncomplicated UTIs [13], Since they are part of the normal flora of the human intestine, it so quickly colonizes;the urinary tract [14]. The susceptibility of E. coli to routine antibiotics is highly location dependant[15•]. Klebsiella species, the Proteus-Providencia-Morganella group and Staphylococcus saprophyticus are other relevant organisms associated with acute uncomplicated UTIs [16]. One previously published literature review found that up to 15% of all antibiotic prescriptions in the United States or specific European countries are for UTI [17],[18]. Urinary tract infections are treated with broad spectrum antibiotics as well. However, misuse of these drugs was increased the widespread availability along with resulted to increase antibiotic resistance in most commonly utilized uropathogens [19], which may be a matter of global health alarm. Which is why UTIs can be impossible to cure. This anomaly can be rectified by continuous monitoring and reviewing of local postsurgical antibiograms.This would therefore help us to select for the most appropriate antibiotics in treatment, allowing UTIs patients improved outcomes. A study carried out in India found the prevalence of UTI was 16.4% (95 % CI; 13.3 –19.9). Of all the bacteria, E. coli was predominantly isolated account for 43.5%, CoNS follow by S.aureus and K.pneumoniae with total number of case are as follows; [Coagulase negative staphylococcus (CoNS) 11(16%), Staphylococcus aureus9(13%)] respectively followed by Pseudomonas aeruginosa[P.A] accounted :-).2bed to MP2000 per piece], Proteaus mirabilis,Morgganella morganii each4 cases[6%] again Citrobacter spp3cases[44]. In vitro, all Gram-negative bacilli were resitant to ampicillin (96%), tetracycline (71.4%) and nearly- half of the coagulase-positive Staphylococcus spp., isolates exhibited resistance against ampicillin(90 %); However only 5S% of them proved not sensitive against tetracycilne Eighty-five percent of isolated bacteria showed multidrug resistance [20]. A study conducted in Teaching hospital Kohat, Khyber Pakhtunkhwa found out that the prevalence of UTI among symptomatic patients is 11.6%, and through interested note mean percentage in males was 8.9% whereas it rolls up to be 13. The isolated bacteria included [[ADV_6]] and [[text of interestx1]]; these constituted the predominance are shown (Table []). 20.7%; 79.3% The most common uropathogenic bacteria E. coli was observed in 41.4% [21]. This study targeted an antibiogram profile from urine samples taken from the UTI patients were analyzed for resistance and sensitivity spectrum under clinical laboratory conditions as DHQ Orakzai Pakistan.

METHODOLOGY

A laboratory based cross-sectional study was conducted from May 2023 to octoberu0536 in the Orakzai District of Khyber Pakhtunkhwa, Pakistan. Of the urine culture, bacterial identification and antibiotics sensitivity testing were done at laboratory of hospital. The verbal consent of all the participants was obtained during data collection. Participants names were not recorded and the data was kept confidential. The study adult patients, male or female from different parts of Orakzai district who attended DHQ hospital with UTI during 2018. Written consent was waived and verbal informed consent obtained from all patients for the present study. We developed an extensive questionnaire to collate the data. Informed consent was obtained from the patients and data were collected through a face-to-face interview. A total of 130 patients using consecutive random sampling technique. Questionnaire: To determine the antibiotic resistant pattern of uropathogen (mainly E.coli) in UTI and its related symptomatology a structured questionnaire was developed based on following literature reviewed. The first part included items that demographic of the participants such as gender, age, marital status and monthly salary were questioned. The second part contained a set of questions regarding health and hygiene risk factors such as history of catheter use, urinary tract infections (UTI), kidney or bladder surgeries performed, how many glasses/cups/beers are consumed daily. Part III was constructed according to clinical data including fever, dysuria and polyuria syndrome /urgency /Lumbago.

Urine Sample Collection

All participants were provided with a wide-necked sterile container to collect urine samples. The samples were processed immediately after collection, or otherwise the samples were stored in a refrigerator at 4°C.

Isolation and Identification of the Organism From the Urine Inoculated all the samples on cystine lactose electrolytes deficient medium (CLED), which is a selective bacteriological media used for isolation of uropathogens. The medium was prepared as described by Oxoid limited (USA); 36.2g powered were dissolved

in distilled water and boiled to dissolve completely then autoclaved at 121°C, dispensed media of volume between15-20 ml in each Petri dish. The plates were incubated at 37°C for 24 hours after they inoculated. Identification of organism was carried out after incubation based on colonial characteristics with biochemical identification (Indole, motility and triple sugar Iron).

Stainless Steel Probe and Antibiotic Disk Syringe Cage

Kirby bar disc diffusion antibiogram was carried out. The MHA(Muller Hinton agar) was prepared as per the manufacturer instruction (Oxoid limited USA). The single colony from overnight fresh bacterial culture was then picked and dissolved in turbidity deionized water equal to 0.5Macfarland standard to prepare the bacteria suspension. Bacterial suspension is spread on the surface of MHA plate to prepare bacterial lawn. A total of 12 antibiotics i.e., Piperacillin, tazobactam Co-Amoxiclav Ciprofloxacin, ceftriaxone ceftotoxime Ceftazidime Fosfomycin Nitrofurantoin Cefepime Amikacin Cefoperzone and sulbactum Imipenem Ertapenem were used in this study Each antibiotic disc was read for the zone of inhibition in millimeter (mm) and, result interpretation made by Clinical Laboratory Standard Institute [CLSI] 2023 guidelines[21].

Statistical Analysis

The analysis was performed using Statistical Package for Social Science (SPSS) Version 27.0. Results were reported as percentages and tables.

RESULTS

In this study, 130 samples with UTI complaints and their associated risk factors were investigated. The majority of participants belonged to the age group 18- 30 years.The mean age of the participants was 35.7 years (±14.53 SD) with a range of 15–80 years, as shown in the table 1 and figure 1. Of the total participants, 74 (56.9%) were female. Most of the participants were married 107 (82.3%). The majority of the participants 90 (69.2%) has a poor socioeconomic status.

Age group	UTI
18 to 30 y	15
31 to 45 y	9
46 to 80 y	5

Prevalence of Urinary Tract Infections

Among the 130 analyzed samples, 109 (77.7 %) were negative, whereas 21 (22.3%) had positive urine culture (105 cfu/ ML)as shown in the table 2.The overall prevalence rate of UTI was 26.6%, and the prevalence of infections in females and males was 19 (65.5%) and 10 (34.5%), respectively. The most
common uropathogen isolated was E.coli which showed growth in 92% of the positive cultures. 80% of the E.coli was ESBL. Two samples showed growth of E. faecalis. As shown in table 3.

Table 2;

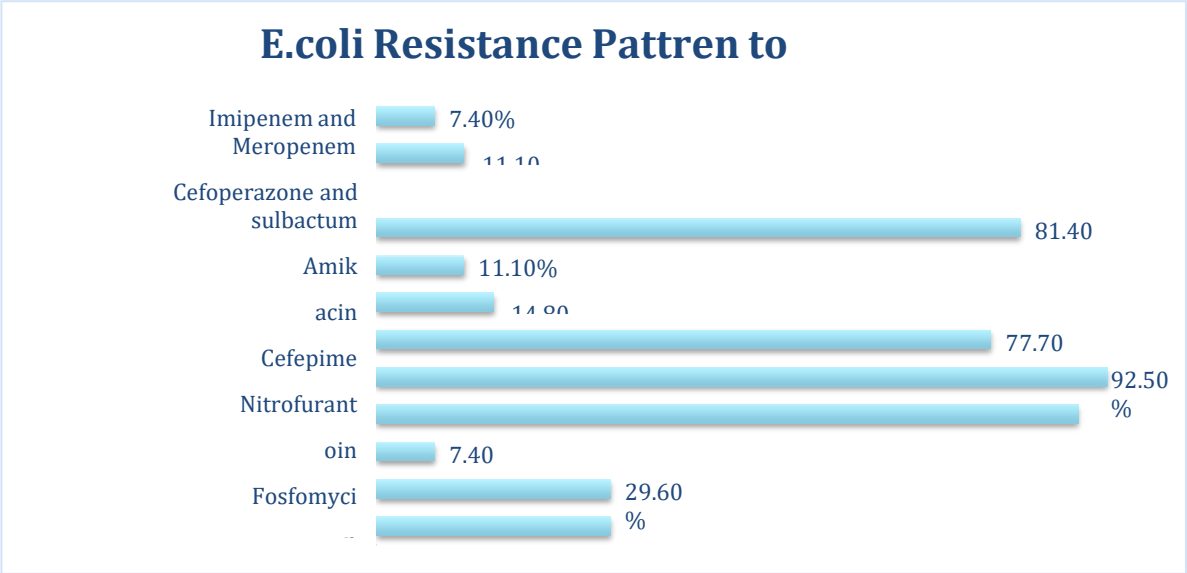
Culture results	Female	Male	Total
culture positive	19	10	29
culture negative	55	46	101
	74	56	130

Table 3;

E.Coli	6
ESBL E.coli	21
E.Feacalis	2

Antibiotics Sensitivity Pattern of E.coli

The pattern of resistance and sensitivity among the uropathogen was consistent among all results.Overall, E.coli was mostly susceptible to Piperacillin and tazobactam (92.5%, n=25) Cefoperazone and sulbactam (88% n=24), Imipenem (92.5%, n=25 and Ertapenem (92.5%, n=25), Amikacin (85.1%, n=23), Fosfomycin (85%, n=23) and Nitrofurantoin (80.7%, n=21).Low sensitivity was observed towards Cefepime (18.5%, n=5), Ceftriaxone (11%, n=3), Ceftazidime (22.2%, n=6), and Cefotaxime (7.4%, n=2).As shown in fig 1.



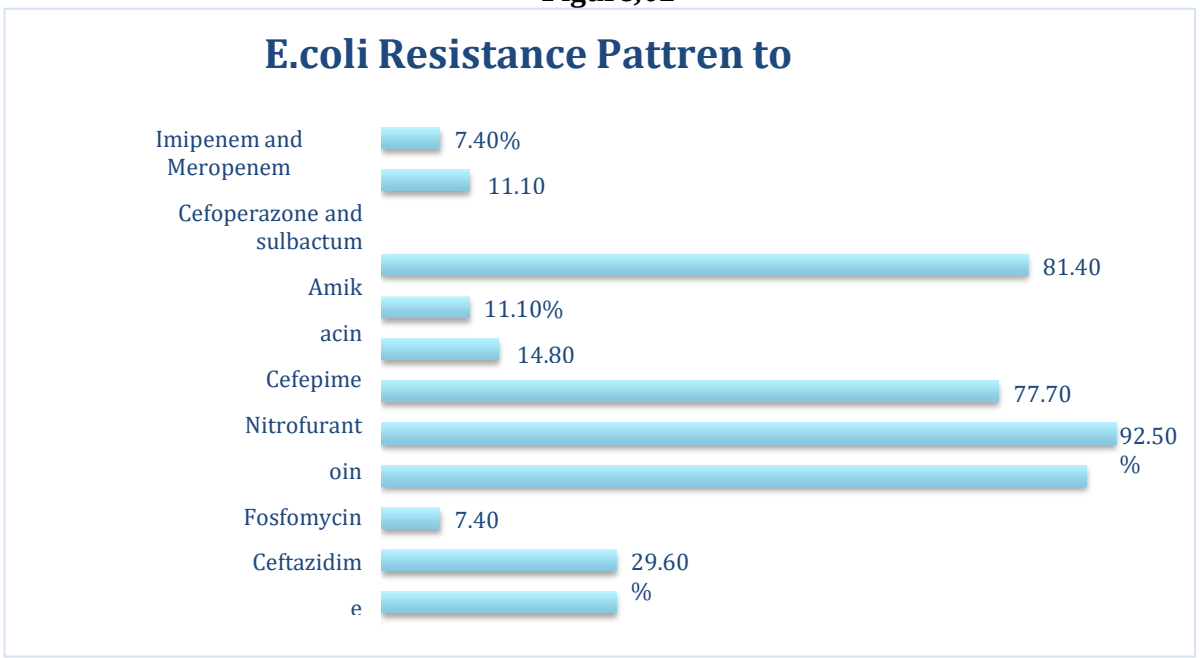
Antibiotics Resistance Pattern of E.coli

A high pattern of resistance for E.coli was observed among the following commonly prescribed antibiotics; Cefepime (81%, n=22), Ceftriaxone (88.8%, n=24), Ceftazidime (77%, n=21), Cefotaxime (92.5, n=25).While the resistance towards other antibiotics was low i.e. Cefoperazone and sulbactam about 12 % (n=3), Fosfomycin 14.8 % (n=4), Piperacillin and tazobactam 7.5% (n=2), Nitrofurantoin 19
% (n=5), and Imipenem and Ertapenem 7% (n=2). As shown in figure 2.Towards the ciprofloxacin and Co-amoxiclav, the E.coli demonstrate partial resistance and susceptibility pattern.

The complete sensitivity of E.coli towards Ciprofloxacin was 44.4% (n=12), While 25.9% (n=7) showed partial sensitivity. The resistance for ciprofloxacin was 29.6% (n=8).

For Co-amoxiclav, the complete sensitivity noted was 22.2% (n=6) while 48.15 (n=13) showed partial sensitivity. The resistance for Co-amoxiclav was 29.6% (n=8).As shown in fig 1 and 2.

Figure;02



DISCUSSION

This study investigated the prevalence, bacterial etiology, and antimicrobial resistance patterns of urinary tract infections (UTIs) among patients attending DHQ Hospital in Orakzai, Pakistan. The findings shed light on the significant burden of UTIs in the local population and underscored the alarming rates of antimicrobial resistance (AMR) among uropathogens, particularly Escherichia coli (E. coli).The prevalence of UTIs in our study population was substantial, with a prevalence rate of 26.6%. This aligns with previous research highlighting UTIs as a common health concern in Pakistan and globally [1], [14]. The predominance of UTIs in females, as observed in our study, is consistent with established epidemiological trends attributed to anatomical differences and other risk factors [2],[15].E. coli emerged as the predominant uropathogen isolated, corroborating findings from similar studies [2],[16]. The high prevalence of ESBL-producing E. coli strains, accounting for 80% of isolates, is concerning and underscores the urgent need for effective antimicrobial stewardship programs to address the escalating threat of AMR[9].

Antibiogram analysis revealed varying sensitivity patterns of E. coli to commonly prescribed antibiotics. While some antibiotics demonstrated high efficacy, including Piperacillin and tazobactam, Imipenem, and Ertapenem, others showed alarmingly low sensitivity rates, such as Ceftriaxone and Ceftazidime. These findings highlight the importance of tailored antibiotic therapy guided by local resistance patterns to optimize treatment outcomes [22].The high rates of resistance observed for key antibiotics emphasize the need for comprehensive strategies to combat AMR, including antimicrobial stewardship initiatives, infection control measures, and surveillance systems[18],[19]. Addressing the drivers of AMR and promoting rational antibiotic use are essential to preserve the effectiveness of available antimicrobials and ensure optimal patient care.Despite the valuable insights provided by this study, several limitations should be acknowledged. These include the reliance on a single healthcare facility, potential selection bias, and the absence of molecular typing methods to characterize resistant strains. Future research should explore these aspects further and investigate the impact of interventions aimed at mitigating AMR in UTIs.

CONCLUSION

this study contributes to our understanding of UTIs and AMR patterns in the Orakzai, Pakistan. The findings underscore the urgent need for concerted efforts to address AMR and ensure effective management of UTIs, ultimately safeguarding public health.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

Authors Contribution

Concept & Design of Study: Hameed Badshah,
Drafting: Saiyad Ali
Data Analysis: Tauseef Hamid
Critical Review: Shafiq Ur Rahman
Final Approval of version: Hameed Badshah,

REFERENCES

1. Demilie T., Beyene G., Melaku S., Tsegaye W. Urinary bacterial profile and antibiotic susceptibility pattern among pregnant women in north west ethiopia. Ethiop. J. Health Sci.2012;22(2):121–128
2. Foxman B. Epidemiology of urinary tract infection. Nat Rev Urol. 2010;7(12):653–660. doi:

10.1038/nrurol.2010.190
3. Oluwole OM, Victoria AA (2016) Asymptomatic bacteriuria:occurrence and antibiotic susceptibility profiles among students of a tertiary institution in Ile-Ife, Nigeria. Afr J Microbiol Res 10:505-510.
4. Rusu A, Petca A, Mares C, Petca RC, Popescu RI, Negotia S,Danau RA, Chibelean CB, Jinga V (2023) Urinary tract infections in a Romanian population: antimicrobial resistance of uropathogens – a multiregional study. Farmacia (Buchurest) 70:165- 173.
5. Rowe TA, Juthani-Mehta M. Diagnosis and management of urinary tract infection in older adults. Infectious Disease Clinics. 2014 Mar1;28(1):75-89.
6. Derese B, Kedir H, Teklemariam Z, Weldegebreal F, Balakrishnan S (2016) Bacterial profile of urinary tract infection and antimicrobial susceptibility pattern among pregnant women attending at Antenatal Clinic in Dil Chora Referral Hospital, Dire Dawa, Eastern Ethiopia.Ther Clin Risk Manag 12:251-260.
7. Khoshbakht R, Salimi A, Shirzad AH, Keshavarzi H (2013) Antibiotic susceptibility of bacterial strains isolated from urinary tract infections in Karaj, Iran. Jundishapur J Microbiol 6:86-90.
8. Gajdács M, Ábrók M, Lázár A, Burián K (2021) Epidemiology and antibiotic resistance profile of bacterial uropathogens in male patients: A 10-year retrospective study. Farmacia (Buchurest) 69:5530-539.
9. Petca RC, Negotia S, Mares C, Petca A, Popescu RI, Chibelean CB (2021) Heterogeneity of antibiotic multidrug-resistance profile of uropathogens in Romanian population.Antibiotics 10:e523
10. Bultitude MF (2012) Campbell-Walsh Urology Tenth Edition, Elsevier Saunders, Philadelphia, PA, USA
11. Olson PD, Hruska KA, Hunstad DA (2016) Androgens enhance male urinary tract infection severity in a new model. J Am Soc Nephrol 27:1625-1634.
12. Petca RC, Mares C, Petca A, Negotia S, Popescu RI, Bot M, Barabás E, Chibelean CB (2020) Spectrum and antibiotic resistance of uropathogens in Romanian females. Antibiotics 9:e472
13. Oluwole OM, Victoria AA (2016) Asymptomatic bacteriuria: occurrence and antibiotic susceptibility profiles among students of a tertiary institution in Ile-Ife, Nigeria. Afr J Microbiol Res 10:505-510.
14. Linhares I, Raposo T, Rodrigues A, Almeida A. Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: a ten-year surveillance study (2000–2009).BMC infectious diseases. 2013 Dec;13:1-4.
15. Tandogdu Z, Wagenlehner FM. Global epidemiology of urinary tract infections. Current opinion in infectious diseases. 2016 Feb 1;29(1):73-9
16. Stefaniuk E, Suchocka U, Bosacka K, Hryniewicz W (2016) Etiology and antibiotic susceptibility of bacterial pathogens responsible for community-acquired urinary tract infections in Poland- Eur J Clin Microbiol Infect Dis 35:1363-1369.
17. Foxman B (2014) Urinary tract infection syndromes: occurrence, recurrence, bacteriology, risk factors, and disease burden. Infect Dis Clin North Am 28:1-13.
18. Wiedemann B, Heisig A, Heisig P (2014) Uncomplicated urinary tract infections and antibiotic resistance epidemiological and mechanistic aspects. Antibiotics 3:341-352.
19. Prah JK, Amoah S, Ocansey DW, Arthur R, Walker E, ObiriYeboah D (2019) Evaluation of urinalysis parameters and antimicrobial susceptibility of uropathogens among outpatients at University of Cape Coast Hospital. Ghana Med J 53(1):44-51.
20. Ali AH, Reda DY, Ormago MD. Prevalence and antimicrobial susceptibility pattern of urinary tract infection among pregnant women attending Hargeisa Group Hospital, Hargeisa, Somaliland. Scientific Reports. 2022 Jan 26;12(1):1419.
21. Ullah A, Shah SR, Almugadam BS, Sadiqui S. Prevalence of symptomatic urinary tract infections

and antimicrobial susceptibility patterns of isolated uropathogens in kohat region of Pakistan. MOJ Biol Med. 2018;3(4):85-9.

22. Clinical and Laboratory Standards Institute. M100-Performance Standards for Antimicrobial Susceptibility Testing. 27th ed. Wayne, PA, USA: Clinical and Laboratory Standards Institute; 2023