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E COLI URINE SUPER BUG AND ITS ANTIBIOTIC SENSITIVITY — A PROSPECTIVE STUDY

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ABSTRACT

Objectives: To determine the sensitivity patterns of E Coli to various antibiotics by urine culture and sensitivity in patients with Urinary Tract Infection (UTI), and to recommend the appropriate empirical antibiotics for UTI while awaiting culture results.

Materials and Methods: This prospective study was conducted in Medical E Unit of Khyber Teaching Hospital, Peshawar, Pakistan from May 2007 to Oct 2009. A total of 354 urine cultures was performed. Urine culture was done using conventional microbiological techniques. Biochemical techniques were used to identify the organisms and antibiotic sensitivity was determined by Kirby Bauer method.

Results: Out of 354 urine cultures, 276 grew E Coli. The gender distribution was 173(62.6%) females as compared to 103(37.31%) males, with age range of 14-70 years. Urine culture of 270 (97.82%) patients was sensitive to Meropenem, 263 (95.28%) to Piperacillin-Tazobactam, 258 (93.49%) to Cefoperazone–Sulbactam, 260 (94.20%) to Imipenem, 257 (93.11%) to Amikacin, 254 (90.57%) to Ceftazidime, 222 (80.43%) to Ceftriaxone, 62 (22.4%) to Co-Amoxiclav, 37 (13.40%) to Pipedemic Acid, 63 (22.8%) to Ciprofloxacin, 85 (30.79%) to Gentamicin and 53 (19.20%) to Cefotaxime.

Conclusion: E Coli resistance against most commonly used antibiotics is on the rise and we recommend using Amikacin or Cefoperazone-Sulbactam as the initial empirical antibiotic of choice for treating UTI while awaiting culture results. We do not recommend using Meropenem, Piperacillin-Tazobactam or Imipenem as initial empirical antibiotic of choice because of the much higher cost as compared to Amikacin or Cefoperazone-Sulbactam.

Key words: Escherichia Coli, Urinary Tract Infection.

INTRODUCTION

Urinary tract infection (UTI) is among the most common infections in both community and hospital settings, and knowledge of its epidemiology and the sensitivity profile of the etiological agent is crucial.[1] Due to rising antibiotic resistance among uropathogens, it is important to have local hospital based knowledge of the organisms causing UTI and their antibiotic sensitivity patterns. This information would be relevant not only to the local hospital but would also be a vital regional database. UTI is frequently encountered in patients with diabetes and in those with structural and neurological abnormalities, which interfere with urinary flow.[2]

The predominance of Gram-negative sepsis, usually Enterobacteriaceae and, particularly, Escherichia coli, remain the principal pathogens causing UTI, accounting for 75-90% of all urinary tract infections in both inpatients and outpatients.[3,4] The in vitro susceptibility of E.coli urinary isolates to the most common antimicrobial agents used for the treatment of patients with UTI varies considerably in different parts of the world.[5,6] Monitoring of the antimicrobial resistance of E.coli is important because resistance has been reported to be associated with increased patient morbidity and mortality, and contributes to escalating health care cost.[7] Antibiotics are usually given empirically before laboratory results from urine culture are available. Empirical treatment of all symptomatic patients is probably the most effective policy.[8]

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MATERIAL AND METHODS

This prospective study was conducted in Medical E unit of Khyber Teaching Hospital, Peshawar which is a 1300 bedded hospital, from May 2007 to Oct 2009. The patients included were between ages of 14-70 years, who were admitted through OPD or Emergency and whose Urine Routine Examination showed numerous pus cells on microscopy. All patients whose Urine Culture and Sensitivity grew E. Coli were included in the study. All types of UTI whether relapse, recurrent, complicated, treatment naïve or

treatment failures were included. Patients who received treatment for UTI on outpatient basis or had a history of antibiotic use in previous ten days were excluded as were patients whose Urine C/S showed no growth, mixed growth or growth other than E. Coli. Sampling technique used was convenience (Non Probability). Fresh midstream urine samples were aseptically collected in sterile containers. A total of 354 urine cultures were performed, out of which 276 cultures grew E.coli. Each sample was plated onto 5% sheep blood agar and MacConkey agar plates using calibrated loop, delivering 0.01ml of the sample. This was incubated at 37°C overnight and the observation was made the next day. All plates showing significant growth (>10 CFU/ml) as per the Kass count[2] were further processed. Fewer colonies (<10 CFU/ml) were processed only if relevant history was present in the form of fever, chills, flank pain, pyuria, history of antibiotic intake, structural abnormalities, diabetes mellitus and any immuno-compromised state.[2] After biochemical identification, anti-microbial sensitivity testing was done for the isolates using Kirby Bauer methods on Mueller Hinton agar and results were interpreted as per the NCCLS guidelines.[2]

RESULTS

Three hundred and fifty-four urine cultures were performed, out of which 276 cultures grew E.Coli. Of these, 173 (62.6%) patients were female as compared to 103 (37.31%) male. Patient age ranged from 14-70 years. In vitro sensitivity of E.Coli is shown in Table 1 (A, B).

DISCUSSION

Antimicrobial resistance is a growing problem and cause of great concern throughout the world.[1] Knowledge of antimicrobial resistance trends among isolates of uropathgens is essential to provide clinically appropriate and cost effective therapy. Guidelines for the empirical treatment of patients with UTI suggest it is important to consider local resistance patterns of E.coli in selecting antibiotic agent. This current study analyses the sensitivity pattern of E.coli to various antibiotics by urine culture and sensitivity in patients with UTI in order to be able to recommend the most appropriate antibiotics for UTI while awaiting culture results.

Uncomplicated UTI is a common clinical problem in women. Approximately one in three women will require antimicrobial treatment for a UTI and 50% of women will have a UTI during their lifetime.[9] E.Coli positive UTI was commoner in females than males in our study. Our data agree with studies from many parts of the world showing these infections are more common in females.[10,11] Despite the fact that women have higher prevalence of UTI because of anatomic and physical factors, male patients have high resistance rates.[3,10,11,12]

The production of beta-lactamases, enzymes that destroy penicillins and cephalosporins by hydrolyzing their b-lactam nucleus, is the most common mechanism of resistance. B-lactamase was first identified in Escherichia coli in 1940.[13] Sulbactam-Cefoperazone and Tazobactam represent the current state of art in B-lactamase inhibition. Sensitivity of E.coli to Meropenem, Piperacillin/ Tazobactam, Imipenem, Cefoperazone-Sulbactam, was 97.82%, 95.28%, 94.20%, 93.49% respectively. Study by Gupta et al,[14] reports low resistance for Imipenem (7.2%), Piperacillin/Tazobactam (2.8%), Cefoperazone-Sulbactam (5.4%). Kiffer CR et al,[15] calculated that sensitivity to Imipenem and Meropenem was 99.96% and 99.90% ($P<0.05$) respectively which is similar to our result. Hence, we conclude that Imipenem, Piperacillin/Tazobactam, Cefoperazone-Sulbactam and Meropenem are effective antibiotics in our environment.

Rai GK et al[16] found E.coli to be most sensitive to Amikacin. Our study demonstrates 93.11% sensitivity of E.coli to Amikacin. A study by Yalmaz et al[17] narrates the rate of resistance to Amikacin and Gentamicin to be 9.5% and 28.4% respectively. But study by Azra et al quotes 33.3% resistance rate of Amikacin. So, Amikacin is a good choice for the empirical treatment of UTI in our population.

Table 1. Antimicrobial Sensitivity Patterns of Urinary E.coli (%) (n=276)

A. Drugs with best sensitivity for urinary E.coli.

Drugs	Meropenem	Piperacillin/ tazobactam	Cefoperazone/ Sulbactam	Imipenem	Amikacin
%Sensitivity	97.82%	95.28%	93.49%	94.20%	93.11%

B. Drugs with low sensitivity for urinary E.coli.

Drugs	Cef-tazidime	Cef-triaxone	Co-Amoxiclav	Pipedemic Acid	Cipro-floxacin	Genta-micin	Cefo-taxime
%Sensitivity	90.57%	80.43%	22.4%	13.40%	22.8%	30.79%	19.20%

The sensitivity of E.Coli to Co-Amoxiclav, Pipemidic acid, Cefotaxime was 22.4%,13.40% and 19.20% respectively. A possible explanation of this fact might be the presence of extended spectrum beta-lactamase (ESBL) in these strains. The increasing frequency of ESBL phenotypes in the community is an emerging problem and risk factors are hospitalization, previous bacterial infection, urinary abnormalities, previous antimicrobial treatment (especially fluoroquinolones, cefuroxime and third-generation cephalosporins), recurrent urinary tract infections, presence of high-level-multi-drug resistance, and older age in males.[1,12]

In our study, only 22.8% of patients were sensitive to Ciprofloxacin. Resistance rates for Ciprofloxacin were reported to be 69% in India, 89.9% in Brazil.[5,6,18] Increasing antimicrobial resistance to fluoroquinolones is being observed world-wide. Some authors have found that quinolone resistance is higher in developing countries than in developed nations because of the use of the less active quinolone, such as nalidixic acid, and the use of low dosages of more potent compounds such as Ciprofloxacin, resulting in selection of mutant isolates.[19] Arslan et al[20] found age over 50, Ciprofloxacin use more than once in the last year, and the presence of complicated UTI to be associated with Ciprofloxacin resistance. High quinolone resistance in our region may occur due to increased fluoroquinolone consumption over years, necessitated by high Trimethoprin-Sulphamethoxazole resistance. Due to this trend, fluoroquinolones should be used with caution, particularly if no antimicrobial susceptibility test result is available.

Antimicrobial resistance is a major public health issue in Pakistan. There has been a steady increase in the level of resistance to commonly used antibiotics. This higher resistance rate seems to be the result of many factors- one of them is high and uncontrolled consumption of these antibiotics by the public during the past decade in our region. This can be explained by the widespread and easy access to first-line antimicrobials in pharmacies in Pakistan without prescription. The relationship between the development and extension of resistance and increased antibiotic use is well established, but the crucial issue is direct demonstration of the reversibility of bacterial resistance following decreased antibiotic use.[21] Kahimeter et al,[22] showed that antimicrobial resistance to one drug does not always correlate to the consumption of the same drug or closely related drugs.

Non-skilled practitioners have also contributed to the high resistance rates in our country. The authors emphasize that broad spectrum and irrational antibiotic usage causes bacterial resistance, increases morbidity and mortality, decreases treatment success and wastes resources. Antimicrobial resistance is a growing problem and a cause of great concern throughout the world.[23] While clear evidence exists of the potential risk for transmission of resistant E.coli coming from animals being fed with antibiotics as growth promoters, recent studies indicate that poor hygienic control measures, overcrowded living conditions, and social deprivation may be related to the high resistance rate.[24]

CONCLUSIONS

Resistant E.Coli superbug is an emerging global problem. We recommend using Amikacin or Cefoperazone/Sulbactam as initial antibiotic of choice while awaiting culture results.

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