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RESEARCH ARTICLE

Changing pattern of resistant pathogens causing urinary tract infections in Karachi

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ABSTRACT

INTODUCTION: The study under view is based under the aim to investigate the prevalence and susceptibility pattern of pathogens, causing urinary tract infections (UTIs), to antibiotics commonly used in routine medication.

MATERIALS AND METHODS: Over a period of 10 months 100 isolates were collected for the determination of their susceptibility to chosen antibiotics, from a laboratory (MedPath Laboratories) in urban area of Karachi. All Gram-negative and Gram-positive urinary tract pathogens were re-identified by their morphological and biochemical characteristics and the susceptibility to seven antibiotics was determined.

RESULTS: Pathogens were found as, *Escherichia coli*, *Pseudomona* spp*, Klebsiella* species*, Enterobacter* spp.*,* and *Staphylococci* spp. In recent study, more than half of the *Escherichia coli* isolates were resistant to one or more of the all antimicrobial drugs tested. Resistance was most common to amoxicillin/clavulanic acid and ofloxacin, cefixime, followed by gentamicin. Our results indicate that *Escherichia coli* and *Pseudomonas* spp. were the most common organisms causing UTI. Other organisms involved were *Enterobacter* spp.*, Staphylococcus* spp.*,* and *Klebsiella* spp. Increasing patterns of resistant to gentamicin, and ofloxacin were also observed.

CONCLUSIONS: In conclusion, pattern of antibiotic susceptibility to first line antibiotics is changing hence antimicrobial susceptibility testing of all isolates is crucial for the treatment of UTI.

KEY WORDS: Resistance, Antibiotics, Pathogens, Infections, Karachi

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INTRODUCTION

Although antimicrobial resistance with *Streptococcus pneumoniae* was first recognized in 1917. However in the late 1930s when Fleming described usage of penicillin, the beginning of the antibacterial era was heralded.[1] Antibiotics have been widely used because of their wide spectrum of activity. For example the fluoroquinolones have been utilized to treat a great variety of infections.[2] A few years ago, ciprofloxacin was pointed out as the most consumed antibacterial agent worldwide.[2-3] This high level of use, and to some extent of abuse in the sense of gratuitous usage, or use of quinolones with poor activity in some developing countries, has been responsible for the rapid development of bacterial resistance to these agents.[1]

Urinary tract infection (UTI) is second on ranking of the most common infection in community practice and has been diagnosed most commonly in outpatients as well as hospitalized.[4] It is the most common diseases encountered in medical practices. However, its impact and frequency fluctuate in different demographic and geographic populations.[5,6] An estimated 10% of the population is diagnosed with UTIs annually.[7] It also constitutes the most common nosocomial infection in many hospitals, plus its occurrence is about 2–3 cases per 100 hospital admissions and accounts for approximately 35%-40% of all hospital-acquired infections reported to the National Nosocomial Infection Surveillance (NNIS) system as in U.S.A.[8,9] An estimated 20–30% of women are expected to have UTI after childhood[6]. UTIs result in approximately 8 million physician visits and more than 100,000 hospital admissions per year in the United States.[10,11]

UTI may involve the lower urinary tract or both the upper and lower tract. In case of lower UTI it is referred to as cystitis, the characteristics of which include a syndrome involving dysuria, frequency, urgency and occasionally suprapubic tenderness. However, the presence of symptoms of lower tract without upper tract symptoms does not necessarily exclude upper tract infection, as well[3]. In female patients uncomplicated cystitis is most common, whereas in male patients complicated UTIs are more common, while the proportion of re-infections and relapses in UTIs amounts to about 35-70%.[12]

Escherichia coli is stated to be the dominant bacterial pathogen of community acquired UTIs. Most cases of UTIs are due to *Escherichia coli* and *Staphylococci* spp. while other agents like *Proteus* spp. and *Klebsiella pneumoniae* account for many of the other infections also.[8] Gram-positive bacteria, such as *Staphylococci saprophyticus* and *Enterococcus* spp. can result in UTIs in certain patients. For example, *S. saprophyticus* is a common pathogen in young, sexually active women and causes approximately 10% of UTIs in them.[13]

The causative agents of UTI and their antibiotic susceptibility have been changing over the years, both in community and hospital-acquired infections which is of great concern.[14,15] Hence knowledge on the present pattern of susceptibility of antibiotics is important for appropriate therapy. UTIs are often treated with different broad-spectrum antibiotics, even if one with a narrow spectrum of activity may be appropriate because of concerns about infection with resistant organisms.[16] Therefore extensive uses of antimicrobial agents have consistently resulted in the development of antibiotic resistance, which, in recent years, has become a main problem worldwide.[8,17] A study showed that though the frequency of resistance differed among laboratories, however, the trend towards increasing resistance was demonstrated in every participating laboratory.[18]

Knowledge of antimicrobial resistance patterns of the major pathogens linked with UTI is essential as a guide in selecting empirical antimicrobial therapy, because several authors have illustrated a relationship between the usage of antibiotics and emergence of resistance.[19] The susceptibility pattern of community-acquired UTI pathogens has been acknowledged in a few studies.[20] It is stated, that the elevated resistance in older age groups (mainly female) might consequence from increased cumulative lifetime exposure in the older patients.[21] Data from the multivariate analysis point out that the effect of age on fluoroquinolone resistance is strongly influenced by gender, maybe due to the different physiological nature of UTI in males and females. The study aims to investigate the prevalence and susceptibility pattern of pathogens, causing urinary tract infections (UTIs), to antibiotics commonly used in routine medication.

MATERIALS AND METHODS

Collection, Storage and Identification of samples

A total of 100 isolates were collected from a diagnostic laboratory (MedPath Laboratories and diagnostic center, Karachi) over a period of 10 month. For the purpose of collecting the isolates, the

respective laboratory was asked to provide only isolates considered significant by their usual criteria. For storage the isolates were sub cultured on to Nutrient Agar (Oxoid) slopes and stored for batched testing, the cultures were checked for purity by sub culturing on to Cysteine Lactose Electrolyte Deficient (CLED) agar (Oxoid) for Gram-negative isolates and blood agar (Oxoid) for Gram-positive isolates. Whereas in the case of mixed cultures, no more than two bacteria (those with the two highest counts) were identified and then later on processed. The significant pathogens were identified by performing Gram staining and by determining their morphological features and via standard biochemical procedures.[22]

Antibiotic Sensitivity Test

After re-identification, the Minimum inhibitory concentration (MIC) for seven different antimicrobials (Oxoid) (Table-1) were determined by the agar dilution method, as described in the National Committee for Clinical Laboratory Standards (NCCLS ; presently called as Clinical Laboratory Standard Institute (CLSI) guidelines, on Mueller–Hinton agar,[24] and interpreted according to CLSI procedures and interpretive guidelines.[13] Antimicrobial susceptibility testing was performed using the disk diffusion method as described by the CLSI.[25]

RESULTS

Out of 100 isolates, 89 were found to be Gram negative and the rest were Gram positive. The following bacteria were classified as uropathogens; *E. coli*, *Klebsiella* spp., other *Enterobacter* spp., *Staphylococci* spp. and *Pseudomonas* spp. Which means 60% of isolates belonged to the *Enterobacteriaceae*, while in many cases like Hryniewicz K *et.al* more than 90% of isolates were found to be of this group.[24] The *Enterobacteriaceae*, were the most frequent pathogens detected, causing 84.3% of the UTIs. The overall frequency of infection and the pathogens involved were broadly as expected and confirm that *E. coli* is the most common pathogen. A very low incidence of community infections caused by Gram-positive bacteria was also observed as by, as only 20% in this study. Identified microorganisms were accounted by *E. coli* (43%), *Klebsiella* spp. (13%). The occurrence frequency of different pathogens and their susceptibility to different antibiotics used are shown in Figure 1.

DISCUSSION

This study like many others indicated that *E. coli* is still the most common (43%) cause of UTI. This corresponds with the data obtained by other investigators.[13] An almost similar results were shown by a study conducted at Aga Khan University (AKU) Pakistan in 1994 where, *E. coli* was found most frequently (61.4%) followed by *Klebsiella* spp. (17.1%). Some have shown, however, that the percentage of *E. coli* is slowly declining, being replaced by other members of the *Enterobacteriaceae* and *Enterococci* spp.[24] In general *E. coli* was susceptible to many drugs (81.39%); this data is similar to those obtained in other countries indicating that *E. coli* is still susceptible to many antimicrobial agents.[24, 26-27] However, a high percentage of multi-resistant strains were found amongst other *Enterobacteriaceae.* In our country (Pakistan), multidrug resistant isolates of *E. coli* are much higher to 3rd generation cephalosporin and quinolones. Findings from routine testing by medical microbiological laboratories also show the growing resistance to several antibiotics in *E. coli* from urinary tract isolates.[18] Though the incidence of resistance differed among laboratories, perhaps owing to different testing methods. However, the trend towards increasing resistance is demonstrated in every participating laboratory.[11]

Albeit, *Pseudomonas species* are fairly uncommon to be sensitive to drugs, as they have many ways of resistance, yet in this study they were found to be susceptible to Imipenem (85%) followed by being sensitive to gentamicin and ofloxacin, 81% and 71.4% respectively. However on the other hand, showing its real devil shadow, giving resistance to the rest of antibiotics, indicating a worrying concern.

Staphylococci are said to be the champion in resistance, and almost the same happened in this study where off 11 *Staphylococci* isolates 95 % proved to be resistant to one or more antibiotics used. Among antibiotics the most resistance was proved to cefixime and ofloxacin where 100 % resistance was shown and even no intermediate range were found to be present, the next antibiotic to be resisted mostly was gentamicin where off only 1 isolate was sensitive. These were followed by amoxicillin. The antimicrobial agent to which *Staphylococci* spp. showed most

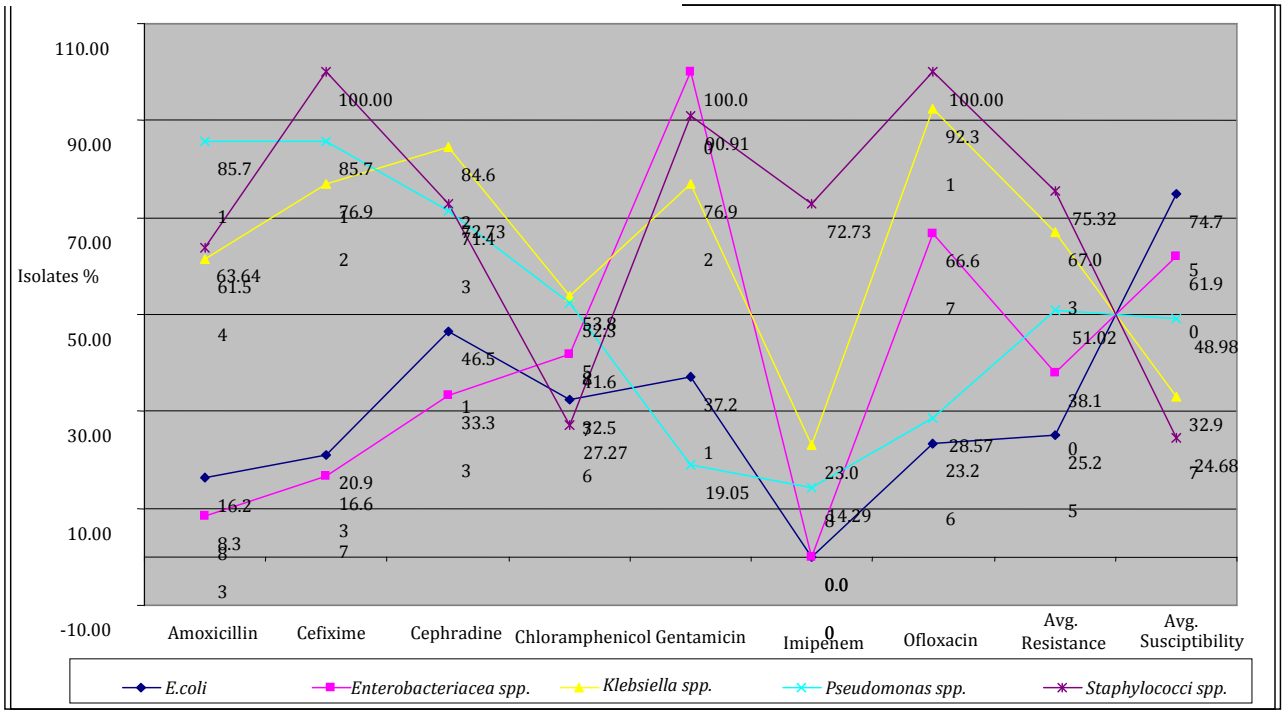

Figure 1. Resistance pattern of uropathogens

sensitivity was chloramphenicol, where 72.72% proved to be sensitive, almost the same conditions, as followed by the other four isolates.

Klebsiella spp. are the third major population to be the etiological agent of most of urinary tract infections, therefore must be considered for their sensitivity tests. This specie showed resistance to most of the agents, in different ratios (Fig. 1). It showed 92% resistant to ofloxacin, the most of all, following cefixime and gentamicin with resistance being 83.3%. The other agent to which it showed it resistance included amoxicillin and chloramphenicol. However, it proved to be sensitive to imipenem with a ratio of 75% followed by 50% by chloramphenicol. In some of agents like amoxicillin it showed no sensitivity but with resistance some of the isolates showed intermediate as 41% in this case and 25% in Gentamycin.

Amoxicillin/ clavulanic acid combination is fairly active against organism sensitive to Amoxicillin for example *Staphylococci* species and also clavulinic acid has been shown to act synergistically with penicillin in vitro against clinical isolates of B-lactamase producing strains of *Staphylococci*, however in this study the *Staphylococci* were found to be resistant to this combination (7/11%). These observations connote to the partial failure of the used of this combination against *Staphylococci*. Albeit, the presence of some vulnerable isolates "4/11% still suggest the utilization of this combination. The efficacy of Augmentin against *E. coli* is quite effective, as 36/41% of isolates proved susceptible to this combination and the similar results were found in a no research works.

Cefixime is the extended spectrum, classified as 3rd generation broad spectrum Cephalosporins. The oral cephalosporin is more stable than narrow spectrum against Gram-negative and other species. The sensitivity of *Enterobacter* spp. and *E. coli* of this scripture are in submission, however it was found to be not as effective in case of other species as *Pseudomonas, Klebsiella* spp. and *Staphylococci*, as given in figure 1.

Data presented in this study also indicate that antibiotics commonly used in UTIs are nevertheless still effective, but species distribution and their susceptibility to antibiotics are changing in general all around the world. Hence it requires regular monitoring in order to make reliable information available for optimal empirical therapy for patients with UTIs.

To prevent a further increase of resistance, it is strictly recommended that antibiotics should be used if urinary tract isolates are susceptible only to these antibiotics or as a second-choice drug for patients in whom treatment with the antibiotic of first choice has failed. Although prudent use of these

antibiotics may help to reduce the prevalence of antibiotic-resistant uropathogens, elimination will be hard to achieve. Therefore, we believe that we can reduce the tide but we will still have to deal with the resistance problem in the future.[7] Because bacterial resistance leads not only to longer and more costly hospital stays but also to increased morbidity and death rates[26] therefore amongst the numerous recommendations to combat resistant bacteria is the necessity for national and international surveillance programmes to monitor the level of antimicrobial resistance. Several programmes have been investigated which have looked at pathogens from a variety of common infections. These include the WHO Antimicrobial Resistance Monitoring Programme, the European Antimicrobial Resistance Surveillance System (EARSS), the Hospitals in Europe Link for Infection Control through Surveillance (HELICS), the European Study Group on Nosocomial Infections, the SENTRY Antimicrobial Surveillance Program has been monitoring antimicrobial resistance worldwide among selected types of infection since January 1997[9] and the Alexander Project on pathogens in lower respiratory tract infections.[22] Similarly the establishment of worldwide antimicrobial resistance surveillance systems seems to be an important step in detecting the emergence of resistance patterns.[9]

CONCLUSIONS

In the conclusion it can be stated that the though resistance UTI pathogens has been increasing rapidly, however with advent of new antibiotics it can be overcome. In this context according to our study the use of ofloxacin is the drug of choice for the treatment of UTI caused by either Gram positive or Gram-negative pathogens. Whereas Gentamicin is additionally recommended for *E. coli*.

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