

Original Article



Development of Antibiotic Resistance, Suggestion For The Safety of Our Future Generation

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Abstract

Background: Rising of multidrug resistance among uropathogenic bacteria is leading our future generation to a crisis. Nevertheless, the era of antibiotic failure due to bacterial resistance has brought interest to other medical science like Traditional Medicine, alternative medicine. **Objectives:** This study was undertaken to determine the current antibiotic resistance situation among common bacterial uropathogens and suggesting prevention measure. **Materials and Methods:** A total of 212 patients male 132, female 80 selected. Mid-urine samples were collected. Isolated organisms were identified by conventional methods. Then different antibiotics representing different families of antibiotics were tested on isolated organisms. **Results:** The most frequently isolated gram negative bacteria was E.Coli (92%) followed by Staphylococcus (7.07%), Klebsiella (7%), Pseudomonas (4.25%). Resistance to Amoxicilline, Ciprofloxacin, Cefixim, Ceftriaxone, Cefuroxim, Cefradin, Cefotaxim was more than 70% of all isolates of E.Coli stains. There was relatively low resistance rate to Nitrofurantoin, Gentamycin, Imipenem, Meropenem, Amikacin, Ceftazidim. However, there was emerging resistance to Ciprofloxacin, specially for common bacteria. **Conclusion:** It is urgent need to make a policy for antibiotics use. We suggest all health care professional of traditional medicine and modern medicine to combat against antibiotics resistance.

Key words: Antibiotic, Uropathogens, Bacterial spectrum, Resistance, Prevention.

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Introduction

The advent of multidrug resistance among uropathogenic bacteria is alarming for our future generation to a crisis. Nevertheless, the evidence of antibiotic failure due to bacterial resistance has brought interest in other medical science like alternative medicine, Chinese traditional medicine etc. The United Nations declared antimicrobial resistance to be one of the biggest threats to global health. Action must be taken to combat the evolving drugs resistance crisis, combining traditional Medicine and other health care provider. Resistance has emerged even to more potent antimicrobial agents day by day. That's why "World Antibiotic awareness Week" has declared. Ancient civilizations used variety of herbs for

infection control. Later on, antibiotic invented and its misuse, over use developed multidrug resistance bacteria which is threat of our society.¹

Present situation regarding antibiotic resistance: According to the Central Disease Control/USA report published in 2019, more than 2.8 million antibiotic-resistance infections occur in USA/year and more than 35,000 people die. The number of people facing antibiotic resistance is still too high.² One article published in Bangladesh stated that half of the E.coli, Staphylococcus aureus, Pseudomonas and Klebsiella showed resistance against older and common antibiotics.³ On an average 48% of tested antibiotics become resistant irrespective of pathogens.

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Pseudomonas aeru. 100% resistant against amoxicillin, *E.Coli* shows 100% resistance against amoxicillin, *E.Coli* 60-85% resistance to Cefuroxim, Ceftriaxone, Cephradine, Cefixim, Cephalexin, Ceftazidime, Gentamycin. Co-trimoxazole.³ We underwent a study to find out the pattern of antibiotics resistance to uropathogens isolated from 212 patients of our urology department.

Materials and Methods

The Phase- I from January 2012 to December 2014, on 111 Patients The Phase-II from March 2017 to March 2018 on 101 Patients It is a hospital based single department prospective study. The aim of the study was to assess the changes in the spectrum of bacteria cultured from urine samples. To compare the annual change in bacterial antibiotic resistance. To give a proposal of collaborative approach to other health care providers for resistance crisis. The hospital is located 150 Km away from the capital city of Bangladesh. A 500 bedded tertiary teaching hospital. All endourological and laparoscopic surgery are performed there. Patients came to Urology OPD or referred from other departments or admitted with urological problems were the study subjects. Initial selection after exclusion criteria were 400 patients. Urine sent for culture and sensitivity. Number of Culture +ve patients were 212. Contaminated sample were excluded. Finally included 212 patients in two phases. Two-tailed Z-test applied for comparison to find significant difference. Data was presented in column, line chart, percentage and cross-tabulation.

Results

In January 2012 to December 2014, a total of 200 (Phase I), and in March 2017 to March 2018 (Phase II), a total of 200 urine specimens were examined for isolations, identification of bacteria and susceptibility testing. Of them 212(53%) showed significant growth in both phases. Of 212 patients 132(62%) were male and 80(38%) were female. Age ranged from 3 to 107 years with mean age 9 +/- 19 SD. Six per cent of them were under 20 years, 21% were under 40, 40% were under 60, and 34% were under 107 years age (Table- I).

Table I: Age, gender distribution of patients with UTI in KYAMCH, Enayetpur (both phases)

Variables	Category	Total no. of pts(N%)
Gender	Male	132(62%)
	Female	80(38%)
Age groups		
A	<20 yrs	12 (5.66%)
B	20-39yrs	44 (20.75%)
C	40-59yrs	85 (40.09%)
D	60yrs and above	71 (33.49%)

We divided the patients in 4 age groups such as A,B,C,D according to age for statistical analysis (Table-I). When calculated the number of patients in different age groups, number of patients affected more in C and D groups. Female were affected more in age group A, but in other groups male were affected more than that of female. When compared male and female in D group, there was significant difference (Z-score = 4.2683). When compared age group B and A, C and B there was significant difference (Z-test at 95% confident interval).

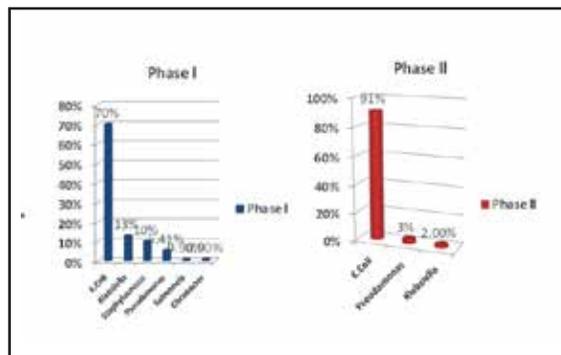


Figure 1: Number of uropathogens in 2 phases

The number of uropathogens was *E. Coli* 70%, *Klebsiella* 13%, *Staphylococcus* 10%, *Pseudomonas* 4.1%, *Salmonella* 0.9%, *Citrobacter* 0.9% in phase I, and *E.Coli* 91%, *Pseudomonas* 3%, *Klebsiella* 2% in phase II study. Gram negative bacteria 83%, and gram positive bacteria 17% in phase I study, and all were gram negative in phase II study (Figure 1). The most frequently isolate bacteria was *E.Coli* in female (63%) and in male it was *itrobacter*(100%), *Salmonella* (100%), *Pseudomonas*(78%), *Staphylococcus*(67%) Figure 1. Amoxicillin, Nalidixic Acid, Cephalosporin, Levofloxacin, Ciprofloxacin, Amoxiclave was resistant to antibiotics with resistant score of 88%,85%,85%, 79%,74%,65% respectively (Table- II), showing high resistance score i than that of sensitivity score (2-tail Z-test. Significant at p<0.05). Low resistance antibiotics were *Astreonom* (0%), *Imipenem* (2%), *Meropenem*(6%), *Amikacin*(12%). Seventy four per cent of Cefixim, 81% of Cefuroxim, and 71% of Ciprocim was resistant to *E.Coli* in phase I study and 91% of Cefixim, 88% of Cefuroxim, and 74% of Ciprofloxacin was resistance in phase II study. All those drugs showed increase trend of resistance against uropathogens. Resistance score of Ciprofloxacin, Erythromycin, Gentamycin, Naidixic acid, Cloxacilline Ampicilline was 86%,83%,80%,80%,75% respectively with significant difference (2-tail Z-score test, p<0.05). Resistance score of Amoxicilline, Nalidixic Acid, Nitrofurantoin, Tetracycline, Co-trimoxazole, Cephalexin, Ciprofloxacin, and Gentamycin, are shown in Table- II.

Table- II: Susceptibility score of conventional antibiotics to uropathogens

Conv. antibiotics	Sensitivity	resistance	Significant level
Amoxicilline	12%	88%	Significant at p<0.05
Nalidixic acid	15%	85%	same
Cephalosporin	16%	85%	same
Levofloxacin	21%	79%	same
Ciprofloxacin	27%	74%	same
Amoxiclave	35%	65%	same

*2 - tail Z-score test, p<0.05

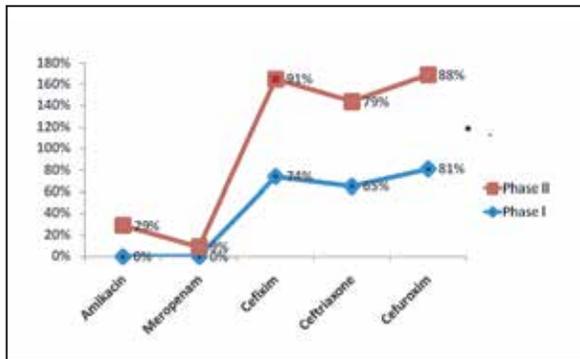


Figure 2: Comparative resistance pattern of drugs against uropathogens in 2 phases.

When compared resistance score of antibiotics against uropathogens in 2 phases, the drugs Cefixim, Ceftriaxone and Cefuroxime shows increase resistance score in phase II than phase I study, which indicate gradual increase of resistance against uropathogens (Figure 2). Staphylococcus isolates were found resistant to Ciprofloxacin(86%), Erythromycin (83%),Gentamycin (80%), Cloxacillin (80%), Ampicilline (75%). The difference of sensitivity and resistance score was significant(2-tail Z-score test at $p < 0.05$). Klebsiella isolates were found resistance to Amoxicillin(100%), Nitrofurantoin (75%),Tetracycline (67%), Co-trimoxazole (63%). The difference of sensitivity and resistance score is significant (2-tail Z-score test at $p < 0.05$).

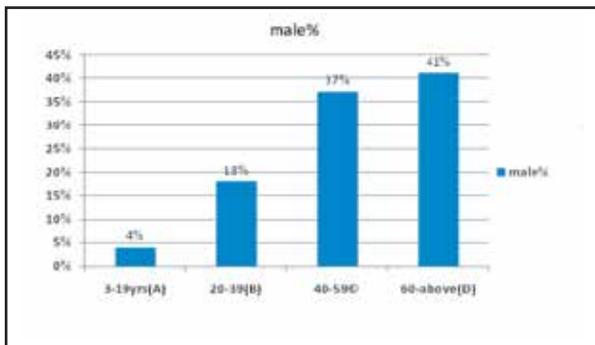


Figure 3: When compared male in different age groups-C & D groups affected more (senior citizens)

When compared male in different age groups, C & D groups (senior citizen group) were affected more than that of other groups (Figure 3).

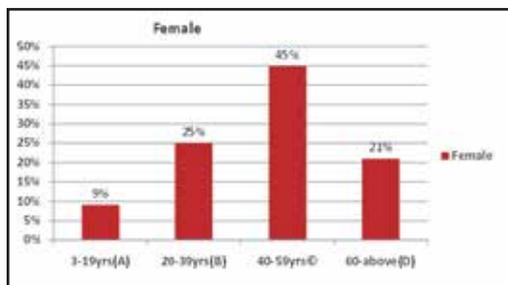


Figure 4: When compared only female in different age groups, B & C groups were affect more.

When compared female in different age groups, B & C groups (reproductive age group) Were affected more than that of other age groups (Figure 4).

Discussion

Development of antibiotics resistance (ABR) is a global threat for empirical treatment of infection control. Due to its misuse, overuse, and use in agriculture, livestock etc, ABR against uropathogens is going up day by day. Now-a-days 1st line antibiotic therapy has become useless. Time will come in near future, no antibiotic will work against infection. Our grand children will die with infection.^{4,5}

There will be significant problem if over treat with antibiotics suspecting UTI and which may lead to the development of multidrug-resistance organism. The incidence of UTI rises in older adult. Age associated changes in immune function, expose to nosocomial pathogens and an increasing number of comorbidities put the elderly at an increased risk for developing infection.^{6,7} The incidence of UTI rises in age group C and D(senior citizens) in our study . Although UTI is higher in women compared with men across all age groups, but in our case it was more in male, may be due to study design, as all the patients were from urology department. Elderly population such as more than 60yrs are at somewhat higher risk for UTIs because of problems going to the bathroom or emptying the bladder.⁶ In our study we found D group men more prone to developed UTI as they are elderly population. In menopausal age of women are also at a greater risk for UTIs due to lower amounts of vaginal estrogen, which can change the vaginal climate.⁶ In our study more women at menopausal age were affected with UTI. Preventive measures accompanying with other health care providers and other nonpharmaceutical measures are recommended as a strategy to reduce antibiotic resistance against pathogenic bacteria. Longtime use of antibiotics poses a risk for the emergence of bacterial resistance. Other therapeutic measures include, use of Cranberry juice and capsule, Methenamine, hippurate, probiotics, immunoprophylaxis and, Acupuncture. Cranberry juice or capsule have been shown to reduce recurrent UTIs as they contain a compound called tannin, or proanthocyanidin, which reduces E.Coli vaginal colonization. Many scientific articles was published in leading medical journal regarding antibacterial effect of cranbotics.⁸⁻¹⁰ Recent studies have shown that acupuncture may prevent RUTs in healthy adult women.¹¹⁻¹³ Studies showed that lactobacillus can prevent UTIs.¹⁴⁻¹⁶ Same study showed that oral immunoprophy laxix with the Uro-Vaxom E.coli extract was effective in preventing RUTs.¹⁷ Another double-blind study showed that E.coli extracts effective for UTIs, reducing the need for antibiotics and preventing RUTs.¹⁷ Among other therapy, Methenamine hippurate is effective for prophylaxis and treatment of RUTs.¹⁸ Older men such as men 70yrs and older are at higher risk for UTIs because of problem going to bathroom and emptying the bladder, older post-menopausal women are also at a greater risk for UTIs due to lower amount of vaginal estrogen, which can change the vaginal climate. We found 41% older men were affected with UTI in age group D, and in female 45% at menopausal age(age group C) and in reproductive age(25% in group B).

Conclusion

The effectiveness of currently available antibiotics is decreasing, as a result of increasing resistant strains among clinical isolates. Worldwide, spread of bacterial resistance to antibiotics may limit the future progress of medicine. Although standard UTI therapy is with antibiotics, alternative strategies for nonpharmacologic approach such as Cranbionics, probiotics, Methenamine salts, immuno prophylaxis, acupuncture, use of vaginal oestrogen in post-menopausal women are available to reduce exposure to antibiotics, and may reduce the number of antibiotics resistance.

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