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A Follow up Study of Bacteriology and Antibiotic Sensitivity Pattern of Urinary Tract Infection in a Tertiary Care Hospital in Bangladesh

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Abstract

Background: Urinary tract infections (UTIs) are a common infection. The aim of this follow up study is to see the changing trends in bacteriology and antibiotic sensitivity pattern among uropathogens in comparison to similar study 5 years back.

Materials and methods: We performed a prospective study in Comilla medical college hospital, Bangladesh during the period of July 2015-June 2016. Urine samples from 658 suspected UTI patients aged above 12 years inoculated for semiquantitative urine culture and sensitivity test. Antibiotic susceptibility pattern was done by Kirby-Bauer disc diffusion method following clinical laboratory science (CLS) program.

Results: Culture positivity were in 198 samples among 658 inoculated samples. *E. coli* was isolated from 171(86%) samples which was the most predominant bacteria followed by *Klebsiella* and *Enterococcus*. UTI with *E. coli* was significantly increased in the year 2016 in comparison to 2011. Meropenem, imipenem, amikacin, tazobactum, gentamycin nitrofurantoin, and mecillinum, found sensitive against 88% to100% of the uropathogens. Bacteria offered high degree of resistance against commonly used antibiotics-amoxycillin, amoxiclav, cephradine and cefixime ranging 60% to 86%. Comparative study of 2016 *vs.* 2011 shows significant reduction in sensitivity for imipenum, ceftriaxone, amoxiclav and increased sensitivity for nalidexic acid, ciprofloxacin, mecillinum, colistin, cotrimoxazole.

Conclusion: UTI with *E. coli* was significantly increased in the year 2016. This study failed to show a steady increase in resistance to all studied antibiotics. Imipenem, meropenem, tazobactum, amikacin and nitrofurantoin still remain more sensitive in this comparative study. Comparative study of 2016 *vs.* 2011 shows significant increasing resistance for imipenum, ceftriaxone, amoxiclav and increasing sensitivity for nalidexic acid, ciprofloxacin, mecillinum, colistin, cotrimoxazole.

Keywords: Urinary tract infection; Follow up comparative study; Changing trends; Culture; Sensitivity; resistance

Introduction

Urinary tract infection (UTI) is a common bacterial infection in mankind and is a major public health problem in terms of morbidity and financial cost which affecting 150 million people each year worldwide [1,2]. In 2007, in the United States alone, there were an estimated 10.5 million office visits for UTI symptoms [3].

Diagnosis and treatment of UTI are empirical mostly because this is imperative to start antibiotics in almost all cases due to low socio economic status, urinary obstruction, unavailability of urine culture facilities for rural patients in Bangladesh. To initiate empirical treatment with appropriate antibiotic is necessary to have current knowledge regarding causative organisms and their antibiotic sensitivity pattern [4]. But alarming fact is that a large number of patient do not respond to conventional antimicrobial agents [5].

Antimicrobial resistance is a well-known important emerging clinical and public health problem. There are various reports available in last two decades about changing pattern of pathogen and their sensitivity pattern to routinely used antibiotics which makes the situation miserable [5], increasing antibiotic resistance among uropathogens to commonly prescribed drugs has become a global reality. Resistance occurs in intestinal bacteria due to antibiotic therapy for treating infections outside the urinary tract [6]. The irrational use of antibiotics has an influence in the spread of antimicrobial resistance among bacteria [7,8]. Controlling antimicrobial resistance is a major issue confronting organized health care today. Therefore this is warranted to know information about rapidly changing sensitivity pattern of micro-organisms towards antibiotics in UTI. To get update information for proper therapeutic interventions, periodic evaluation and regional surveillance programs is necessary for the development

local data about the antimicrobial sensitivity to uropathogens for in UTI.

The present study was undertaken to observe the current bacterial uropathogens and their antibiotic sensitivity pattern in a tertiary hospital in Bangladesh to compare previous same pattern of study in 2011 [9]. It will be helpful for awareness and antibiotic use in UTI in this tertiary level hospital and country level.

Materials and Methods

It was a prospective study in department of medicine Comilla medical college hospital during the period of July 2015-June 2016. All the patients included in this study ware above 12 years of age, presented with the suspected UTI (dysuria, frequency, fever and pain in lower abdomen). The patients presented with active menstruation, PID, tubo-ovarian disease, appendicitis, colitis, epididymitis and orchitis diagnosed either clinically or by investigations were excluded from this study. Those patients were on antibiotic advised to stop drug for 48 h and were included in this study.

Freshly voided midstream clean-catch urine samples were collected from each 658 patients of different age and sex groups in a sterile screw capped universal container. The specimen was labeled and transported to the microbiology laboratory for processing and cultured within half an hour of collection. A modified semi-quantitative technique using a standard calibrated bacteriological loop of urine was performed to transfer 0.001 ml of sample on blood agar and MacConkey agar media. After allowing the urine to be absorbed into the agar, the plates were then inverted and incubated aerobically at 37°C for 24 h. The plates were then examined macroscopically for bacterial growth. The colony count was done using semi quantitative method. Number of colonies obtained was multiplied by 1000 to obtain the colony forming units (CFU)/ml [10].

A significant growth is considered if the number of colony is $\geq 10^5$ CFU/ml. Colonial appearance and morphological characters of isolated bacteria was noted and gram staining was done for identification of the isolated organisms. The characteristic bacteria on the culture media were aseptically isolated.

Antimicrobial sensitivity tests were carried out by disc diffusion technique using Muller Hinton Agar. Interpretation of results was expressed in sensitive and resistant depending upon the size of the zone of inhibition. The antibiotics used for susceptibility testing in our study were amoxycillin, amoxyclav, cefotaxime, ceftriaxone, cephalexin, nalidexic acid, nitrofurantoin, mecillinum, amikacin, cefixime, ceftazidime cefuroxime, cephradine ciprofloxacin cotrimoxazole, gentamycin, tazobactum, meropenem, and imipenem.

Results

A total of 658 urine samples were collected from suspected UTI patients.

	Frequency (Total – 460)	Percentage
Residence		
Urban	136	30
Rural	334	70
Education		
Educated	303	66
Not educated	157	34
Marital status		
Married	338	73
Unmarried	122	27
Sexual activity		
Active	285	62
Not active	175	38
Economical status		
Lower class	49	11
Middle class	393	85
Higher class	18	4
Dysuria		
Present	321	68
Absent	139	32
Urgency		
Present	359	78
Absent	101	22
Fever		
Present	336	73
Absent	124	27
Abdominal pain		
Present	354	77
Absent	106	23
Treated with antibiotics		
Yes	221	48
No	239	52
Co-morbid condition		
DM	55	12
HTN	15	3
ISD	8	2
Others	34	7
Pressure ulcer		
Present	40	9
Absent	420	91

Table 1: Base line characteristics in patients without growth in urine culture.

	Frequency (Total-198)	Percentage
Residence		
Urban	66	33
Rural	132	67
Education		
Educated	134	68
Not educated	64	32
Marital status		
Married	163	82
Unmarried	35	18
Sexual activity		
Active	143	72
Not active	55	28
Economical status		
Lower class	10	5
Middle class	180	91
Higher class	8	4
Dysuria		
Present	152	77
Absent	46	23
Urgency		
Present	175	88
Absent	23	12
Fever		
Present	133	67
Absent	65	23
Abdominal pain		
Present	150	76
Absent	48	24
Treated with antibiotics		
Yes	94	48
No	104	52
Co-morbid condition	68	34
DM	45	23
HTN	27	14
IHD	4	2
Pressure ulcer		
Present	22	11
Absent	176	89

Table 2: Base line characteristics in patients with growth in urine culture.

Base line characteristics in patients in urine culture without growth and with growth had shown in Tables 1 and 2.

SL No.	Bacterial Isolates	Frequency		
		Number (%)	Male (%)	Female (%)
1	*E. coli*	171 (86)	69 (35)	102 (51)
2	*Klebsiella*	17 (9.6)	4 (2)	13 (7)
3	*Enterococcus*	10 (5)	2 (1)	8 (4)
	Total	198	75 (38)	123 (62)

Table 3: Frequency of Isolation of organism in relation to sex of patient and their overall percentage.

Among 198 culture positive samples, *E. coli* was ranked highest 171 (86%). Growth of *Klebsiella pneumonia* and *Enterococcus* was found in 17 (9.6%) and 10 (5%) samples respectively. It was also observed from this table that the maximum numbers of isolates were distributed among the females 123 (62%) (Table 3).

Name of organism	No (%) 2016	No (%) 2011	Chi-Square Value (x^2)	P. value
E. coli	171 (86)	98 (75)	3.17	<0.01
Klebsiella	17 (9.6)	14 (10.4)	0.29	>0.1
Enterococcus	10 (5)	8 (6)	0.38	>0.1
Pseudomonas	0	2 (1.5)	0.16	>0.1
Proteus	0	2 (1.5)	0.16	>0.1
Staph. aureus	0	4 (3)	0.47	>0.1
E. coli and *Klebsiella*	0	3 (2.29)	0.35	>0.1

Table 4: Comparative study between the common isolated uropathogenic bacteria in the year 2016 and 2011. UTI with *E. coli* was found statistically significant increase in the year 2016 with p values <0.01.

Sl. No	Name of antibiotics	Total No Sensitive	Percentage
1	Meropenem	198	100
2	Imipenem	197	99.5
3	Amikacin	196	99
4	Tazobactum	196	99
5	Gentamycin	178	90
6	Nitrofurantoin	175	88

7	Mecillium	174	88
8	Colistin	167	84
9	Ceftazidime	114	53
10	Cotrimoxazole	105	53
11	Ciprofloxacin	104	52
12	Ceftriaxone	102	45
13	Nalidexic acid	89	45
14	Cephlalexine	86	43
15	Cefuroxime	84	42
16	Cefotaxime	84	42
17	Cefixime	80	40
18	Cephradine	68	34
19	Amoxiclav	49	24
20	Amoxicillin	28	14

Table 5: *In vitro* antibiotics sensitivity pattern of the bacteria (n=198).

Study shows, meropenem, imipenem, amikacin, tazobactum, gentamycin nitrofurantoin, and mecillinum, were found to be most effective antibiotic against most of the uropathogens. *In vitro* sensitivity of the isolates to these antibiotics was shown to be varied from 88% to 100%. This table also shows high degree of resistance against commonly used antibiotics-amoxycillin, amoxiclav, cephradine and cefixime Tables 4 and 5. *In vitro* resistance of the isolates to these antibiotics was varied from 60% to 86%.

Antibiotic	**2016 (n=198)**	**2011 (n=131)**	**Chi-Square Value (x^2)**	**P value**
Carbapenem				
Imipenem	197 (99.5%)	131 (100.0%)		0.0001
Meropenem	198 (100.0%	128 (98.0%)	0.51	0.4751
Cephalosporins				
1st Generation				
Cephradine	68 (34.0%)	48 (37.0%)	0.09	0.7642
Cephlalexine	86 (43.0%)	46 (34.7%)	1.13	0.2878
2nd Generation				
Cefotaxime	84 (42.0%)	51 (39.0%)	0.08	0.7773
Ceftazidime	114 (53.0%)	-	-	-
Cefuroxime	84 (42.0%)	49 (37.0%)	0.33	0.5657
3rd Generation				
Ceftriaxone	102 (51.5%)	100 (76.0%)	12.08	0.0005
Cefixime	80 (40.0%)	40 (30.0%)	1.78	0.1821
Quinolones				
Nalidexic acid	89 (45.0%)	33 (25.0%)	7.93	0.0049
Ciprofloxacin	104 (52.0%)	45 (34.5%)	5.6	0.018
Aminoglycosides				
Amikacin	196 (99.0%)	128 (98.0%)	0	1.0
Gentamycin	178 (90.0%)	113 (86.0%)	0.43	0.512
Penicillin				
Amoxiclav	49 (24.0%)	100 (76.0%)	52.02	0.0001
Amoxicillin	28 (14.0%)	17 (13.0%)	0	1.0
Mecillinum	174 (88.0%)	92 (70.0%)	8.71	0.0032
Colistin	167 (84.0%)	114 (58.0%)	15.18	0.0001
Nitrofurantoin	175 (88.0%)	119 (91.0%)	0.21	0.6468
Tazobactum	196 (99.0%)	-	-	-
Cotrimoxazole	105 (53.0%)	50 (38.0%)	3.95	0.0469

Table 6: Comparative study between 2016 and 2011 of trend of antibiotic sensitivity pattern of uropathogenic bacteria.

There was statistically significant reduction in sensitivity pattern in year 2016 in comparison to 2011 was detected for imipenum, ceftriaxone, and amoxiclav. On the other hand significant increase in sensitivity pattern was found for nalidexic acid, ciprofloxacin, mecillinum, colistin and cotrimoxazole. No statistically significant change in sensitivity pattern was shown for other antibiotics (Table 6).

Discussion

This study demonstrates the distribution and antibiotic susceptibility pattern of bacteria isolated from patients with suspected UTI from a tertiary care center. The patients attending in our center with symptoms suggestive of UTI, 31% had culture positive, which was nearer to our previous study in 2011 where growth was 24% [9]. Studies by BHN Yasmeen et al. [11] on 2014 in Bangladesh shows 21% urine sample were positive for pathogenic organisms. Our study showed a high prevalence of UTI in females (73.57%) than in males (35.14%) which is similar to other reports where it was shown that the frequency of UTI is greater in females as compared to males [12-14]. It has been extensively reported that adult women have a higher prevalence of UTI than men, principally owing to anatomical and physical factors [15-17].

In this study, the most predominant isolated organism was *E. coli* (86%) which was significantly higher (p value was <0.01) than our previous studies in 2011 where *E. coli* was 75% [9].

In this study the most powerful antibiotic was meropenem, imipenem, tazobactum and amikacin. These antibiotics show their efficacy against 99-100% of the uropathogens which was similar to our previous study on 2011 [9]. Uropathogens shows higher degree of resistance against most of the antibiotics used for sensitivity. This increasing resistance is due to irrational consumption of most of the antibiotics during the past decade in our region [8,18,19]. As meropenem imipenem and tazobactum are highly expensive medicine which makes it very difficult to purchase by most of the peoples of our community. So like our previous study still our recommendation is in

favor of using amikacin regarding empirical antibiotics in UTI. The most sensitive oral antibiotics were nitrofurantoin. It shoes its effectiveness against 88% of the isolates. This drug exhibited low resistance rate in the major part of the world (0–5.4%), despite of its use for many years which was because of localized action of this drug only on the urinary tract [20]. So, nitrofurantoin can be considered as first line, cost saving and effective oral therapy in UTI. There was significant reduction in sensitivity pattern in year 2016 was detected for imipenum, ceftriaxone, and amoxiclav, possibly because random use of these antibiotics in past few years with inadequate dose and duration. Uropathogens resistance to antibiotic has now become a public health concern in Bangladesh [21]. There was significant increase in sensitivity pattern in year 2016 was detected for Nalidexic acid, Mecillinum and Colistin because these antibiotics are not commonly used in our community in last few years. According to guideline by Infectious Diseases Society of America (IDSA) in the year 2011, an antibiotic is no longer recommended for empirical treatment of acute UTI if there is >20% resistance prevalence to that particular antibiotic [22]. According to this guideline of IDSA, most of the antibiotics used in our study should not be used for empirical treatment of acute UTI and our standard treatment guidelines for UTI is not sufficient which requires a large scale study.

There is urgent need of constant monitoring with culture and sensitivity pattern of specific pathogens in different health care centre's in our country. Community awareness program should be undertaken for adherence to treatment protocol considering bacterial resistance and emerging multidrug resistant strains. It is necessary to conduct a regional research on the culture and sensitivity patterns of the bacteria. All the authors contributed equally in this study.

Conclusion

UTI with *E. coli* was significantly increased in the year 2016. This study failed to show a steady increase in resistance to all studied antibiotics. Imipenem, meropenem, tazobactum, amikacin and nitrofurantoin still remain more sensitive in this comparative study. Comparative study of 2016 *vs.* 2011 shows significant increasing resistance for imipenum, ceftriaxone, amoxiclav and increasing sensitivity for nalidexic acid, ciprofloxacin, mecillinum, colistin, cotrimoxazole.

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