Pattern and types of resistance in Carbapenemase Producing Imipenem Resistant *E. coli* of urine sample in Dhaka Medical College.

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Abstract

Background: Antimicrobial resistance is a serious public health problem. The emergence of metallo-β-lactamase-producing *Enterobacteriaceae* is a worldwide health concern. **Objectives:** To determine pattern and types of resistance in Carbapenemase Producing Imipenem Resistant *E. coli* of urine sample in Dhaka Medical College. **Methods:** An observational study was carried out over a period of one year in Dhaka Medical College. A total 280 urine samples were collected purposive sampling with aseptic precaution from the attended suspected UTI patients. The collected specimens were inoculated in blood agar, nutrient agar and MacConkey agar media and incubated aerobically at 370C for 24 hours. Antibiotic susceptibility pattern was determined by double disk method for all the isolated *E.coli* strains. *Results:* A total of 280 urine samples, 83 (29.6%) samples were identified as culture positive. Among 83 culture positive urine, *Esch.coli* was identified as the most common (60, 72.29%) pathogens. Among the isolated uropathogenic *E.coli,* the most resistance was found against cotrimoxazole (90%) and lowest resistant was found against tigecyline (6.67%). Out of 60 uropathogenic *Esch.coli* 43 (71.67%) were multidrug resistance (MDR) followed by 14 (23.33%) and 3 (5.00%) were XDR and PDR respectively. **Conclusion:** Antimicrobial resistance has become a global issue now a days. So, we should use appropriate antibiotic according to the sensitivity pattern for bacteria to prevent emergence of resistance.

Key words: uropathogenic E.coli, antimicrobial susceptibility pattern, antimicrobial resistance pattern, antimicrobial resistance types.

Introduction

Antimicrobial resistance (AMR) is a worldwide nuisance to health community and globally 700,000 deaths are annually reported.[1] *Esch.coli* is increasingly associated with multidrug resistance, including the resistance to the last-resort carbapenems.[2] The prevalence of ESBLs producing *Esch. coli* is reported in 62.9-100.0% from Asia.[3,4]

Colistin is a drug of last resort for CREBs. Colistin resistance implies a pan drug resistant state, with virtually no therapeutic options.[5] Recently the use of fosfomycin has attracted renewed interest for the treatment of serious systemic infection caused multi drug resistance Enterobacteriaceae. WHO has classified fosfomycin in the category of a critically important antimicrobial for investigation in light of its efficacy MDR gram negative organism and has been identified as an antimicrobial which holds great promise worldwide for managing MDR gram negative infection , due to affordable cost and efficacy as carbapenem sparing regimen.

So, development of novel antibiotics for treating AMR infections has been actively persuading, but has not been successful. Such present situation calls for efforts on various levels in order to better manage AMR infections.

Methods

An observational study was carried out over a period of one year in the Microbiology department of Dhaka Medical College (DMC) and the outpatient department of Dhaka Medical College Hospital (DMCH). Ethical clearance for the study was taken from the Instutional Review Board and concerned authority, Dhaka Medical College & Hospital. A total 280 urine samples were collected by purposive sampling with aseptic precaution from the attended suspected UTI patients at both the department. Informed written consent was taken from each patient or patient's attendant before selecting the patient in this study. The collected specimens were inoculated in blood agar, nutrient agar and MacConkey agar media and incubated aerobically at 370C for 24 hours. Growth of >=105 cfu/ml was considered as positive urine culture. Antibiotic susceptibility pattern was determined by double disk method for all the isolated E.coli strains. Data were analysed in the computer using SPSS for windows. Data analysis involved simple descriptive as well as analytical techniques. Chi-square test for categorical variables (e.g., pus cells /HPF) was applied to determine the association between pus cells /HPF in urine and urine culture result.

Results

Table I: Pus cells/HPF in urine and Urine culture result (n=280).

Pus cells in HPF	Urine culture result		Total N(%)	P value
	Culture Positive N(%)	Culture Negative N(%)		
5-10	18(13.3)	117(86.7)	135 (48.2)	73.12
11-20	21(24.7)	64(75.3)	85 (30.4)	
>20	44(73.3)	16(26.7)	60 (21.4)	
Total N(%)	83(29.6)	197(70.4)	280 (100.0)	

A total of 280 urine samples, 135 (48.2%) samples had pus cell count 5-10/HPF, 85(30.4%) had pus cell 11-20/HPF and 60(21.4%) samples had pus cell count >20/HPF. Out of 135 urine samples having pus cells count 5-10/HPF, only 18 (13.3) urine samples were culture positive. Culture positive cases were increasing with the increasing the level of pus cell count/HPF. Culture positive cases were remarkably high among the samples having pus cells count >20 /HPF than the others groups. There was an association between pus cells count /HPF and culture positivity ($p < .05$)(Table I).

Table II: Bacteria isolated from urine culture (n=83).

Bacteria	Frequency (Percentage) N (%)
Escherichia coli	60(72.29)
Klebsiella spp.	6(7.23)
Pseudomonas spp.	5(6.02)
Proteus spp	3(3.61)
Enterobacter spp	2(2.41)
Acinetobacter spp	1(1.20)
CONS	3(3.61)
Staphylococcus aureus	2(2.41)
Enterococcus spp	1(1.20)

Among 83 culture positive urine, 60(72.29%) were Esch.coli, The least common (1.2%) uropathogens were Acinetobacter spp and Enterococcus spp (Table II).

Table III: Antibiotic resistance patterns of isolated uropathogenic Esch.coli (n=60).

Antimicrobial drugs	Resistant N (%)
Amikacin	24(40.00)
Amoxyclav	42(70.00)
Aztreonam	48(80.00)
Cefotaxime	42(70.00)
Cefoxitin	42(70.00)
Ceftazidime	48(80.00)
Cotrimoxazole	54(90.00)
Ceftriaxone	50(83.33)
Ciprofloxacin	51(85.00)
Gentamicin	42(70.00)
Piperacillin/Tazobactum	39(65.00)
Nitrofurantoin	24(40.00)
Colistin	08(13.33)
Imipenem	09(15.00)
Fosfomycin	14(23.33)
Tigecycline	04(06.67)

A total of 60 isolated uropathogenic Esch.coli, 54 (90.0%) were resistant to cotrimoxazole followed by 51(85%) ciprofloxacin, 50(83.33)% ceftriaxone and only 4(0.6.67%) were resistant to Tigecycline (Table III).

Table IV: Types of antibiotic resistance pattern of isolated uropathogenic *Esch.coli* (N=60).

Type of resistant	Number (Percentage) N (%)
MDR	43 (71.67)
XDR	14 (23.33)
PDR	03 (5.00)

Out of 60 uropathogenic *Esch.coli,* 43 (71.67%) were multidrug resistance (MDR), 14 (23.33%) and 3 (5.00%) were XDR and PDR respectively (Table IV).

Discussion

A total of 280 specimens (urine) were collected from clinically suspected infected patients from Dhaka Medical College.

In the present study, majority 92.77% of UTI were due to gram negative bacilli(GNB) and remaining 7.23% due to gram positive cocci (GPC). In a study in the Department of Microbiology, All India Institute of Medical Sciences, New Delhi, India, conducted by Mohapatra *et al.* (2022)[6] reported GNB and GPC among uropathogens were 94.4% and 5.6%, respectively, which is almost similar to with the present findings. In this study, Mohapatra *et al.* (2022)[6] also reported that prevalence of *Esch.coli* and Klebsiella pneumoniae among total isolated uropathogens were 65.57% and 16.19% respectively, which are in accordance with the present study findings. In an another study in Pakistan by Akter *et al.* (2016)[7] reported that the other gram-negative bacteria were Pseudomonas spp.(7.61%), Proteus spp.(4.01%), Enterobacter spp.(2.31%) and Acinetobacter spp.(1.03%), which are consistent with the present study. The present study findings revealed that isolated Esch.coli were susceptible to Cotrimoxazole and ciprofloxacin with the high resistance of 90% and 85%, respectively. These findings are in agreement with the study by Bhowmik *et al.* (2021)[8] who reported 86.6% resistance of *Esch.coli* to Cotrimoxazole and 79.92% to ciprofloxacin. In the present study, resistance pattern of *Esch.coli* to colistin and fosfomycin were 13.33% and 23.33%, respectively. Padhi *et al.* (2020)[9] from India reported 9.8% resistant to colistin and 15.9% resistant to Fosfomycin for *Esch.coli.* Chowdhury *et al* (2019)[10] from Bangladesh reported that resistance of *Esch.coli* to colistin and fosfomycin were 12.19% and 17.47% respectively.

Among the 60 isolated *Esch.coli* in this study, 43(71.67%) were multidrug resistant (MDR), 14(23.33%) were extensively drug resistant (XDR) and 03(5.00%) were pandrug resistant (PDR). In Tehran, a study conducted by

Saderi and Owlia (2015)[11], who reported that 74.5% of isolates were MDR, 21.73% were XDR and 3.77% were PDR which are similar to the findings of this study. There are four general antimicrobial resistance mechanisms that bacteria use. These are limiting uptake of the drug, modifying the target of the drug, inactivating the drug, and active efflux of the drug. These mechanisms may be located on the bacterial chromosome and occur naturally in all members of a species (intrinsic) or come from other bacteria, usually via a plasmid (acquired). Antimicrobial resistance has become a global issue for all of us. That's why, we should use appropriate antibiotics according to the sensitivity pattern for bacteria to prevent emergence of resistance.

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