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SPECTRUM OF ANTIBIOTIC SUSCEPTIBILITY PATTERN IN EXTENDED SPECTRUM BETA LACTAMASE (ESBL) PRODUCING ESCHERICHIA COLI IN CASE OF URINARY TRACT INFECTION IN TERTIARY MEDICAL CENTRE.

General Medicine

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ABSTRACT

Background: In India females are most vulnerable to both community acquired and hospital acquired urinary tract infection caused by Escherichia coli. Due to improper use of antibiotics there is emergence of multidrug-resistant ESBL producing E coli as a result mortality and morbidity of the patient are increased.

Aims & Objectives: Aim of this study was to show the pattern of antibiotic susceptibility and thus resistance to different types of antibiotics against ESBL producing Escherichia coli induced urinary tract infection so that proper antibiotic can be prescribed and to know the which antibiotic should be prescribed in the local geographical area to treat urinary tract infection.

Materials and method: Midstream morning clean-catch urine from the patients was sent to the nearest laboratory for culture and sensitivity without delay. After culture of the organism ESBL production was detected followed by testing of antibiotic sensitivity.

Results: Urine samples from 348 patients (out of total 1800 samples, 800 males and 1000 females) demonstrated highest sensitivity to carbapenam group and nitrofurantoin, moderate sensitivity to netilmicin, amikacin, piperacillin-tazobactum, polymyxin B and colistin but highly resistant to ampicillin, chloramphenicol, ticarcillin, fairly resistant to ofloxacin group of drugs except levofloxacin, 4th generation cephalosporin.

Conclusion: Progressively increasing resistance to common antibiotics against ESBL producing Escherichia coli due to unnecessary, inadvertent and over the counter use of antibiotics warn the internist to use antibiotics only after getting the result of culture-sensitivity of urine from the laboratory.

KEYWORDS

ESBL producing E Coli, Urinary tract infection, Antibiotic susceptibility, Tertiary Medical Centre

Introduction:

Escherichia coli, gram negative bacteria, is most common cause of both community acquired and hospital acquired urinary tract infection and 25% of female experienced this disease in any time of their life[1,2,3].

In the clinic physicians usually give empiric treatment to the patients come with urinary tract infection prior to getting the results of urinary culture/sensitivity. As a result there is evidence of increasing resistance to ampicillin, ciprofloxacin[4, 5]. Now-a-days extended spectrum beta lactamase (ESBL) producing gram negative bacteria, Escherichia coli, pose a great threat to treat the UTI throughout the World including certain studies in India showing 50 percent prevalence of this ESBL producing E coli. There are three organisms produce this ESBL; these are Escherichia coli, Klebsiella pneumoniae, Enterobacteriaceae[6,7,8,9].

ESBLs are a composite group of plasmid mediated complex rapidly evolving enzymes capable of hydrolyzing the several groups of drugs, like, penicillin, broad-spectrum cephalosporins and monobactums[7]. ESBLs are derived from TEM and SHV type enzymes, CTX-M type enzymes which are being isolated from ESBL producers and these are recognized as important subtype responsible for multidrug resistance[10]. The plasmid bearing genes encoding ESBLs are responsible for developing resistance to the few other antimicrobial agents, like, aminoglycosides and quinolones[11]. These ESBL producing organisms are responsible for spectrum of urinary tract infection from asymptomatic cases to severe urosepsis. Physicians prescribe cephalosporins, fluoroquinolones like antibiotics but recently there is evidence of emerging resistance against these antibiotics[11]. In case hospital acquired infection carbapenem are prescribed for these organisms but resistance also developed against this antibiotic[11]. As a result the choice of antibiotics is very limited against these organisms. There are several risk factors for this UTI by ESBL producing organisms. These are repeated hospitalization, recent antibiotic treatment with second and third generation cephalosporins, quinolones and penicillin, diabetes mellitus, male sex, recent Klebsiella infection[12].

AIM & OBJECTIVES:

So our aim is to evaluate the prevalence of antibiotic sensitivity of ESBL producing Escherichia coli isolated from urinary tract infection in hospitalized patients.

MATERIALS & METHODS:

This is a descriptive cross-sectional study done over a period of 5 years done in **our hospital** after receiving ethical clearance from our local ethical committee. Total 3220 urine samples were sent for culture and sensitivity.

Patient selection: All the patients clinically suffered from fever of more than 100°F with or without chill and rigor, nausea with or without vomiting, increased frequency of micturition, burning sensation during micturition, tender renal angle. Laboratory findings demonstrated white blood cell count of more than 11000/cc with predominant neutrophil positivity, high C reactive protein, ultrasonographic evidence of acute renal parenchymal disease were considered for this test. All the participants after treatment with culture-sensitivity guided antibiotics repeat urine culture demonstrated negative for any growth.

Method of collection and bacteriology: Midstream urine was collected in a sterile container for semi-quantitative urine culture and inoculated in blood agar and MacConkey agar with the help of calibrated loop and kept it incubated at 37° C for 24 hours. Samples with colony count more than 10^5 are considered as significantly positive. From that growth E coli was identified by Gram stain and different biochemical tests containing different substrates, like, oxidase, indole, lysine decarbonize, methyl red, indole, simmons citrate, urease and glucose fermenting in Triple Sugar Iron (TSI) agar medium as described in standard bacteriological methods[13].

Antibiotic susceptibility tests: Disc diffusion method on Muller-Hinton agar determines antibiotic susceptibility pattern to clinical Laboratory Standard Institute (CLSI) guidelines[14]. Different antibiotics disc obtained from MAST chemical corporation, England were tested to get the pattern of sensitivity. E coli ATCC 25922 was used for quality control as per CLSI recommendation.

Detection of ESBL production: Double disc diffusion (combined-disc) method determines ESBL producing organisms. Bacterial suspension was prepared with 0/5 Mcfarland dilution followed by culture on Muller-Hinton agar plates. Four antibiotics disc were placed on four agar plates, these were ceftazidime (30 µgr) and cefotaxime (30 µgr) alone as well as in combination with clavuronic acid (10 µgr) (CAZ:30 µgr / CA 10µgr) and CTX:30 µgr / CA 10 µgr. These were incubated for 24 hours at 35±2°C for evaluation of ESBL production. Indication of ESBL production was determined by ≥5 mm increase in diameter of zone of inhibition produced by one combination disc versus its zone when tested alone. As per recommendation of CLSI, Klebsiella ATCC 700603 was used as quality control.

Data analysis:

All the data were analyzed by SPSS software version 16.

RESULTS:

The result showed high percentage of sensitivity (75.28% to 86.21%)

were demonstrated in case carbapenem group as well as nitrofurantoin, moderate sensitivity (65.52% to 62.93%) in case of amikacin, netilmicin, polymyxin B, colistin, piperacillin-tazobactum, low sensitivity (57.18% to 47.70%) in gentamicin, tobramycin and cefoparazone-sulbactam. Third and fourth generation cephalosporins except Cefoxitin (40.23%), amoxycillin group, aminoglycoside group, fluoroquinolone group demonstrated very low sensitivity.

Table: Pattern of antimicrobial Sensitivity of ESBL E Coli infection of urinary tract (n=348)

Antibiotic	Sensitivity	Percentage
Amoxycillin	3	0.86
Amoxycillin-Clavulanic acid	35	10.05
Piperacillin-Tazobactam	219	62.93
Cefoparazone-sulbactam	166	47.70
Cefuroxime	6	1.72
Cefotaxime	10	2.87
Cefoxitin	140	40.23
Ceftazidime	7	2.01
Ceftriaxone	6	1.72
Cefepime	7	2.01
Azithromycin	0	0
Aztreonam	14	4.03
Ertapenem	262	75.28
Imipenem	300	86.21
Meropenem	294	84.48
Gentamicin	199	57.18
Tobramycin	179	51.43
Netilmicin	229	65.81
Amikacin	240	68.96
Norfloxacin	34	9.77
Ciprofloxacin	38	10.92
Ofloxacin	48	13.80
Levofloxacin	82	23.56
Cotrimoxazole	77	22.12
Chloramphenicol	3	0.86
Polymyxin B	227	65.23
Colistin	228	65.52
Ticarcillin	46	13.22
Nitrofurantoin	274	78.74

DISCUSSION:

Now-a-days ESBL producing E coli are responsible for community acquired urinary tract infection in the world and antibiotic resistance is the major problem due to limited choices of treatment[14,15]. According to the reports of World Health Organization Iran was described as highest consumption of antibiotics in the world but global statistics gave no report of antibiotic use in Iran[16]. This present study demonstrated all the patients suffered from community acquired UTI which was similar to the study done by Baziboroun M. et al[17].

This present study demonstrated 75.28% to 86.21% sensitivity to carbapenem group of drugs which was similar to the study done by Baziboroun M. et al[17]. This study demonstrated 57.18% to 68.96% sensitivity to aminoglycoside group drugs; it was similarly demonstrated in a Spanish study as a cause of significant reduction in mortality in carbapenem group resistant ESBL producing E coli[18]. A large number of studies demonstrated susceptibility to carbapenem, aminoglycosides and nitrofurantoin which was similarly demonstrated in this present study[19, 20, 21]. In Nepal and Korea it was reported as 100 percent in case of meropenem[19,20]. In India ESBL producing E coli was 80% resistant to nitrofurantoin; it was contradictory to the present study, it may be due to wide spread use of this drug in case community acquired UTI in that isolated region[22].

In this region as there is no definite antibiotic guideline the physicians use 3rd or 4th generation cephalosporins at random in community acquired UTI, as result these drugs became resistant in this infection[23, 24].Again, in Iran ciprofloxacin is the most preferred treatment in case of community acquired UTI whereas in Shiraz, Iran, resistance to ciprofloxacin and ceftazidime were 38.5% and 63.5% respectively [19,24, 25, 26]. This present study showed only 10.92% and 2.01% sensitivity to ciprofloxacin and ceftazidime respectively.

In Jaipur, Rajasthan, community acquired UTI is ESBL producing E coli are sensitive to Piperacillin-tazobactum which was similar to this present study where the sensitivity was 62.93%[27]. In Turkey, Korea resistance to ciprofloxacin was lower as compared to the present study[19,28,29].

So there should be some strategies to be implicated in every hospital to reduce the spread of ESBL producing E coli by minimizing the contact with the hospital patients[30].

If patients are infected with multidrug-resistant organisms, they should have restricted contact with already admitted patients. So less seriously ill patients even infected with ESBL producing organisms should be discharged as early as possible and the patient should be treated with potent and effective antibiotic Ertapenem[31]. One study demonstrated that there was no evidence of resistance against carbapenem in 167 patients in India in 2014 and 115 patients in Bangladesh in 2008[32,33].

CONCLUSION:

Multidrug-resistant ESBL producing E coli responsible for UTI was mostly associated with previous hospitalization, contact with hospitalized patients, repeated antibiotic use. Without proper culture and sensitivity random antibiotic use to treat UTI gives rise development multidrug resistant E coli. India being the third world country with free health care system, occurrence of carbapenem resistant ESBL producing E coli add significant health budget to the existing health budget. So, proper antibiotic guidelines should be followed to prevent emergence of multi drug-resistant E coli in different infections in the body.

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