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Extended Spectrum B Lactamase (ESBL) Producing Uropathogens in the Intensive Care Unit in A Tertiary Care Hospital, Tamilnadu.

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Abstract: *Urinary tract infections are one of the most common infection in human beings, especially in intensive care unit due to the impaired immunity and invasive procedures. The changing pattern of resistance to antibiotics may lead to therapeutic failure and it is a major public health issue. We aimed to see the prevalence of UTI among ICU patients, its bacterial profile and to evaluate its ESBL production among the GNB. E.coli and Klebsiella were the predominant uropathogens. 39.5% were ESBL producers among this GNB. They were maximum sensitive to amikacin, nitrofurantoin and nalidixic acid, followed by norfloxacin and ciprofloxacin. This study reveals the emergence of ESBL producers among urinary isolates in ICU, which makes the treatment failure. The clinician must be aware of the antibiotic resistance as well as sensitivity knowledge in their locale. So that, to avoid treatment failure, proper infection control which in turn, will reflect on good patient outcome.*
Key words*: ICU, ESBL, GNB, uropathogens.*

I. Introduction

Infections in urinary tract is one of the commonly encountered infections in humans and gram negative bacteria (GNB) are the predominant causative agents of urinary tract infections (UTI) [(1).]Among the GNB, the members of Enterobacteriaceae are commonly isolated. For UTI, β lactum group of antibiotics are commonly used to treat these organisms [(2)]

ESBL are enzymes secreted by bacteria and there are capable of hydrolysing all β lactum drugs except cephamycin and carbapenem. This resistance is encoded by transferrable conjugative plasmid [(3).] The common classification of β Lactamase are the ambler molecular (A-D), and Bush-Jacoby-Medeiros functional classification. (7)

β lactum antibiotics are among the most commonly prescribed antimicrobials in intensive care units, globally, which is due to their broad spectrum, efficacy and less toxicity. [(4)] In intensive care unit (ICU), the incidence of hospital acquired infections and the antibiotic resistance are in rise, due to their clinical diseases with altered immunity and use of invasive procedures and indiscriminate use of empirical antibiotics. [(5)]

The emergence of antimicrobial drug resistance is major public health issues and threat to treatment failure. [(6)] Now the increasing frequency of ESBL producing organisms are of concern due to the treatment failure and it may leads to complications, morbidity and mortality.[(8)]

With this background, we have undertaken this study to characterise the GNB causing UTI in ICU, and to evaluate the ESBL production among these GNB.

II. Materials And Method

This study was done in intensive care unit of Govt Stanley medical college. A total of 75 urine samples were collected with all aseptic precaution and in a sterile wide mouth container from these patients and transported immediately to the microbiology laboratory for further bacteriological processing. All urine samples were inoculated into nutrient agar, MacConkey agar and blood agar and incubated at 37 ^{o}c, overnight. All the isolates were identified using standard biochemical tests. [(9)]

Drug susceptibility test was done by Kirby Bauer disc diffusion method using 3rd generation cephalosporin, gentamycin, amikacin, norfloxacin, ciprofloxacin, nitrofurantoin, and nalidixic acid. The results were interpreted according to CLSI guidelines. [(10)]

All the isolates showing resistance to 3rd generation cephalosporin's were subjected to phenotypic screening and combined disc confirmatory testing for ESBL production.

Phenotypic ESBL Screening method [(10)]

According to the CLSI Screening procedures for ESBLs production was done, using indicator cephalosporins, ceftriaxone (30µg), ceftazidime (30µg), and Cefotaxime (30µg). Isolates exhibiting zone size ≤

25mm with ceftriaxone ≤ 22mm for ceftazidime and ≤ 27mm with cefotaxime were considered as ESBLs producer.

Combined Disc Diffusion Method ([10])

From the colonies of gram negative bacilli, 0.5 McFarland's turbidity standard suspension was prepared. Lawn culture was made on Muller Hinton Agar plate with this inoculum. Discs of Ceftazidime and Ceftazidime + Clavulanic acid (30 mcg/10 mcg) were placed aseptically on the surface of MHA. The distance of 15mm was kept between the disc and overnight incubation was done at 37^{o}C. An increase of ≥ 5mm in zone diameter of Ceftazidime + Clavulanic acid in comparison to the zone diameter of Ceftazidime alone confirmed the ESBL production by the organisms.

III. Results

Among the 75 urine samples, 48 were gram negative bacilli (64%), and 8 were gram positive cocci (10.7%). 19(25.3%) showed no growth.

Table 1: Distribution of urinary isolates

Organisms	Number (n=48)	Percentage(%)
Escherichia coli	22	45.9
Klebsiella pneumoniae	12	25.0
Proteus vulgaris	10	20.8
Pseudomonas aeruginosa	3	6.3
Acinetobacter species	1	2.0

Table 2: ESBL producers among uropathogens

Organisms	Number	Percentage (%)
Escherichia coli	14	29.1
Klebsiella pneumoniae	5	10.4
Proteus vulgaris	-	-
Pseudomonas aeruginosa	-	-
Acinetobacter species	-	-
Total	19	39.5

Table 3: Antibiotic sensitivity pattern of ESBL producers

Antibiotics (n=19)	Sensitivity	Percentage
Amikacin	15	78.9
Nitrofurantoin	12	63.1
Nalidixic acid	12	63.1
Norfloxacin	10	52.6
Ciprofloxacin	8	42.1
Gentamycin	6	31.5
Cotrimoxazole	2	10.5
Cephalexin	0	0

IV. Discussion

Infections among ICU patients might be community or hospital acquired and UTI are very common infection here. The emergence of resistance to antibiotics among ICU patients are double burden to the patients as well as physicians, and if not monitored properly, he may go for renal and life threatening complications.

In our study, out of 48 urinary GNB isolates, E.coli was the predominant bacterial (45.8%) isolate, followed by Klebsiella pneumoniae (25%). The similar observations has been made by Anuradha *et al*., Supriya *et al*, Melten *et al* , (11, 12,13) in which E.coli & Klebsiella were 44.7% & 11.2%, 49.8%& 37.8% and 45.5% &13.3% respectively. In a study by Akram *et al*, Klebsiella species were the predominant isolate in urine sample. All these GNB were screened and confirmed for ESBL production. We observed 39.5% GNB were ESBL producers, in our study. The similar percentage has been reported with Saeide *et al.,* and Babek *et al*., which were, 44.5% & 42% respectively. But the lower percentage, 11.7% were ESBL producer in the study of Deepti *et al*., Slightly high rate of 58%, by Mathur *et al*., and very higher rates of 71.7% & 84.6% has been reported with Hasan *et al*., & Rejitha *et al*., respectively. Studies conducted from various part of India states that the ESBL production ranges from 10% - 80%. This variation could be attributed to the geographical locale and the environment from where the study conducted. Most of the ESBL strains (78.9%) were sensitive to amikacin, which is followed by nitrofurantoin and nalidixic acid, which were 63.1% & 63.1%, respectively. This is a good choice in the treatment of UTI. Moderate sensitivity was seen with norfloxacin (52.6%) and ciprofloxacin (42.1%). This is preferred compared to amikacin; if the patient could able to take oral antibiotics. Very low sensitivity was noted with co- trimoxazole (10.5%). None were sensitive to cephalexin, as it is the very often prescribed drug for UTI; the resistance could be explained in relation with inappropriate prescription of this

drug.This study reveals the emergence of ESBL producers among urinary isolates in ICU, which makes the treatment failure. The clinician must be aware of the antibiotic resistance as well as sensitivity knowledge in their locale. So that, to avoid treatment failure, proper infection control which in turn, will reflect on good patient outcome.

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