Research Paper

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# Extended Spectrum Beta – Lactamase (ESBL) Mediated Resistance to Antibiotics Among Klebsiella Pneumoniae in In Tertiary Care Hospital, Jamnagar, Gujarat

Medical Science

KEYWORDS : Klebsiella Pneumoniae, Extended Spectrum Beta – Lactamase, antimicrobial resistance.

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## ABSTRACT

*INTRODUCTION: Resistance bacteria are emerging worldwide as a threat to the favourable outcome of common infections in community and hospitals. Now a days ESBL producing strain in Klebsiella pneumoniae lead to resistance among the organism toward cephalosporin and other antibiotics. AIM: To determine the prevalence and antibiotic susceptibility patterns of Extended Spectrum Beta- Lactamase producing Klebsiella pneumoniae isolated from various clinical samples. MATERIAL & METHODS: Clinical isolates of Klebsiella pneumoniae were confirmed by culture, staining & biochemical reaction. The isolates were subjected to susceptibility testing using Kirby- Bauer method of determining antimicrobial susceptibility and ESBL production was phenotypically determined using double disc synergy test. RESULTS: ESBL production was determined among 115 isolates of Klebsiella pneumoniae, out of 91 (79.13%) were express ESBL. CONCLUSION: Regular monitoring of antibiogram of organism, and avoiding misuse and overuse of antibiotics may reverse the undesired effects of multidrug resistant and ESBL producing Klebsiella pneumoniae.*

**INTRODUCTION:**

Klebsiella pneumoniae is a successful opportunistic pathogen and has been associated with various ailments such as urinary tract infections, septicaemia, respiratory tract infections and diarrhoea.1 Infection by Klebsiella pneumoniae is now complicated because of emergence of resistant strains. The resistant strains gain their resistance by producing Extended-spectrum b-lactamase (ESBL) which is class-A enzymes. ESBL are the derivatives of common b-lactamase (TEM and SHV b-lactamase) that have undergone one or more amino acid substitutions near the active site of the enzyme, thus increasing their affinity and the hydrolytic activity against third generation cephalosporin and monobactams. Extensive use of newer generation cephalosporin has been the strong factor for the evolution of newer b-lactamase such as ESBL. ESBL are encoded by transferable conjugative plasmids, which often code resistance determinants to other antimicrobial agents such as amino glycosides. These conjugative plasmids are responsible for the dissemination of resistance to other members of gram negative bacteria specially E.coli & Proteus species in hospitals and in the community.[2, 3, 4, 5]

ESBL are distinguished into more than 30 types based on their physical properties and all are inhibited by Clavulanate, Sulbactam and Tazobactam, a property which has been used to detect them in the laboratory.[6]

ESBL are more prevalent in Klebsiella pneumonia than in any other Enterobacter species, and outbreaks of infections caused by ESBL producing strains have been reported widely. ESBL producing strains are probably more prevalent than currently recognized because they are often undetected by routine susceptibility testing methods. Occurrence of ESBL producing Klebsiella spp. has been also reported from south India[7] and central India.[8] Recent reports have highlighted the emergence of ESBL producing strains endowed with an extremely wide spectrum of antibiotic resistance, including resistance to Trimethoprim, Amikacin, Streptomycin and gentamicin.[9] Due to the extensive spread of multidrug resistant ESBL producing strains, there has been renewed interest in Klebsiella infections. The present study was conducted with an objective to examine the incidence of ESBL producing strains among Klebsiella pneumoniae.

**MATERIAL AND METHOD**

This study was done in microbiology department, Government Guru Gobindsingh Hospital, Jamnagar. A total 115 Klebsiella pneumoniae were isolated from different samples include 41 from blood, 21 from urine, 39 from pus, and 14 from other sample (Sputum, E.T. tube or secretion, Throat swab) obtained during June 2012 to November 2012. These organisms were identified and characterized based on colony morphology and biochemical reactions.[11]

Routine disc diffusion susceptibility testing was performed by modified Kirby - Bauer's disc diffusion method. The sensitivity of the isolates to Third Generation Cephalosporin (3GC) viz., Ceftizoxime (CI), Cefotaxime (CF) , each 30 µg/disc ,Cefadroxil (CFD), Cephalexin (CFL) , and Cefuroxime (CFR) (first and second generation cephalosporin specially for urinary isolates) 30 µg/disc and to the other antibiotics such as Amikacin (AMK) (30 µg), Ampicillin-Sulbactum (AS) (20 µg), Gentamycin (GM) (10 µg), co-Trimoxazole (BA) (25 µg), Tetracycline (TE) (30 µg), Imipenem (I) (30 µg), ciprofloxacin (CFX) (5 µg), Getifloxacin (GFX) (10 µg), Ofloxacine (ZN) (5 µg) were tested by disc diffusion method.[12] The results were interpreted as per National Committee for Clinical Laboratory Standards (NCCLS) recommendations.[13] Escherichia coli ATCC 25922 strain was used for quality control.

Isolates with resistance or with decreased susceptibility (intermediate by NCCLS criteria) to any of the Third Generation Cephalosporin were selected for further study. ESBL detection done by Double Disc Diffusion Synergy Test (DDST) In the DDST, synergy was determined between a disc of Ceftizoxime & Clavulanic acid (30 µg Ceftazidime and 10 µg Clavulanic acid) and a 30 µg disc of Ceftazidime antibiotic placed at a distance of 30 mm apart on a lawn culture of the resistant isolate under test on Mueller-Hinton Table-1: Antibiotic sensitivity of klebsiella isolate in percentage from various samples. Agar (MHA, Hi-Media).[14] The test organism was considered to produce ESBL, if zone size of Ceftazidime individual disc is less than 27 mm & in combination with Clavulanic acid the zone diameter is increased up to 5 mm.(Figure 1)

**Figure1.**

CAC: Ceftazidime (30 µg) + Clavulanic acid (10 µg)
CAZ: Ceftazidime (30 µg)

**RESULT**

Out of 115 isolated klebsiella pneumonia 91(79.13%) isolate were ESBL. Out of 115 klebsiella isolates, 91 isolates showed resistance or decreased susceptibility to at least one of the two 3GC used for the study. And this resistance to all the three 3GC was found to coexist with resistance to other antibiotics. All the isolates were found sensitive to the antibiotic Imipenem. (Table 1.) Shows the antibiotic resistance pattern of the K. pneumonia isolates. Out of 79.13% ESBL producers' klebsiella pneumonia were 57.14% from urine, 79.48% from pus, 92.68% from blood & 71.42% other sample.

**Table 1. Antibiotic sensitivity of 115 klebsiella from various clinical samples.**

| Antimicrobial agents | Urine 21(%) | Pus 39 (%) | Blood 41(%) | Other 14(%) |
|---|---|---|---|---|
| Ceftizoxime (CI), | 2.56 | 2.56 | 4.87 | 22.9 |
| Cefotaxime (CF) | 9.5 | 2.56 | 7.31 | 6.2 |
| Cefadroxil (CFD), | 4.7 | 00 | 00 | 00 |
| Cephalexin (CFL) | 9.5 | 00 | 00 | 00 |
| Cefuroxime (CFR) | 14 | 2.56 | 7.31 | 6.2 |
| Amikacin (AMK) | 52.38 | 28.20 | 21.95 | 85.4 |
| Ampicillin-Sulbactum (AS) | 2.56 | 2.56 | 9.75 | 6.2 |
| ciprofloxacin(CFX) | 19 | 43.58 | 41.46 | 35.4 |
| Getifloxacin(GFX) | 85 | 97.43 | 85.36 | 83 |
| Ofloxacine (ZN | 58.97 | 58.97 | 39 | 35.4 |
| Gentamycin (GM) | 42.85 | 12.82 | 14.63 | 37.5 |
| Co-Trimoxazole (BA) | 53.84 | 53.84 | 4.87 | 37.5 |
| Tetracycline (TE) | 30.76 | 30 | 48 | 12.5 |
| Imipenem (I) | 100 | 100 | 100 | 100 |

**DISCUSSION**

ESBL producing organisms pose a major problem in clinical therapeutics. The incidence of ESBL producing strains among clinical isolates has been steadily increasing over the past few years, resulting in limitations of therapeutic options20. In our study 79.13% ESBL producers klebsiella pneumonia were detected which was comparable with study of Mathur P. et al 2002 (80%)[21] & Hadi Mehrgan et al 2010 (77.7%)[22]. Our study highlights the emergence of ESBL producing strains endowed with extremely wide spectrum of antibiotic resistance, including resistance to sulphonamides, Streptomycin, Gentamycin and Amikacin. Studies have shown that ESBL prevalence was more from blood (92.68%) which was also compaired with similar study R.M. Parveen et all 2011(97.2%) [23]. This high ESBL frequency may have been caused by the excessive use of broad-spectrum antibiotics in our hospital and to a higher level in our community setting, together with a lack of attention to laboratory screening of ESBL production by clinical isolates. On the other hand, the high rate of ESBL production could possibly be due to the spread of one single clone and/or plasmid within our hospital setting.

**Conclusion**

In present study, high prevalence of ESBL-producing K. pneumoniae was observed in our hospital setting. As the available treatment options are limited, antibiotic control policies together with the implementation of infection control measures remain of high importance. Because of the new challenges presented by the changing nature and distribution of these enzymes, clinicians need to be familiar with the clinical significance of these enzymes, and clinical microbiology laboratories require adopting a technique most appropriate to them for their detection.

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