

Original Research Article

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## ***Klebsiella pneumoniae*: Prevalence of ESBL Producing Clinical Isolates and their Antimicrobial Susceptibility Pattern in a Hospital Setting**

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### ABSTRACT

The incidence of infections caused by multidrug resistant ESBL producing *K.pneumoniae* is on rise. The treatment of these infections have become increasingly difficult and life threatening. Knowledge on prevalence of these infections and corresponding antimicrobial susceptibility patterns is essential regionally. Routine standard operative procedures were followed in the laboratory in processing the clinical specimens for culture and sensitivity. ESBL producing *K.pneumoniae* were identified by phenotypic combination disc test. Majority of *K.pneumoniae* were isolated from respiratory specimens and pus, followed by urine and blood respectively. 42 (40.38%) isolates were confirmed as ESBL producing *K.pneumoniae*. The resistance demonstrated to 3<sup>rd</sup> generation cephalosporins was significant and to non  $\beta$  lactam antibiotics was moderate. Resistance exhibited to piperacillin/tazobactam was low and nil to carbapenems and tigecycline. The infections caused by multidrug resistant ESBL producing *K.pneumoniae* are significant. Due to their multidrug resistant nature the treatment options available are limited. Therefore, active surveillance and appropriate infection control measures are necessary to control the spread of these pathogens.

#### Keywords

ESBL producing *K.pneumoniae*, cephalosporins, piperacillin/tazobactam, carbapenems

#### Article Info

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### Introduction

*Klebsiella pneumoniae* causes a variety of infections, ranging from pneumonia, urinary tract infection, bacteremia, meningitis, sepsis and abscesses. In the past, *K. pneumoniae* has caused serious infections mainly in immunodeficient individuals and in those with comorbid diseases. But, in the recent times due to the rise of hypervirulent strains, the frequency and severity of infections has increased in healthy and immunocompetent

individuals also.<sup>1</sup> Furthermore, in recent decades, the incidence of infections caused by multidrug resistant extended spectrum  $\beta$  lactamase (ESBL) producing *K.pneumoniae* is on rise. Due to this, the treatment of these infections have become increasingly difficult and life threatening.<sup>2,3</sup>

The resistance to multiple antibiotics seen in *K.pneumoniae* is due to the ability to produce enzymes like ESBLs and carbapenemase. ESBL producing strains exhibit resistance to

cephalosporins and monobactams. Carbapenemase producing strains show resistance to nearly all the available beta lactams, including the carbapenems.<sup>4</sup> Due to the lack of effective treatments the infections caused by these multi drug resistant strains along with the possibility of subsequent bacteremia and sepsis are associated with higher rates of morbidity and mortality.<sup>5</sup>

The rise in incidence of hypervirulent strains, spread of resistance to multiple antibiotics, the morbidity and mortality associated with infections by these strains and the cost of management warrant efforts to better understand the epidemiology of *K.pneumoniae*. Knowledge on prevalence of *K.pneumoniae* infections and corresponding antimicrobial susceptibility patterns is essential particularly in our region where the information available is insufficient to guide in the management of these infections.

### Materials and Methods

This observational cross section study was carried out at GSL general hospital, Rajamahendravaram, Andhra Pradesh, India between September 2018 and December 2018. Routine standard operative procedures were followed in the laboratory in processing the clinical specimens for culture and sensitivity that were obtained from patients admitted in the hospital.<sup>6, 7, 8, 9</sup>

Antimicrobial susceptibility test was done on Mueller-Hinton agar medium by the conventional modified Kirby-Bauer disc diffusion method. Disks Commercially available from HIMEDIA containing a known concentration of antimicrobial agent were used in the test. CLSI recommendations were followed.

Detection of ESBL producing *K.pneumoniae* was done by phenotypic combination disc

test. The isolates that have demonstrated zones of inhibition to cefotaxime  $\leq 27$  mm and to ceftazidime  $\leq 22$  mm in the initial screen test were subjected to combination disc test using both cefotaxime and ceftazidime, alone and in combination with clavulanic acid. Then the zone of inhibition to cephalosporin disc with clavulanic acid was compared with the zone of inhibition to cephalosporin alone (Figure.1). The isolate was considered as ESBL producer when the inhibition zone diameter was  $\geq 5$  mm larger with clavulanic acid than without. Quality control: *K.pneumoniae* ATCC 700603.<sup>10</sup>

### Results and Discussion

A total number of 926 clinical specimens were processed for culture and sensitivity during the study period. Bacterial culture was positive in 688 clinical specimens and out of them 104 (15.11%) isolates were identified as *K.pneumoniae* (Figure.2). Majority of *K.pneumoniae* were isolated from respiratory specimens (42) and pus (37), followed by urine (21) and blood (4) respectively (Table 1). Among these 104 clinical isolates, 42 (40.38%) were confirmed as ESBL producing strains of *K.pneumoniae* (Figure. 3).

All the strains of ESBL producing *K.pneumoniae* have demonstrated resistance to ampicillin, amoxicillin/clavulanate, cefazolin, ceftriaxone, ceftazidime and aztreonam. Resistance to Piperacillin/tazobactam exhibited was 12% and to carbapenems was nil. Resistance noted to non  $\beta$  lactam antibiotics like aminoglycosides was 40.5%, quinolones was 50%, cotrimoxazole was 42.8% and tigecycline was nil (Table.2).

*K.pneumoniae* is a common cause of bacterial infections in hospitalized individuals. It is seen in water and soil and it readily colonizes mucosal surfaces of human gastrointestinal tract, conjunctiva, respiratory tract, and the

genitourinary tract.<sup>11</sup> From these sites, it can gain access to other tissues and cause severe infections in humans.

Epidemiological studies indicate that the inappropriate use of 3<sup>rd</sup> generation cephalosporins has resulted in the emergence of multidrug resistant ESBL producing *K.pneumoniae*.<sup>12</sup> In the present study, the prevalence of these pathogens was noted as 40.38%. The prevalence varies between hospitals as it depends on various factors like infection control measures, antibiotic policy and carriage rate of these pathogens among the patients and hospital personal.<sup>13, 14</sup>

The colonization rates of these organisms increase dramatically in hospitalized patients in direct proportion to the duration of their stay in the hospital.<sup>15</sup> Several risk factors like vascular catheterization, invasive procedures, urinary catheterization, mechanical ventilation, prior antibiotic use and poor adherence to infection control policies have been implicated in acquisition of ESBL producing *K.pneumoniae* in hospitalized patients.<sup>16</sup> All the strains of ESBL producing *K.pneumoniae* have demonstrated resistance to ampicillin, amoxicillin/clavulanate, ceftazidime, ceftazidime and aztreonam.

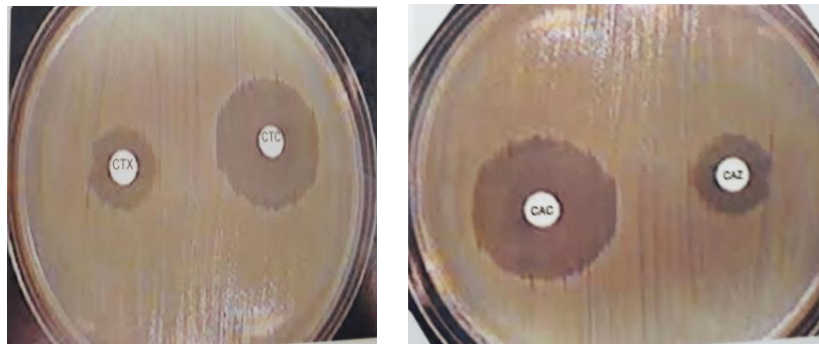


Figure.1 ESBL detection by phenotypic combination disc test

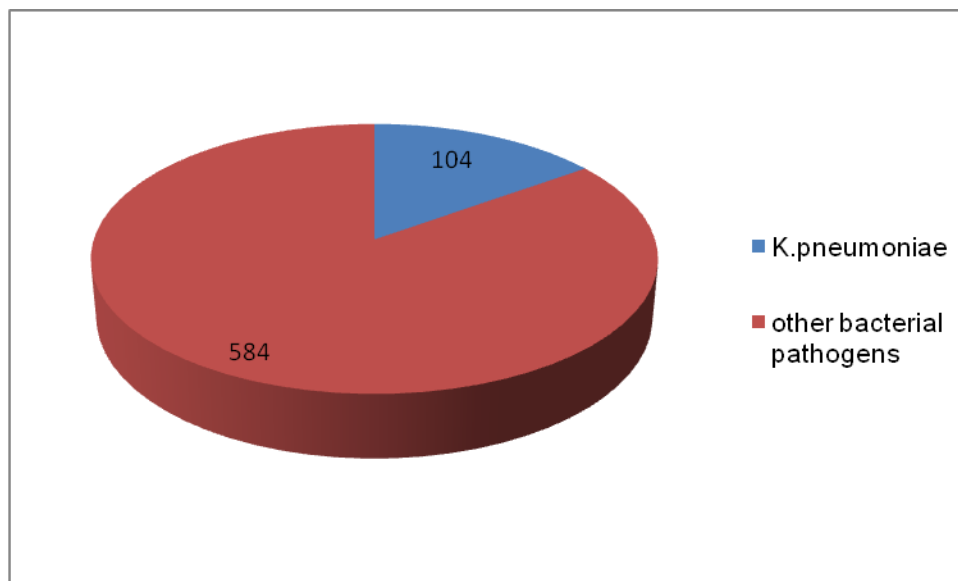
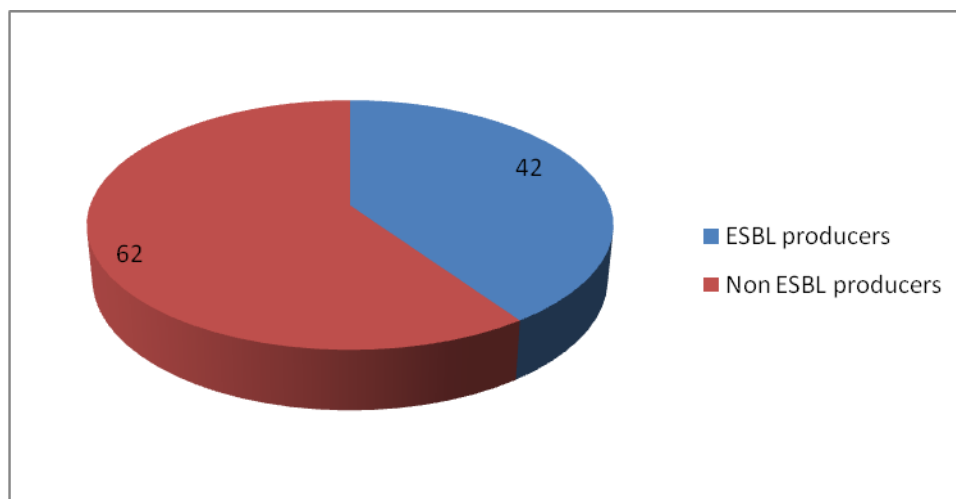


Figure.2 Frequency of *Klebsiella pneumoniae* among the study group (n = 688)



**Figure.3** Frequency of ESBL producing *Klebsiella pneumoniae* among the study group (n = 104)

**Table.1** Clinical site wise distribution of *Klebsiella pneumoniae* among the study group (n=104)

S.No	Clinical site involved	No.of isolates	%
1	Respiratory specimen	42	40.38
2	Pus	37	35.57
3	Urine	21	20.19
4	Blood	4	3.84

**Table.2** Antibiotic susceptibility pattern among ESBL producing *Klebsiella pneumoniae* (n=42)

S. No	Drug name (Strength µg)	Sensitivity (%)	Resistance (%)
1	Cotrimoxazole (25)	57.2	42.8
2	Gentamicin (10)	59.5	40.5
3	Amikacin (30)	59.5	40.5
4	Tobramycin (10)	59.5	40.5
5	Tigecycline (15)	100	0
6	Aztreonam (30)	0	100
7	Ampicillin (10) and Amoxicillin-clavulanic acid (20/10)	0	100
8	Cefazolin (30), ceftriaxone (30), ceftazidime (30)	0	100
9	Ciprofloxacin (5)	50	50
10	Levofloxacin (5)	50	50
11	Piperacillin-Tazobactam (100/10)	88	12
12	Imipenem (10)	100	0
13	Meropenem (10)	100	0

ESBL producing *K.pneumoniae* pose challenging situations during the treatment of infections caused by these multidrug resistant strains. Due to the rise of these strains the effectiveness of broad spectrum cephalosporins is restricted.

High level resistance demonstrated to cefotaxime (70%) and ceftazidime (75%) in this study therefore indicate that these broad spectrum antibiotics are empirically not recommended in the management of serious infections caused by these pathogens.<sup>17</sup>

Piperacillin and tazobactam combination is a broad spectrum antibiotic against a variety of bacterial pathogens including ESBL producing organisms. Low level resistance (12%) exhibited to this combination may be examined as a choice of antibiotic in the empirical treatment of serious infections caused by these pathogens. However, it should be used with a caution as susceptibility in vitro may not necessarily estimate the effectiveness in vivo.<sup>18</sup>

All the *K.pneumoniae* isolates were sensitive to imipenem and meropenem. Carbapenems are valuable against ESBL producing organisms as they are resistant to ESBL enzymes and also due to their small size they can easily enter through the porins into the periplasmic space of Gram negative bacilli. Thus, carbapenems are usually evaluated empirically in the treatment of serious infections caused by these pathogens. However, liberal and widespread use of these drugs might facilitate the emergence of carbapenem resistance.<sup>19</sup>

Resistance level shown to non  $\beta$  lactam antibiotics such as aminoglycosides, quinolones and cotrimoxazole was moderate ranging from 40.50% to 50%. This could be due to pathogens possessing the plasmids with resistance genes that encode ESBL genes also carry resistance genes to other groups of

antibiotics. Thus, these pathogens are multidrug resistant and therefore reduce the treatment options for infections caused by these pathogens to carbapenems and newer drugs like tigecycline.<sup>18, 19</sup>

In conclusion, the infections caused by ESBL producing *K.pneumoniae* in our hospital setting is significant. Due to their multidrug resistant nature the treatment options available are restricted. Therefore, active surveillance for these organisms should be conducted regularly which helps in designing more effective antibiotic policies. Appropriate infection control measures like effective hand hygiene and contact precautions should be strictly implemented to control the rise and spread of these organisms.

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