Carbapenem Resistance *Klebsiella* Species Isolated from Various Clinical Samples in a Tertiary Care Hospital

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**Abstract**

Carbapenems are one of the β-Lactam antibiotics with a broad spectrum of antibacterial activity. Inappropriate use of this antibiotic can produce resistance strains by production of carbapenemases enzyme. The *Klebsiella pneumoniae* carbapenemase (KPC) is the most important mechanism of enzymatic resistance seen in Enterobacteriaceae isolated especially *Klebsiella pneumoniae*. The aim and objectives of this study was isolation and detection of the Carbapenem resistant *Klebsiella species* strains with phenotypic methods. Out of 11248 samples, 602 *Klebsiella species* (33.7%), were isolated by standard Microbiological protocol & Antibiotic susceptibility test was performed by disk diffusion method with CLSI guidelines. A total 602 *Klebsiella species* strains were isolated. Of the 602 isolates of *Klebsiella species*, *Klebsiella pneumoniae* were 323 (54%) and *Klebsiella oxytoca* were 279 (46%). Antibiotic sensitivity pattern revealed maximum resistant to Cephalosporins (22%) followed by Ciproflaxacin (14%), Gentamycin (10%), Ceftriaxone - Clavulanate (8%), Piperacillin - Taxobactum (7%), Amikacin (7%). Out of 602 *Klebsiella spp*, Carbapenems resistant isolates were 28 (5%). All the 28 (100%) isolates were resistant to Meropenem and 23 (83%) isolates were resistant to Imipenem. Carbapenems are the drug of choice for multidrug resistant infections, like ESBL and AmpC producing isolates, but resistance to carbapenems by the production of carbapenemases and various other mechanisms has limited therapeutic options to use carbapenem drugs.

**Keywords**

*Klebsiella pneumoniae*, Carbapenem Resistance.

**Accepted:** 23 June 2017

**Available Online:** 10 July 2017

**Article Info**

Carbapenems are one of the β-Lactam antibiotics with a broad spectrum of antibacterial activity. Improper and inappropriate use of this drug induces Carbapenem resistance by an enzyme, *Klebsiella pneumoniae* carbapenemase (KPC).

*Klebsiella pneumoniae* carbapenemase (KPC) is a enzyme produced by Enterobacteriaceae family mainly *Klebsiella species* that offer resistance to carbapenems and other Beta lactam antibiotics by direct hydrolyzing activity on this drugs, reduced in bacterial outer membrane permeability and increased production of ESBL, AmpC lactamases and carbapenemase (KPC) (Masoume, 2015; Nordmann et al., 2012)

*Klebsiella pneumoniae* carbapenemase (KPC) was, first described in 1996 in North Carolina, USA (Yigit et al., 2001)
The main purpose of this study was to detect the carbapenem resistant *Klebsiella* species among various clinical samples. Because the emergence of *Klebsiella pneumoniae* carbapenemase (KPC) producing bacteria has become a significant global health challenge.

**Materials and Methods**

The study was a retrospective study conducted over a period of one year in a tertiary care hospital. *Klebsiella* species isolates from various clinical samples like Urine, pus, Blood, sputum and throat swab received during the study period (April 2016 to March 2017) were included in the study.

Out of 11248 clinical samples received and processed, identification of *Klebsiella* species was done by morphology of the colonies on the MacConkey plate and blood agar plate, Catalase test, Oxidase test, Hanging drops method, Nitrate reduction test, IMViC test and sugar fermentation test.

The Antibiogram test done by Kirby Bauer disc diffusion method was carried on Cationic adjusted Mueller Hinton agar with the following antibiotic disc as per CLSI guidelines, Amikacin- 30µg, Gentamycin -10µg, Ciproflaxacin -5µg, Ceftriaxone -30µg, Cefotaxime -30µg, Ceftriaxone / Clavulanate -30µg/10µg, Piperacillin/ Taxobactum -30µg/10µg, Imipenem -10µg and Meropenem -10µg.

**Results and Discussion**

Out of 11248 samples, 602 *Klebsiella species* were isolated from various clinical samples. Of the 602 isolates *Klebsiella pneumoniae* were 323 (54%) and *Klebsiella oxytoca* were 279 (46%) (Table 1).

The more number of pathogen isolated from urine 300 (50%). Organisms isolated from pus, sputum, blood and swab were 165 (27.4%), 68 (11.2%), 42 (7%) and 27 (4.4%) respectively.

Antibiotic sensitivity pattern revealed maximum resistant to Cephalosporins (22%) followed by Ciproflaxacin (14%), Gentamycin (10%), Ceftriaxone -Clavulanate (8%), Piperacillin- Taxobactum (7%), Amikacin (7%).

Out of 602 *Klebsiella spp*, Carbapenems resistant isolates were 28 (5%). All the 28 (100%) isolates were resistant to Meropenem and 23 (83%) isolates were resistant to Imipenem.

In this study, 28 Carbapenems resistance isolates, 23 were male patients, 5 were female patients.

Carbapenems resistant strain was isolated from pus 12 (43%) followed by urine 9(32%), sputum 5 (18%) and blood 2(7%).

Of 28 Carbapenems resistant strains, 16 (57%) were belongs to *Klebsiella oxytoca* and 12 (43%) were belongs to *Klebsiella pneumoniae*. All the strains were isolated from hospitalized patients.

*Klebsiella pneumoniae* carbapenemase (KPC) is a enzyme produced by Enterobacteriaceae family mainly *Klebsiella species* that offer resistance to carbapenems and other Beta lactam antibiotics. This is by direct hydrolyzing activity on the drugs, reduction in bacterial outer membrane permeability for the drugs and increased production of ESBL, AmpC lactamas and carbapenemase (KPC).

Acquisition of Carbapenem resistant *Klebsiella* spp may be due to reduced permeability of drugs (Nordmann *et al*., 2012). Falagas *et al*., (2007) have reported as previous use of antipseudomonal penicillins, quinolones and Carbapenems are the
important risk factors for development of Carbapenem resistant strains. Prolonged hospitalization, intensive care unit stay, improper infection control measures and use of H2 receptor antagonist reduces gastric acidity and leads to colonization of Carbapenem resistant *Klebsiella* spp (Table 2). Out of 11248 samples, 602 *Klebsiella* species were isolated from various clinical samples. Of the 602 isolates *Klebsiella pneumoniae* were 323 (54%) and *Klebsiella oxytoca* were 279 (46%). The more number of pathogen isolated from Urine 300 (50%). Organisms isolated from Pus, Sputum, Blood and Swab were 165 (27.4%), 68 (11.2%), 42 (7%) and 27 (4.4%) respectively.

**Table.1** *Klebsiella* species isolated from various clinical samples

| Samples | Organisms | Total |
|---------|-----------|-------|
|         | *Klebsiella pneumoniae* | *Klebsiella oxytoca* | No | % |
| Urine   | 162       | 138   | 300 | 50 |
| blood   | 23        | 19    | 42  | 7  |
| sputum  | 36        | 32    | 68  | 11.2 |
| pus     | 91        | 74    | 165 | 27.4 |
| swab    | 11        | 16    | 27  | 4.4 |
| Total   | 323       | 279   | 602 | 100 |

**Table.2** Antibiotic sensitivity and resistant pattern of *Klebsiella* species isolated from various clinical isolates

| Antibiotics | Sensitive pattern | Resistant pattern |
|-------------|------------------|-------------------|
|             | Number of isolates | Percentage | Number of isolates | Percentage |
| Amikacin- 30µg | 562 | 93 | 40 | 7 |
| Gentamycin -10µg | 541 | 90 | 61 | 10 |
| Ciproflaxacin -5µg | 519 | 86 | 83 | 14 |
| Ceftriaxone -30µg | 470 | 78 | 132 | 22 |
| Cefotaxime -30µg | 472 | 78 | 130 | 22 |
| Ceftriaxone / Clavulanate -30µg/10µg | 555 | 92 | 47 | 8 |
| Piperacillin/ Taxobactum -30µg/10µg | 562 | 93 | 40 | 7 |
| Imipenem -10µg | 574 | 95 | 28 | 5 |
| Meropenem -10µg | 579 | 96 | 23 | 4 |
All the carbapenem resistance strains were isolated from Inpatient (100%). This is due to prolonged antibiotic therapy, Intensive care unit stay, Multiple Invasive devices and Immunosuppressive drugs (Chia et al., 2010; Yigit et al., 2001).

In this study, among 28 Carbapenem resistant, Klebsiella spp 25 (89%) isolated from male patients, 3 (11%) isolated from female patients. This is agreement with the study conducted by Alves et al., in which they have reported as male (72.3%) predominantly affected by KPC (Alves et al., 2013) (Fig. 1).

Among 28 Carbapenem resistant strains, 12 (43%) isolated from Pus followed by Urine 9 (32%), Sputum 5 (18%) and Blood 2 (7%), this is similar to study conducted by Gabriela Seibert et al., (2014) in which most of the Carbapenem resistant strains was isolated from surgical ward. Infections produced by Carbapenem resistant Klebsiella spp mainly in immunosuppressed patients who are hospitalized and/or who use invasive devices, such as catheters and tubes.

Of 28 Carbapenems resistant strains, 16 (57 %) belongs to Klebsiella oxytoca and 13 (43 %) belongs to Klebsiella pneumoniae. This is not correlated with other studies because they found out that the Klebsiella pneumoniae mainly induces Carbapenemase enzymes that will degrade Carbapenem drugs and produces resistance.

Out of 28 Carbapenem resistant Klebsiella spp, 28 (100%) isolates were resistant to Meropenem, 23 (82%) isolates were resistant to Imipenem and the remaining 5 (18%) were sensitive to Imipenem. A similar study conducted by Bratu et al., (2005) has reported as 80% resistant to Imipenem, 83% resistant to Meropenem. The different sensitivity pattern between imipenem and meropenem is due to different pharmacodynamic property among the carbapenem drugs (Joseph et al., 2004).

Antibiotic sensitivity pattern revealed maximum resistant to Cephalosporins (22%) followed by Ciproflaxacin (14%), Gentamycin (10%), Ceftriaxone -Clavulanate (8%), Piperacillin- Taxobactum (7%), Amikacin (7%). This multidrug resistance of Carbapenem resistant Klebsiella spp is due to carbapenems share a common structure with cephalosporins and penicillin. Carbapenem
resistant organism can confer resistance to multiple various antimicrobial classes, like β-lactams, fluoroquinolones and aminoglycosides (Endimiani et al., 2009). Bratu et al., (2005) and Gasink et al., (2009) reported as KPC infections are always associated with high therapeutic failure and mortality rates.

Our study showed that 86% sensitive to amikacin and 61% sensitive to gentamicin. In a study conducted by Alves et al., (2013) reported as 97.5% sensitive to amikacin and 70% sensitive to gentamicin. The aminoglycoside is a good alternative drug for carbapenem resistant organisms.

In conclusion, carbapenems are the drug of choice for multidrug resistant infections, like ESBL and AmpC producing isolates, but resistance to carbapenems by the production of carbapenemase and various other mechanisms has limited therapeutic options to use carbapenem drugs. To combat the drug resistance we have to adhere strict infection control measures, and antibiotic policy.

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How to cite this article:

Rajeswari Jayakumar, Vijayalakshmi Arumugam and Meera Srinivasagam. 2017. Carbapenems Resistance *Klebsiella* Species Isolated from Various Clinical Samples in a Tertiary Care Hospital. *Int.J.Curr.Microbiol.App.Sci.* 6(7): 2194-2199.

doi: [https://doi.org/10.20546/ijcmas.2017.607.318](https://doi.org/10.20546/ijcmas.2017.607.318)