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

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A B S T R A C T

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 carbapenamases and various other mechanisms has limited therapeutic options to use carbapenem drugs.

Introduction

Carbapenems are a most important antibacterial drugs used for the treatment of Extended spectrum Beta Lactamases and AmpC lactamases producing organisms mainly Enterobacteriaceae family. 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, 5were 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 lactamases 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.

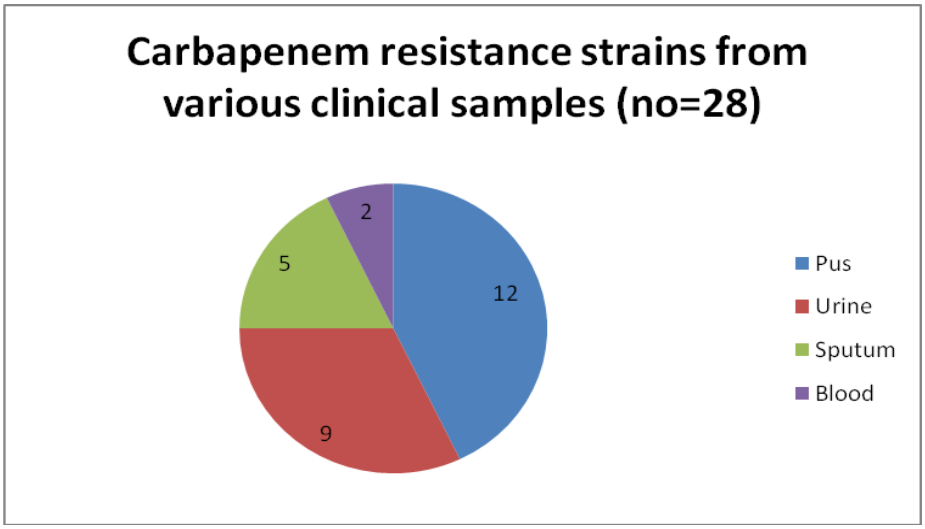
Table.1 *Klebsiella* species isolated from various clinical samples

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**

Fig.1 Cabapenem resistant strains



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 Carbapenems 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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