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RESEARCH ARTICLE

CARBAPENEM RESISTANT KLEBSIELLA PNEUMONIAE IN A TERTIARY CARE HOSPITAL IN NORTHERN INDIA

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Abstract

Background:-Antibiotic resistance is a global public health problem. The foundation of modern medicine is built on the availability of effective antibiotics, especially in economically deprived areas of the world. Identification of carbapenem-resistant *Klebisella pneumoniae* infection may assist in the empiric therapeutic decision-making process and allow for early implementation of appropriate infection-control measures. **Aims & objectives:-** To find out the prevalence of *Klebsiella pneumoniae* strains resistant to carbapenems, to ascertain antibiogram of strains and formulate an advisory for control and treatment of infections. **Material & Methods:-**The study was conducted in the department of Microbiology, SKIMS, Soura, Srinagar (J&K). Patients attending the OPD or admitted during one year were taken for the study. Different samples were processed according to the standard microbiological techniques. Antimicrobial sensitivity of *Klebsiella* isolates was performed according to CLSI guidelines. The minimum inhibitory concentration of imipenem for isolates that were resistant to imipenem was done by microbroth dilution method. **Results:-** Overall prevalence of Carbapenem resistant *Klebsiella pneumonia* was 27.9%. Majority (84.2%) of the imipenem resistant *Klebsiella* isolates were found to be carbapenemase producers. The predominant source of both imipenem resistant and Modified Hodge test positive isolates were urine, pus and blood. The recovery of *Klebsiella* isolates from urine and blood was found to be statistically significant ($p<0.05$). Maximum numbers of carbapenem resistant isolates were recovered from patients with sepsis (15.78%). Antibiogram showed a high degree of resistance to cephalosporins (>90%) with maximum sensitivity to tigecycline and polymyxin B (100%). **Conclusion:-** Carbapenem resistant *Klebsiella* is a major problem in our hospital. Early detection of carbapenemase producing *Klebsiella spp*. may avoid future spread of these isolates and ensure better patient care and timely introduction of appropriate infection control measures.

Introduction

Antibiotic resistance is a global public health problem [1, 2]. The foundation of modern medicine is built on the availability of effective antibiotics, especially in economically deprived areas of the world where the disease burden due to bacterial infections remains high. The World Health Organization (WHO) and European Commission (EC) recognized the importance of studying the emergence and determination of resistance and the need for control strategies. The need for strategies to control antibiotic resistance is greater in resource constraint settings because antibiotic resistance puts further strain on an already fragmented health care system in developing countries [3]. Well known multi-resistant bacteria causing problems in many countries all over the world are Methicillin-resistant *Staphylococcus aureus,* Vancomycin-resistant *Enterococci,* Penicillin-resistant *Pneumococci,* Extended-spectrum beta-lactamase producing *Klebsiella pneumoniae,* Carbapenem-resistant *Acinetobacter baumannii,* and multi-resistant *Mycobacterium tuberculosis*[4]. Carbapenem-resistant gram-negative pathogens present an increasing threat to the management of hospital-acquired infections. Although the isolation of carbapenem-resistant *Enterobacteriaceae* was unusual, the frequency of carbapenemases producing *Klebsiella pneumoniae* had increased in different geographic regions [5].

In India, rapid evolution of bacterial resistance may be due to a complex interaction of several factors such as higher burden of infectious disease, treatment uncertainty, lack of treatment guidelines, inadequate access to standard laboratory facilities, self-medication, prescription based on availability, government support to pharmaceutical industries, market forces, antibiotics prescribed by unqualified health professionals, less strict law enforcement, fragmented public health system, poor population-wide insurance coverage, inadequate adherence to universal hygiene and infection control measures and a education level. Antibiotic stewardship programs are thus urgently needed in India [6,7]. A recent eye opener was the spread of *Enterobacteriaceae,* with resistance to carbapenem conferred by New Delhi metallo-β-lactamase1 (NDM-1). NDM-1 received extensive media coverage [8].

Although antimicrobial development efforts remain a cornerstone of Carbapenem Resistant *Enterobacteriaceae* response efforts [9], interventions aimed at preventing the transmission of and infections with, these organisms are also important. Delaying the emergence of carbapenem resistance, particularly in areas where this resistance is still uncommon, can decrease the impact of these organisms as we await additional treatment options. More research is needed to determine the best ways to prevent CRE transmission, but single-center studies and national effort have suggested that bundled prevention strategies can be successful in outbreak and endemic settings[10].The escalating prevalence of carbapenem-resistant *K. pneumoniae* infection and the increasing incidence of this pathogen in United states, India and worldwide mandate further investigation into the epidemiology of and clinical outcomes associated with carbapenem-resistant *K. pneumoniae* infection. Identification of risk factors associated with carbapenem-resistant *K. pneumoniae* infection may assist in the empiric therapeutic decision-making process and may allow for early implementation of appropriate infection-control measures[11,12]. So far very limited studies have investigated the prevalence of carbapenem resistant *Klebsiella pneumoniae* in this part of the country. This study was therefore undertaken to report the prevalence of such isolates in our setup and to look for the antimicrobial susceptibility pattern of *Klebsiella* from clinical specimens in this tertiary care hospital in Kashmir valley.

MATERIAL AND METHODS

The study was conducted in the department of Microbiology, Sheri-i-Kashmir Institute of Medical Sciences, Srinagar (J&K) over a period of one year i.e. from January 2011 to December 2011. All the patients attending the OPD or admitted in the hospital during the period of one year were taken for the study purpose. Different samples like blood, sputum, urine, wound swabs, catheter tips, pus and other body fluids obtained from patients admitted in the hospital and attending the OPD were processed for isolation and identification of bacterial pathogens according to the standard microbiological techniques. Gram negative bacilli that were catalase positive, non motile, encapsulated and lactose fermenting on Mac Conkey agar and decarboxylated lysine were identified as *Klebsiella.*

Antimicrobial Sensitivity Testing:- Antimicrobial sensitivity of *Klebsiella* isolates was performed on Mueller Hinton agar plates by Kirby-Bauer disk diffusion method according to CLSI guidelines. The following antibiotic discs were used; amikacin-30µg, gentamicin-10µg, ciprofloxacin-5µg, ofloxacin-5µg, moxifloxacin-5µg, levofloxacin-5µg, ceftazidime-30µg, cefotaxime-30µg, cefipime-30µg, piperacillin-100µg and tazobactum-10µg, cotrimoxazole 25µg, imipenem-10µg, tigecycline-15µg and polymyxin B-300 units. In addition nitrofurantoin-300µg discs were used for isolates recovered from urine. All the discs were procured from Hi media, Mumbai.

The sizes of the zones of inhibition were interpreted as per CLSI guidelines.

Screening for carbapenemase - Inclusion criteria: - All the isolates resistant to imipenem were included in the study.

Determination of Minimum inhibitory concentration (MIC):- The minimum inhibitory concentration of imipenem for isolates that were resistant to imipenum was done by microbroth dilution method. MIC is defined as the lowest concentration of a drug that will inhibit the visible growth of an organism after overnight incubation. MIC endpoint was read as the lowest concentration of antibiotic at which there was no visible growth. MIC of $\leq 4\mu g/ml$ was taken as sensitive and $\geq 16\mu g/ml$ as resistant.

Phenotypic confirmation of carbapenemase

Modified Hodge Test: Carbapenemase production was then confirmed by Modified Hodge test. The test isolate produces the enzyme and allows growth of a carbapenem susceptible strain (*E. coli* ATCC 25922) towards a carbapenem disk.

Procedure: - 0.5 McFarland dilution of *E.coli* ATCC 25922 was prepared in 5 ml of broth or saline. 1: 10 dilution was prepared by adding 0.5 ml of the 0.5 McFarland to 4.5 ml of MHB or saline. A lawn of 1: 10 dilution of *E.coli* ATCC 25922 was made on a Mueller Hinton agar plate. 10 µg ertapenem susceptibility disk was placed in the center of the test area. Test organism was streaked in a straight line from the edge of the disk to the edge of the plate. Plate was incubated overnight at 35^0C+2^0C. **MHT Positive** test has a clover leaf-like indentation of the *E. coli* 25922 growing along the test organism growth streak within the disk diffusion zone. **MHT Negative** test has no growth of the *E. coli* 25922 along the test organism growth streak within the disc diffusion. **Quality Control:-** Positive Control: an in house known carbapenemase producing *Klebsiella* strain. Negative Control: an in house known carbapenemase negative *Klebsiella* strain.

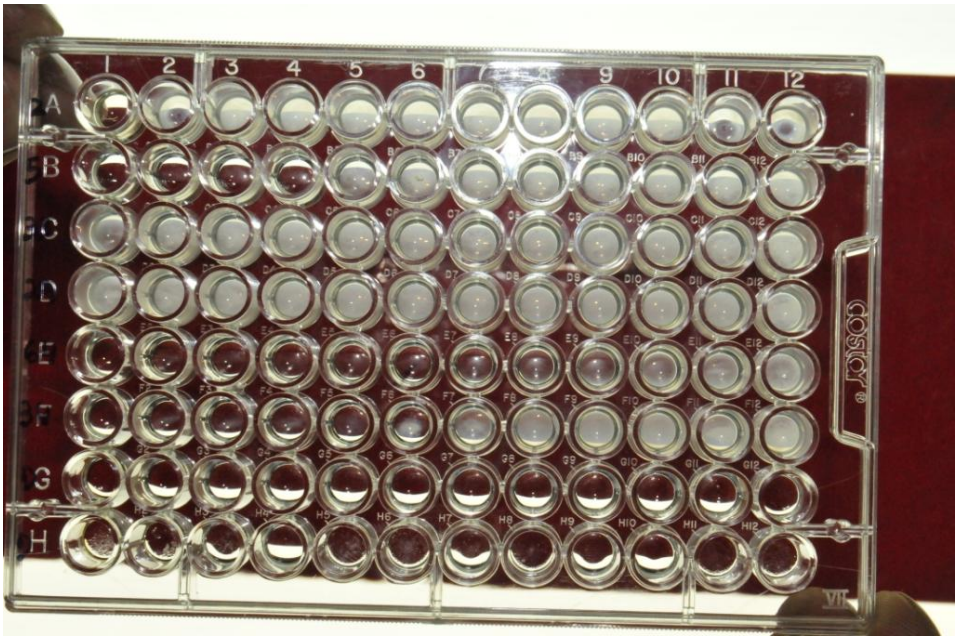
Data collection: Detailed information of the patients and isolates was recorded in a separate proforma. The medical records of the patients were reviewed for age, sex, underlying illness, source from which the isolate was recovered, presence of invasive devices (urinary catheters, CVC), previous antibiotic use etc. **Statistical analysis:** The statistical analysis was performed using SPSS version 17 software. Data is represented in the form of tables, bars and proportions. Categorical variables were compared employing non parametric tests (chi-square, fisher exact test) whereas continuous variables were compared by using student's t-test. Values have been expressed as mean ± SD and p value <0.05 was considered significant.

RESULTS

A total of 204 non duplicate *Klebsiella* strains (belonging to various species) were isolated from patients admitted or attending the OPD. Out of the total samples; 27.9% were imipenem resistant and 72.1% were imipenem sensitive. Among imipenem resistant isolates, 61.4% were males and 38.5% were females whereas among imipenem sensitive isolates 59.8% were males and 40.1% were females respectively **(Table-1)**. Most of the patients from whom carbapenem resistant *Klebsiella* species were isolated were in the age group of 50-59 yrs (26.31%), followed by 40- 49 yrs (17.5%) and >60 yrs (15.7%), respectively. The distribution of the patients according to age was similarly dispersed amongst the carbapenem sensitive and resistant category. There was no statistical significant difference in age between patients with carbapenem resistant and those with carbapenem sensitive *Klebsiella* infection ($p>0.05$) **(Table-2)**. In our research it was found that maximum number of *Klebsiella* strains were recovered from urine; (40.1%), followed by blood; (23.1%) and pus; (17.6%). In imipenem resistant isolates (n=57), most of the *Klebsiella* strains were found in urine (54.38%), followed by pus (19.2%), swab (8.77%) and blood (7.0%) respectively. The isolation of *Klebsiella* isolates from urine and blood was found to be statistically significant ($p<0.05$). On the other hand isolation of *Klebsiella* from other specimens was not statistically significant ($p>0.05$) **(Table-3)**. The antimicrobial sensitivity patterns of the various isolates are depicted in **(Table-4)**. 28% (n=57) of the isolates were resistant to imipenem and there was a variable sensitivity to other antimicrobials tested. The isolates exhibited a high degree of resistance to beta-lactam antibiotics including penicillins and cephalosporins. There was a variable sensitivity to quinolones. Maximum isolates (84.3%) were resistant to moxifloxacin followed by levofloxacin (78.9%) and ofloxacin (72.1%). Among the quinolones, least amount of resistance was seen against ciprofloxacin (71.6%). Gentamicin resistance was seen in (98.5%) isolates and (72.7%) isolates were resistant to amikacin. Nitrofurantion was tested against 70 isolates recovered from urine, out of which (42.9%) were resistant to this antimicrobial. Amongst the other class of antibiotics, (70.6%) were resistant to co-trimaxazole. Maximum numbers of *Klebisella* isolates were sensitive to tigecycline and polymyxin-B 204 (100%). The present study revealed that out of the total imipenem resistant isolates, 48 were Hodge test positive and remaining 9 were Hodge test negative. Of the Hodge test positive, maximum number of isolates were found in the age group of 50-59 yrs (25%), followed by 40-49 yrs (18.8%), >60 yrs (16.7%) and 20-29 yrs (16.7%), respectively. However there was no statistically significant association between a particular age group and Hodge test ($p>0.05$) **(Table-5)**. The

predominant source of carbapenemase producing isolates were found in urine (54.1%) followed by pus (22.8%), swab (8.3%), pleural fluid (6.3%) and blood (6.2%) respectively. Less number of carbapenemase producing isolates were recovered from samples like ascitic fluid, drain fluid and sputum; 2.1% each. However the isolation of carbapenemase from various specimens was found to be statistically non-significant ($p>0.05$) **(Table-6)**. The antibiogram of carbapenem resistant isolates is shown in **(Table-7)**. It was observed that among carbapenemase producing isolates, maximum resistance was seen for cephalosporins (ceftazidime 97.9%, cefotaxime 97.9%, cefepime 95.8% and ceftriaxone 97.9%) and piperacillin plus tazobactum 97.9%) whereas least resistance was seen against tigecycline (4.16%) and polymyxin-B (2.08%). Further the antimicrobial susceptibility pattern of carbapenemase producers and non-carbapenemase producers did not vary much except that a significantly higher proportion of carbapenemase producing isolates were resistant to cotrimaxazole ($p<0.05$). While all of the non-carbapenemase producers 9 (100%) were sensitive to tigecycline and polymyxin-B. Minimum Inhibitory Concentration (MIC) was done on all the 57 imipenem resistant isolates by Micro-broth dilution method. For 26 (45.61%) isolates MIC was greater than 256 µg / ml; followed by an MIC of 128 µg/ml, which was seen in 14 (24.56%) isolates. Similarly 10 (17.54%) isolates had MIC of 64 µg/ml where as 5(8.77%) and 2(3.5 %) of isolates had MIC of 32 µg/ml and 16 µg/ml respectively. **(Table-8)**.

MIC (by micro broth dilution) of imipenem for Carbapenem resistant Klebsiella pneumoniae.



Modified Hodge's Test (MHT) for detection of Carbapenemase production. Positive test with clover leaf -like indentation.

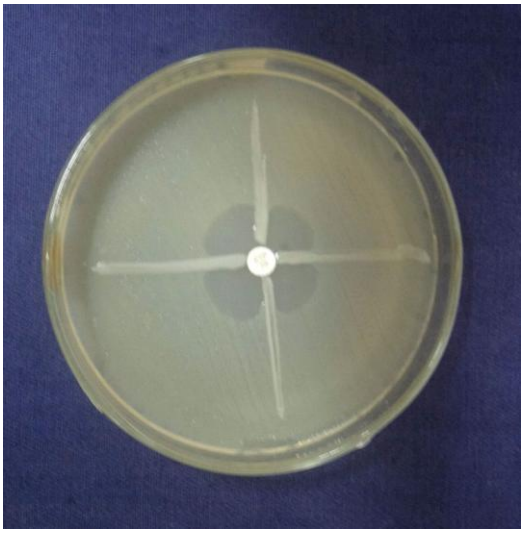


Table1: Overall distribution of *Klebsiella pneumoniae* isolates (resistant and sensitive).

Total sample	No. (%)	Sex	
		Male No. (%)	Female No. (%)
Carbapenem resistant	57(27.9)	35(61.4)	22(38.5)
Carbapenem sensitive	147(72.1)	88(59.8)	59(40.1)
Total	**204**	**123**	**81**

Table 2: Age wise distribution of Carbapenem (imipenem) sensitive and resistant *Klebsiella pneumoniae* isolates.

Age in years	Imipenem Sensitive	Imipenem Resistant	P-value
0 – 9	15(10.2)	3(5.2)	Chi-square=4.69, P=0.58(NS)
10 – 19	6(4.0)	5(8.7)	
20 – 29	14(9.5)	9(15.7)	
30 – 39	20(13.6)	7(12.2)	
40 – 49	27(18.3)	10(17.5)	
50 – 59	35(23.8)	15(26.3)	
≥60	30(20.40)	8(14.03)	
Total	**147**	**57**	

Table 3: Sample wise distribution of *Klebsiella pneumoniae* isolates

Specimen	Isolates (204) No. (%)	Imipenem Sensitive (147) No. (%)	Imipenem Resistant (57) No. (%)	P-value
Blood	47(23)	43(29.5)	4(7.0)	*0.001
Pus	36(17.6)	25 (17.0)	11 (19.2)	0.85(NS)
Catheter tip	3(1.4)	3 (2.04)	0 (0)	0.56(NS)
Drain fluid	2(0.9)	1 (0.68)	1(1.75)	0.48(NS)
Swab	15(7.3)	10 (6.80)	5 (8.77)	0.56(NS)
Sputum	7(3.1)	6 (4.08)	1 (1.75)	0.6(NS)
CSF	0(0)	0(0)	0(0)	-

Urine	82(40.1)	51 (34.6)	31 (54.38)	*0.01
Bile	1(0.4)	1 (0.68)	0 (0)	1.0(NS)
BAL	1(0.4)	1 (0.68)	0 (0)	1.0(NS)
Pleural fluid	5(2.3)	2 (1.36)	3 (5.26)	0.13(NS)
Tracheal tip	2(0.9)	2(1.36)	0 (0)	1.0(NS)
Ascitic fluid	2(0.9)	1 (0.68)	1 (1.75)	0.48(NS)
Hydatid fluid	1(0.4)	1 (0.68)	0 (0)	1.0(NS)

*Statistically Significant

Table 4: Antimicrobial susceptibility profile of *Klebsiella pneumoniae* isolates

ANTIBIOTIC	**Number tested N=204 (*Nitrofurantion=70)**	
	Sensitive No. (%)	**Resistant No. (%)**
Amikacin	104 (50.9)	100 (49)
Gentamicin	3 (1.5)	201 (98.5)
Ciprofloxacin	58 (28.4)	146 (71.6)
Ofloxacin	57 (27.9)	147 (72.1)
Moxifloxacin	32 (15.7)	172 (84.3)
Levofloxacin	43 (21.1)	161 (78.9)
Ceftazidime	20 (9.8)	184 (90.2)
Cefotaxime	18 (8.8)	186 (91.2)
Cefipime	21 (10.3)	183 (89.7)
Ceftriaxone	19 (9.3)	185 (90.7)
Piperacillin + Tazobactam	31 (15.2)	173 (84.8)
Imipenem	147 (72.1)	57 (27.9)
Tigecycline	204 (100)	0 (0)

Polymyxin B	204 (100)	0 (0)
***Nitrofurantoin**	40 (57.1)	30 (42.9)
Co-trimoxazole	60 (29.4)	144 (70.6)

Table 5: Age wise distribution of Hodge test positive and Hodge test negative isolates

Age (yrs)	Hodge test +ve No. (%)	Hodge test –ve No. (%)	Total	P-value
0 to 9	1(2.1)	1(11.1)	2	Chi-square=5.02 P=0.54(NS)
10 to 19	6(12.5)	0(0)	6	
20 to 29	8(16.7)	1(11.1)	9	
30 to 39	4(8.3)	2(22.2)	6	
40 to 49	9(18.8)	1(11.1)	10	
50 to 59	12(25)	3(33.3)	15	
≥60	8(16.7)	1(11.1)	9	
Total	**48**	**9**	**57**	

Table 6: Sample wise distribution of Hodge test positive and Hodge test negative isolates.

Specimens	Hodge test +ve(48) No. (%)	Hodge test –ve(9) No. (%)	Total (57)	P-value
Blood	3(6.2)	1(11.1)	4	Fischer exact test = 3.157 P=0.977(NS)
Pus	9(18.75)	2(22.2)	13	
Catheter tip	0(0)	0(0)	0	
Tracheal tip	0(0)	0(0)	0	
Drain fluid	1(2.1)	0(0)	1	
Swab	4(8.3)	1(11.1)	5	

Sputum	1(2.1)	0(0)	1	
CSF	0(0)	0(0)	0	
Urine	26(54.1)	5(55.5)	31	
Pleural fluid	3(6.3)	0(0)	3	
Bile	0(0)	0(0)	0	
BAL	0(0)	0(0)	0	
Ascitic fluid	1(2.1)	0(0)	1	
Hydatid fluid	0(0)	0(0)	0	

Table 7: Antimicrobial susceptibility profile of the Hodge test positive and Hodge test negative isolates.

Antibiotic	**Hodge test +ve (48)**				**Hodge test –ve (9)**				**P value**
	S		**R**		**S**		**R**		
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	
Amikacin	13	27.1	35	72.9	1	11.1	8	88.9	0.42
Gentamicin	2	4.16	46	95.8	0	0	9	100	1.00
Ciprofloxacin	5	10.4	43	89.6	0	0	9	100	0.58
Ofloxacin	6	12.5	42	87.5	3	33.3	6	66.7	0.14
Moxifloxacin	4	8.3	44	91.7	2	22.2	7	77.8	0.07
Levofloxacin	3	6.2	45	93.8	1	11.1	8	88.9	0.50
Ceftazidime	1	2.1	47	97.9	0	0	9	100	1.0
Cefotaxime	1	2.1	47	97.9	0	0	9	100	1.0
Cefipime	2	4.16	46	95.8	0	0	9	100	1.00
Ceftriaxone	1	2.1	47	97.9	0	0	9	100	1.00
Piperacillin + tazobactam	1	2.1	47	97.9	0	0	9	100	1.00
Tigecycline	46	95.8	2	4.16	9	100	0	0	1.00
Polymixin B	47	97.9	1	2.08	9	100	0	0	1.00
Nitrofurantoin	2	4.16	16	33.3	1	11.1	0	0	0.15
Co-trimoxazole	0	0	48	100	2	22.2	7	77.8	*0.02

*Statistically Significant

Table 8: Minimum Inhibitory Concentration (MIC) of carbapenem resistant *Klebsiella pneumoniae* isolates

MIC (µg/ml)	**Carbepenum resistant No. (%)**	**Hodge test +ve No. (%)**	**Hodge test -ve No. (%)**
16	2(3.50)	-	2(22.22)
32	5(8.77)	4(8.33)	1(11.11)
64	10(17.54)	8(16.66)	2(22.23)
128	14(24.56)	13(27.08)	1(11.11)
>256	26(45.61)	23(47.91)	3(33.3)
Total	**57**	**48**	**9**

DISCUSSION

Spread of multidrug-resistant (MDR) gram-negative pathogens is one of the major hazards for patients requiring long-term hospitalization or hospitalization in intensive care units (ICU) [13]. As carbapenems have long been considered the antibiotic class of last resort in the treatment of infections caused by multidrug-resistant gram-negative organisms, the dissemination of carbapenem resistance among pathogenic bacteria has been declared a "global sentinel event" [14]. In the present study, a total of 204 strains of *Klebsiella pneumonia* were isolated over a period of one year, out of which 27.9% strains isolated were resistant to imipenem whereas 72.1% were sensitive to imipenem. 84.2% were carbapenemase producers while 15.7% were carbapenemase non-producers. Among carbapenemase non-producers the resistance is likely to be mediated by presence of extended spectrum β – lactamases or plasmid borne Amp C in combination with impermeability due to porin loss and efflux pumps. The findings of the present study were in accordance to a study done by Patel JB et al [15] in New York City and Debby et al[16] in Israel who in their respective studies found the prevalence of carbapenem resistant *Klebsiella pneumonia* to be 26% and 27%. The present study found that out of the 57 imipenem resistant isolates, 61.4% were males and 38.5% were females. There was no statistically significant difference in age between patients with carbapenem resistant and those with carbapenem sensitive *Klebsiella pneumoniae* infection. The findings of the above results are in accordance to a study done by Amin A et al[17] in Pakistan who found that majority of the patients were males (60%) than females (40%). Patel G et al [18] in a similar study, revealed that male patients were (59%) and female patients were (41%) and further it was found that there was no significant differences in age ($p=0.70$) or sex ($p=0.51$). The possible reason for the majority of our patients being in the adult age group is that ours is mainly an adult facility with only a small number of patients admitted to the neonatology and pediatric surgery wards. Thus a proportionate pattern of the distribution stands exhibited in the age groups. In the present study it was found that maximum numbers of *Klebsiella* strains were recovered from urine 40.1%, followed by blood 23.1% and pus 17.6%. Further it was observed that the isolation of *Klebsiella* isolates from urine and blood was found to be statistically significant ($p<0.05$) whereas from other specimens it was found to be statistically non-significant ($p>0.05$).The findings of the above study are in accordance with a study done by Gaibani P et al[19] and Leavitt A et al[20] who also found that most of the *Klebsiella* strains were isolated from urine (19 strains). The reason for maximum isolation of *Klebsiella* spp. from urine and blood samples in our study could be attributed to the fact that was that majority of the patients were catheterized and had sepsis/sepsis syndrome with bacteremia. The present study highlighted the most alarming situation of highly diverse antibiotics resistance rates against cephalosporins ranging from 89.7% to 91.2%. About 84.8% were resistant to piperacillin plus tazobactam. There was a variable sensitivity to quinolones. Nitrofurantion was tested against 70 isolates recovered from urine, out of which 30 (42.9%) were resistant to it. Maximum numbers of *Klebsiella* isolates were sensitive to tigecycline and polymyxin B (100%).The results of the present study were similar to a study done by Amin A et al[17], who found that the maximum resistance was seen against cephalosporin's ranging from 82.5% to 100%. The present study observed that among carbapenemase producing isolates, maximum resistance was seen for cephalosporins and piperacillin plus tazobactum (97.9%) whereas least resistance was seen for tigecycline (4.16%) and polymyxin-B (2.08%). Further the antimicrobial susceptibility pattern of carbapenemase producers and carbapenemase non- producers did not vary much except that a significantly higher proportion of carbapenemase producing isolates were resistant to co-trimoxazole ($p<0.05$), while all of the non-carbapenemase producers (100%) were sensitive to tigecycline and polymyxin-B. The results of our study were in accordance with Parveen M et al [21] who in their study found higher level of resistance to cephalosporins (100%), cotrimaxazole (100%), piperacillin plus tazobactum (100%) whereas least resistance was found among polymyxin-B. In the current study, Minimum Inhibitory Concentration (MIC) was done on all the 57 imipenem resistant isolates by Micro-broth dilution method. For 45.61% isolates MIC was greater than 256 µg/ml, followed by MIC of 128 µg/ml which was shown by 24.56% isolates. The results of our study were similar to a study done by Parveen M et al[21] who in their study found a high MIC range of >128 µg/ml for meropenem which could be because of selective pressure due to extensive or inadequate meropenem use.

CONCLUSION:- Carbapenem resistant *Klebsiella* is a major problem in our hospital with a prevalence of 27.9%. As these strains are resistant to nearly all the available antimicrobial agents, their dissemination may lead to treatment failures with increased morbidity and mortality. An insight into the risk factors associated with infections due to these bacteria may equip the clinicians better in dealing with them. The early detection of carbapenemase producing *Klebsiella spp*. may avoid future spread of these isolates & ensure better patient care and timely introduction of appropriate infection control measures. It is imperative to do Modified Hodge test (MHT) in the microbiology laboratory and if the MHT reveals the presence of a carbapenemase a comment should be added to the microbiology report to inform clinicians and infection preventionists.

RECOMMENDATIONS:- In the absence of new effective agents the spread of carbapenemase producers may lead to therapeutic dead ends. Till the time such agents, which can tackle this increasing menace are available the most effective way of preventing the increase and spread of carbapenemase producers is early detection and institution of appropriate control measures. Methods like Modified Hodge test that are cost effective and easy to perform should be used routinely to assess whether carbapenemase producers are present or not. An alert should be released from clinical laboratories when carbapenemase-producing isolates are found, independently of their MIC values, since the correct identification of carbapenemase production also has implications for the implementation of infection control measures to control their dissemination. Judicious prescribing of antibiotics, antibiotic resistance surveillance program and antibiotic cycling should be tried whenever possible.

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