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Original Research Article

A Trend of Antibiotic Resistance Pattern of Klebsiella Pneumoniae Isolates from Sputum

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Abstract

Klebsiella pneumoniae, Gram Negative, capsulated rod shaped Bacilli is responsible for causing life threatening infections in humans and also opportunistic bacterial pathogen of clinical relevance for its association with both nosocomial infections and community acquired infections.Moreover, increased resistance to these antibiotics complicates and limits the available therapeutic drug options for the clinicians. Hence this study was taken to investigate the antimicrobial drug resistance and Prevalence of ESBL producing *Klebsiella pneumoniae*. This is a Retrospective study conducted at from JANUARY 2018 to DECEMBER 2018 at Saveetha Medical College and Hospital included Sputum sample of 3125 in patients from various Department, out of which 2154 had growth, from which 1320 *Klebsiella pneumoniae* isolates were collected. Patient's demographic details, co-morbid conditions other associated risk factors were also collected. Antibiotic susceptibility testing (AST) was done on Muller Hinton agar by Kirby bauer method as described by the Clinical Laboratory Standard Institute (CLSI). The result shows 1320 Isolates, resistance to antibiotics like (Amoxicillin intrinsically resistance), Cefepime (70.8%),Ceftriaxone (67.5%), Cefuroxime (58.3%), Gentamycin (43.3%) and 726 ESBL producers (55%) which clearly point towards the multi-drug resistance of *Klebsiella pneumoniae* isolates and ESBL producers were significantly more resistant compared to ESBL nonproducers. Hence, Routine ESBL testing should be done along with antibiogram for the proper treatment of patients and also to prevent the development of multi drug resistance.

Keywords: The antimicrobial drug resistance and Prevalence of ESBL producing *Klebsiella pneumoniae*.

INTRODUCTION

Klebsiella pneumonia a Gram-negative, rod-shaped, non-motile, lactose-fermenting, facultative anaerobic, wide-spread nosocomial pathogen with polysaccharide capsule belongs to the family Enterobacteriaceae was named after Edwin Klebs, a German microbiologist .Respiratory tract infection (RTI) is common infection worldwide and numerous patients are presenting to general practice daily caused by both Gram positive and Gram negative. Among Gram negative, *Klebsiella pneumoniae* aerobic bacterial flora of the human intestine is one of the common causative agents causing RTI and it has become most important pathogens in causing nosocomial and opportunistic infections like pneumoniae, pyogenic infections, meningitis, urinary tract infections (UTI), rarely diarrhoea ,chronic pulmonary, cardiac, renal and neoplastic diseases, and attack immunocompromised hospitalized individuals associated with diabetes mellitus [1]. This Organism exhibits an increased antimicrobial resistance making it essential for the identification of resistant bacteria.

Treatment of any bacterial infections depends heavily on effective antimicrobial therapy. Delayed use of treatment with antibiotics has been associated with a higher mortality in patients with severe infections. Therefore, presence of multidrug resistance would adversely affect the treatment outcome. One major drug resistance mechanism in *Klebisella pneumoniae* is the production of β-lactamases enzymes, especially extended-spectrum β-lactamases (ESBLs) and AMPC lactamase, which hydrolyse and inactivate betalactam in drugs like penicillin and Cephalosporins.

Recent reports shows *Klebsiella* spp producing ESBL are resistant to drugs like aminoglycosides, flouroquinolones, tetracycline, chloramphenicol, and sulphonamides [2]. A major risk factor for ESBL producing *Klebsiella pneumoniae* is over usage of Cephalosporins. ESBLs are enzymes coded by

transferable, conjugative plasmids which can lead to outbreaks [3]. Multi drug resistant (MDR) bacteria mostly do not respond to available antibiotics,hence drug of choice for ESBL producers is carbapenems, but inappropriate and over usage use of these drugs is also leading to emergence of carbapenem resistant organisms [4]. *Klebsiella pneumoniae* resistant Carbapenem is associated with high risk of morbidity and mortality and the treatment options have been narrowed further to polymyxins, which can be prevented by the judicious use of carbapenems [5]. High levels of antibiotic resistance have left only few treatment options available . However, we found no change in mortality rates over time. This could partially be attributed to the effective management of source control.

The overall prevalence of ESBL-producers of *Klebsiella pneumoniae* isolates varies widely in different studies, from 3.6% in Canada, 16% in USA, to 26.2% in Korea, and 39.3% in Eastern European nations.Study for Monitoring Antimicrobial Resistance Trends (SMART) has shown that the Prevalence of *Klebsiella pneumoniae* ESBL producers from intra-abdominal infections also.

Moreover,some epidemiological studies shows high virulent *Klebsiella pneumoniae* strains causing infections, like pneumoniae have also been reported. Despite this recent focus on the virulence factors underlying severe bacterial infection and their relationship with infection severity, the difference in the prevalence of the highvirulent *Klebisella pneumoniae* strains and other strains, and the characteristics between infection and colonization/asymptomatic status are still poorly understood. The risk factors associated with ESBL-KP are severe underlying illness, long-term treatment with multiple antibiotics, incomplete antibiotic course, Prolonged duration of hospital stay, surgical intervention, Presence of instrumentation, intravenous catheters, and endotracheal intubation and Mechanical ventilation common among intensive care unit's patients.

Therefore, we conducted a retrospective study to investigate the prevalance , antibiogram and ESBL production of *Klebisella pneumoniae* from sputum samples in ward patients of saveetha medical college and hospital.

MATERIALS AND METHODS

This Retrospective study was done at Saveetha medical college from JANUARY2018 – DECEMBER 2018 included Sputum sample of 3125 in patients from various Department, out of which 2154 had growth, from which 1320 *Klebsiella* pneumoniae strains were isolated. Patients demographic data, clinical comorbidities ,and microbiological data were retrieved from the medical records.

Continuous sample collection technique was used. sputum samples were immediately transported in a sterile container to the Microbiology laboratory and are processed. After initial direct Gram staining, samples were streaked on blood agar, Mac-conkey agar, and chocolate agar, and incubated at 37°C for 24 hours. Any significant growth was identified and antibiotic sensitivity testing (AST) was done only for pathogenic bacteria by following CLSI guidelines. ESBL screening was done as per CLSI guidelines and confirmed by combined disc method.

RESULTS

This study, conducted at Saveetha Medical College and Hospital included sputum sample of 3125 patients from various Department, out of which 2154 had growth, from which 1320 *Klebsiella pneumoniae* isolates were collected.A higher rate of culture positivity is seen in male patients (924 patients out of 1320) than from female patients (396 patients out of 1320).The age group 61-70 years showed the highest confirmed cases of *Klebsiella pneumoniae* isolates, followed by other age groups. Sample isolated from ICU patients showed higher degree resistance compared to ward patients. Resistance to antibiotics like Ampicillin intrinsically resistant (100%), Cefepime (70.8%), Ceftriaxone (67.5%), Cefuroxime (58.3%), gentamycin (43.3%) clearly point towards the multi-drug resistance of *Klebisella pneumoniae with* least resistance 33% to Amikacin. Amomg 1320 Isolates of *Klebsiella pneumoniae* 726 (55%) were ESBL producers and 594 (45%) were ESBL non producers. ESBL-KP isolates showed a higher degree of antimicrobial resistance as compared to non-ESBL producers.

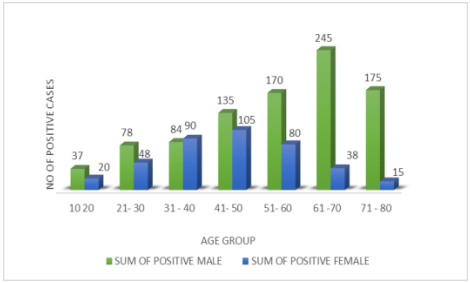

Fig-1: Age wise distribution of *Klebisella pneumoniae*

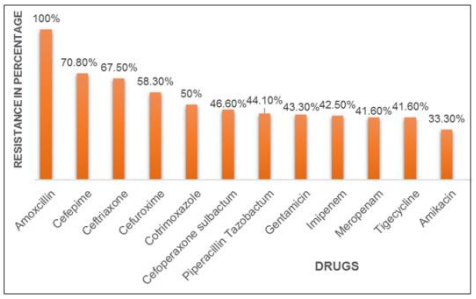

Fig-2: Shows drug resistance among *Klebsiella pneumoniae* culture isolates from sputum sample, with intrinsic resistance to Ampicillin followed by Cefepime 70.8% with least resistance to Amikacin 33.3%

In this study, most of the patients were multidrug-resistant. Some patients were sensitive only to colistin and tigecycline and Some patients were even resistance to colistin and tigecyclin. All the MDR organisms were isolated from patients with multiple comorbidies and on hospitalization of >4 days.

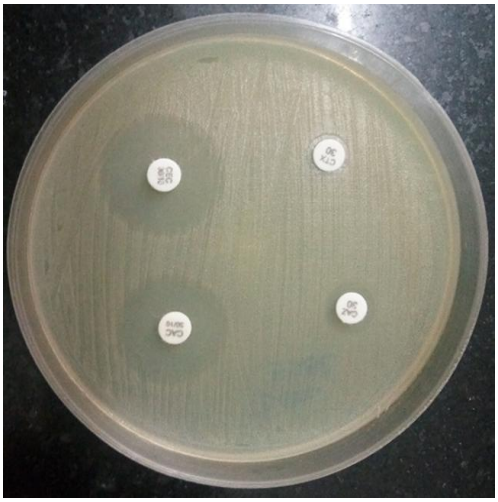

Fig-3: ESBL production by combination disc method

Table-1: ESBL Distribution

Organisms	ESBL Producers	ESBLnon-producers
Klebsiella spp	726 (55%)	594 (45%)

All the ESBL positive isolates were recovered from patients with history of prolonged hospital stay of more >3 days (Fig-5).

DISCUSSION

In 1983 ESBL Producers was discovered in Europe and the detection frequency has been increasing since then probably because of Multifactorial causes. In India,there is a high prevalence of *Klebsiella pneumoniae* strains Producing ESBL. Hence this study was done at Saveetha Medical College and Hospital.Studies showed a higher rate of culture positivity from the samples of male patients (924 patients out of 1320) than from female patients (396 patients). The duration of stay in hospital differed between stable patients and the patients with comorbid conditions and other illness. Sputum samples were isolated from Patients with comorbid conditions like chronic obstructive pulmonary disease, tuberculosis pneumonia and bronchitis.Similarly, multi drug resistance was more common in elderly male patients as they have more pre-existing lung diseases and incidence of smoking (Meatherall et al., 2009) and other co-morbid illness than compared to female's patients. The age group 61-70 years showed the highest confirmed cases of *Klebsiella pneumoniae* isolation, because of weaker immune system and predisposing factors for bacterial infection like exposure to adverse weather and environmental conditions, dietary challenges and other associated comorbidities.Risk of ESBL and multidrug resistance increases with previous History of hospitalization in the old age people. Lowest rate of isolation was observed among new-borns and 10-20 years.

All ESBL positive isolates were recovered from patients with history of hospitalisation of more than 3 days. Classification of patients on basis of previous hospital exposure revealed that of 45 % of cases (non-ESBLs-producers) does not have history of prior hospitalisation, and however ESBLs-producers of 55% of the patients were hospitalized previously. According to report published in 2013, the global rate of the, ESBL *Klebsiella* -phenotype was 32.5%. In recent years significant increase in *Klebsiella* ESBL producers was also reported from Turkey 78.6% ,China 51%, Taiwan 28.4%, Spain 20.8%, Algeria 20%, USA 4.2–44%, Canada 4.9%, and in india Overall ESBL producers ranged from 4% to 83%. Rodrigues *et al.*, [6] reported the lowest percentage in Maharashtra ie 4 positive (8.5%) ESBL producers among 47 *Klebsiella pneumoniae* isolates . Probably, it reflects the emerging **phase** of ESBL producers which would have raised in the same locality if a similar study is conducted by now. In our study , we noticed the prevalence of ESBL-producing *Klebsiella* 55% which is almost similar to other studies done elsewhere. Multidrug resistance was commonly seen in Ampicillin (100%), Cefepime (70.8%), Ceftriaxone (67.5%), Cefuroxime (58.3%), followed by Gentamycin (43.3%). These findings are quite comparable to earlier study results as mentioned above. The Study for Monitoring Antimicrobial Resistance Trends (SMART) has shown the prevalence of ESBL-producing *Klebsiella pneumoniae* isolates from intra-abdominal infections also. The comparatively lower rate in our hospital can be justified by the fact that there is a good infection control practices followed here.Regarding the treatment for affected cases, recommendations of antibiotics are based on the pathogen, disease severity, and patient's comorbidity. When ESBL-producing organism are isolated from sputum or when the organism are expected to be the causative agent, use of carbapenems has been recommended. However, some carbapenems resistance have also been reported.

Our study highlights the Prevalence of multidrug resistance and *Klebsiella pneumoniae* ESBL Producers in Saveetha Medical college and Hospital .Routine detection of ESBL- by standard detection methods is required to be done by each laboratory for controlling the spreading of these infections and to prevent the emergence of Multidrug resistance.However, there is a need to emphasize on the rational use of antibiotics on patients. In addition, regular antimicrobial susceptibility surveillance is essential since only few High levels of antibiotic treatment options available.

Here are some limitations to our study. First, it is a Retrospective and single-center surveillance study, which may explain the resistance levels observed in our hospital alone. Second, we did not perform polymerase chain reaction (PCR) and DNA sequencing of isolates.

CONCLUSION

Appropriate antimicrobial therapy is possible only with proper specimen collection, culture and sensitivity. Multidrug-resistant organisms are becoming increasingly associated with nosocomial infections. Hospital Infection Control protocols need to improve in high-risk settings such as in all intensive care units. Gram-negative bacteria especially *Klebsiella spp*, are most commonly encountered pathogens isolated from sputum samples in various patients.

Klebsiella pneumoniae shows high ESBL positivity, with some patients being resistance, to colistin and tegecycline especially in ICU patients. The occurrence of resistant pathogens may be used to determine trends in antimicrobial susceptibilities to formulate local antibiotic policies and to assist clinicians in the rational choice of antibiotic therapy which will leads to decreased prevalence of ESBL producers in the community.

Hospital infection control commite should have an updated hospital antibiotic status and susceptibility profiles which guides for the initial empirical treatment . In this regard, the VAP bundle checklist is to be implemented strictly to all the ICUs. It contains five components ie , elevation of the head end of bed to 30◦, daily 'sedation vacation' and daily assessment of readiness to extubate, daily oral care with chlorhexidine, peptic ulcer prophylaxis, and deep venous thrombosis prophylaxis.

Conflict of Interest

There is no conflict of interest.

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