

Klebsiella pneumoniae Carbapenamase (KPC) Outbreak in a Multispeciality Cancer Hospital—An Emerging Superbug

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Abstract

Aim: To identify, analyse and control the outbreak of Carbapenamase producing *Klebsiella pneumoniae*. **Objectives:** 1) To detect multidrug resistant *K. pneumoniae* at the earliest and isolate patients. 2) To find out the predisposing causes for the occurrence of this outbreak. 3) To break the chain of infection transmission. 4) To reduce the risk of Hospital acquired infections. **Methods:** This retrospective study along with the surveillance was conducted from January 2017 to March 2017 at HCG multispecialty cancer hospital, Bangalore, India. **Results:** Total 15 patients were diagnosed with KPC infection during the first month of the study period. Those affected were mostly Male patients (73%), admitted in ICU (73%) for further treatment. In our study, the incidence of KPC infection was mostly found with bloodstream infections (60%), mostly seen in those with central lines (80%) followed by patients on ventilatory support (66%). Before the outbreak of KPC infection, all the patients (100%) had already been treated with higher antibiotics including Carbapenems. In our study, only nine out of fifteen patients (60%) could be salvaged with treatment and were discharged. **Conclusions:** Hospital Infection Control Committee's regular screening and the training of healthcare professionals are vital for the control of the outbreak.

Keywords

Intensive Care Unit (ICU), *Klebsiella Pneumoniae* Carbapenamase (KPC), Outbreak

*Original Article.

1. Background

Hospital acquired infections (HAI) especially pan-drug resistant infections are the most notorious infection encountered in multi speciality cancer hospitals with major implications like increased morbidity, mortality, financial burden and longer duration of hospital stay. Among the pan drug resistant infections, *Klebsiella Pneumoniae* Carbapenamase (KPC) is one of the emerging and challenging bugs in our setting. As per the worldwide data, KPC-producing Enterobacteriaceae were first reported in a clinical specimen from a patient in North Carolina in 2001 [1].

In the United States of America, the dissemination of KPC producing CRE isolates appeared to be clonal [2]. A sample of KPC-producing *K. pneumoniae* isolates sent to the CDC for reference testing from 1996 to 2008 was characterized using PFGE and multilocus sequence typing (MLST). This analysis revealed that a dominant strain, ST258, accounted for approximately 70% of all KPC-producing *K. pneumoniae* isolates sent to the CDC during that time period [2]. As per the Indian data, in 2009 a novel MBL, the New Delhi MBL (NDM), was described [3]. NDM was first identified in a *K. pneumoniae* isolate from a Swedish patient who had received medical care in India and was soon recognized as an emerging mechanism of resistance in multiple species of Enterobacteriaceae in the United Kingdom. Our hospital data shows that there is a seasonal trend of outbreaks of KPC with occasional 1 or 2 cases per month.

Antibiotics treatments for KPC are very limited and include Aminoglycosides, Colistin, Tigecycline and Fosfomycin [4] [5]. The activity of these antibiotics against KPC seems to depend on pk/pd parameters [6] [7] [8]. Irrational use and abuse of these higher antibiotics have been a major concern especially in developing countries which have lead to the emergence of Gram-negative isolates resistant to these agents [9] [10] [11].

Klebsiella pneumoniae is one of these multidrug resistant organisms (MDR) identified as an urgent threat to human health by the World Health Organization, the US Centers for Disease Control. The lineage defined as sequence type (ST) 258 is a notorious example of MDR *K. pneumoniae*. ST-258 frequently carries the *K. pneumoniae* carbapenamase (KPC) gene, as well as numerous other acquired AMR determinants, and has been responsible for outbreaks on several continents [12]. Our hospital, being a multi speciality cancer hospital, deals with immunocompromised patients and KPC infection shows a higher mortality rate.

According to Grinbaum [13], "One of the objectives of Epidemiological Surveillance carried out by the Hospital Infection Control Service is to detect outbreaks before the propagation results in further harm." We have a similar body, named Hospital Infection Control Committee (HICC) which is a committee responsible to investigate the outbreaks that include the source of the agent, means of transmission and control measures.

Minor breach in the prevention and control measure leads to an outbreak of any infection and the most common route of transmission of nosocomial infec-

tion is via pathogen contaminated hands of care givers. Following any outbreak of infection, according to our Hospital customized protocol, which is similar to that of CDC guidelines with minor changes; the HICC scrutinizes the patient and the environment. The possible source/host is identified and measures to control the transmission are taken.

2. Material and Methods

This retrospective study was conducted from January 2017 to March 2017 at HCG Multispecialty Cancer Hospital, Bangalore, India. The population under investigation consisted of 200 hospitalized patients over the aforesaid period.

There was an outbreak of *Klebsiella Pneumoniae* Carbapenamase (KPC) infection in January 2017, which was identified by our HICC surveillance system following which urgent meeting of HICC was held which suggested the urgent need of study of the outbreak along with hospital environment and staff surveillance by hospital Infection Control Team (ICT) which comprised of Microbiologist, Medical Oncologist, Radiation Oncologist, Surgical Oncologist, Intensivist, Pharmacologist, Statistician and Infection Nurse practitioners. The methods of study were as depicted in **Figure 1**.

This study is a surveillance study post KPC outbreak. All the microbiologically proven KPC positive cases were included in the study, while all the *Klebsiella pneumoniae* carbapenamase sensitive (KPC negative) cases were excluded from the study.

An investigation into the predisposing causes was initiated, using computer based database as the data source. Cases were defined as symptomatic patient with culture positivity for KPC. A number of predisposing factors and risk factors were included:

- 1) Presence of neutropenia; 2) Central lines; 3) Catheterisation; 4) Parenteral

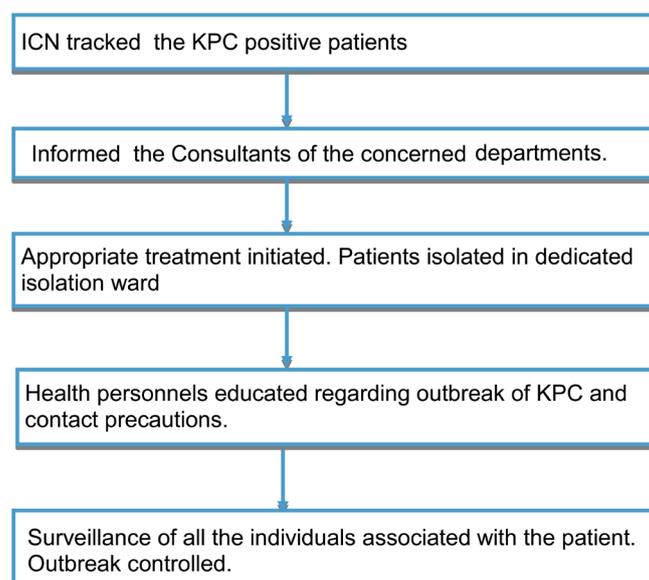


Figure 1. Design of the study.

nutrition; 5) Blood products; 6) Intensive care unit (ICU) stay; 7) Medical or surgical cases; 8) Intubation/ventilation; 9) Steroids use; 10) Prior use of higher antibiotics.

An investigational proforma was created, which included patient identification, duration of hospitalization, culture reports as well as above selected predisposing factors. All the tests were done on automated Blood Culture System (Bact Alert) for blood and other samples were processed on routine media and then subjected to automated Vitek 2 Compactor identification and antibiotic sensitivity pattern with MIC's value. After the collection of reports statistical analysis was done using SPSS Software.

3. Results

Total 15 patients were diagnosed with MDR KPC infection during the study period. The results of the investigation are presented in **Tables 1-3**. Due to technical reasons, it was not possible to carry out molecular typing, however, all of the positive culture samples had the same phenotypic antibiogram profile which is depicted in **Table 4**.

In our study, most commonly affected were males (73%) with blood stream infections (60%). 80% of the patients had central line and 73% were admitted in

Table 1. Characteristic features of patients (N/%).

CHARACTERISTICS	NUMBER OF PATIENTS	PERCENTAGE %
Mean Age	50	-
Male	11	73
Co-morbidity	2	13
International patients	4	26
Solid tumors	10	66
Haematological	5	34
Surgical cases	9	60
Medical cases	6	40

Table 2. Characteristic features of Infections (N/%).

CHARACTERISTICS	NUMBER OF PATIENTS	PERCENTAGE %
Fever	13	86
Neutropenic sepsis	3	20
Blood stream Infection	9	60
Surgical site infection	2	13
Lower Respiratory Infection	3	20
Urinary Tract Infection	1	6
High Procalcitonin level (>0.5)	10	66
Death	4	40

Table 3. Predisposing factors for *Klebsiella pneumoniae* (N/%).

FACTORS	Number of Patients	Percentage %
Neutropenia	3	20
Central Lines	12	80
Surgical Cases	9	60
ICU stay	11	73
Steroid use	7	46
Diabetic patients	2	13
Intubated/Ventilated	10	66
Blood Products	10	66
Parenteral Nutrition	5	34
Higher Antibiotics used before	15	100
Urinary catheter	11	73

Table 4. Antimicrobial susceptibility of pathogen.

Antimicrobial	MIC(microg/ml)	Interpretation
Ampicillin	≥32	R
Piperacillin/Tazobactam	≥128	R
Cefoperazone/Sulbactam	32	R
Imipenem	≥16	R
Meropenem	8	R
Amikacin	≥64	R
Gentamycin	≥16	R
Colistin	1	S
Tigecycline	2	S

Footnote: R: Resistant; S: Sensitive.

ICU for further management. 66% of the cases were on ventilator support. All the patients (100%) were being treated with higher antibiotics, including carbapenems, prior to this outbreak. Nine out of fifteen patients (60%) recovered with the treatment and were discharged.

Initially, the following intervention measures were introduced to control the outbreak: 1) Contact isolation; 2) Alcohol gel containing hand rubs; 3) Special care during vascular access and foley catheterization; 4) Hand washing and strict personal protective equipments; 5) Training of the staffs; 6) Refrain sharing of bedpans, instead use of disposable bedpans. Along with the intervention measures, screening of the hospital environment and healthcare staffs including consultants was done in March 2017. Hospital environment including room air, beds, tables etc were found to be sterile. Seven out of Sixty four health care staffs, who were screened by nasal, throat and hand swabs, were found to be harbour-

ing pan sensitive *Klebsiella pneumoniae* but not KPC. Basic treatment was given to the healthcare staffs till the subsequent cultures were found to be negative. Apparently there was colonization of *Klebsiella pneumoniae*, and all healthcare professional were asymptomatic.

The only limitation of this study was inability to do a detailed PCR study of the organism for comparison of isolates.

4. Discussion

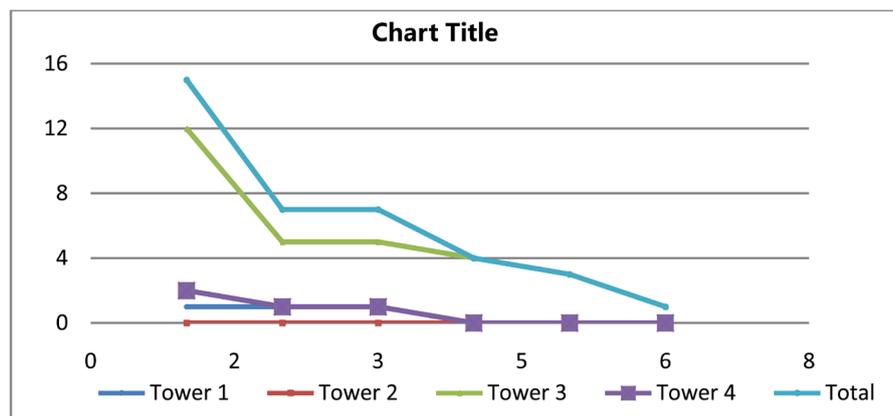
K. pneumoniae, is a part of the respiratory and intestinal microflora of humans and can be isolated from the oropharyngeal cavity at a frequency up to 6%. It is strongly associated with infections, such as pneumonia, urinary infections and septicemias. Between half and three-quarters of all the bacteremias caused by this agent originate in the hospital, therefore they are resistant to ampicillin and carbenicillin, and are frequently susceptible to cephalosporins, cotrimoxazole, aminoglycosides and carbapenem [14]. Later due to genetic material exchange by plasmids and transposons, these organisms become resistant to higher antibiotics including carbapenems. This pattern was also found in our study, as the HAI cases were caused by ampicillin-resistant *K. pneumoniae*.

Most of these infections occurred in Tower 3 of our hospital which included high risk area consisting of Surgical ward, Hematology ward and ICU having critical patients who had undergone surgery, chemotherapy and immunosuppressant medicines. The first case among these patients was an international patient with diagnosis of blood cancer (AML) admitted in ICU. Since there was inability to perform molecular testing of KPC so the above mentioned patient could not be identified as an Index case in our study. In order to deal with the shortcoming of performing molecular testing, the hospital management is now taking necessary measures. Ideally perianal and rectal cultures are most reliable sites to screen for resistant Enterobacteriaceae for surveillance according to CDC usually obtain surveillance cultures for Enterobacteriaceae from the wound and perirectal area, during outbreak investigations. Our study is retrospective and for the screening of healthcare professional we have taken hand, nasal and throat swabs for cultures which is not according to the CDC guidelines. However on screening all the staffs were asymptomatic and only seven were found harbouring/colonising pan-sensitive *Klebsiella pneumoniae*. They were given basic treatment.

After the implementation of surveillance strategies and adoption of the intervention measures, marked reduction in the infection rate was observed with only four cases reported in April and one in June as described in **Table 5** and **Figure 2**. This justifies the appropriate adoption of intervention measures to control the outbreak and interruption of transmission chain. A fall in the incidence of Hospital infections was also observed when compared with indices prior to the outbreak. Quality Improvement Program (QIP) report was prepared and implemented for next three months. We have also started Infection Board Meeting

Table 5. Monthly KPC incidence after surveillance (N).

Months	Tower 1	Tower 2	Tower 3	Tower 4	Total
January	1	0	12	2	15
February	1	0	5	1	7
March	1	0	5	1	7
April	0	0	4	0	4
May	0	0	3	0	3
June	0	0	1	0	1



Footnote: X axis: Number of months after surveillance; Y axis: Number of patients.

Figure 2. Monthly KPC incidence after surveillance.

every weekly to handle such complicated multi drug resistant organisms cases in our hospital which has helped a lot.

Long term sustainable plans and policies were proposed and implemented which included:

- 1) Strict hand hygiene and Personal Protection Equipment (PPE);
- 2) Training of all staffs, cross evaluations and motivations;
- 3) Maintain strict follow up of HICC policies/practices;
- 4) Strict adherence to bundles;
- 5) Antibiotics stewardship policy.

The mortality rate of carbapenem-resistant *Klebsiella pneumoniae* (CRKp) infections in North America, South America, Europe, and Asia is reportedly 33.24%, 46.71%, 50.06%, and 44.82%, respectively [15] which was similar to our mortality rate of 40%.

5. Conclusions

Despite of our efforts, the source of this agent couldn't be identified however we came to a conclusion that cross contamination of the organism was the major determinant for this outbreak during the patients care. Hospital Infection Control Committee's regular screening and the training of healthcare professionals are vital for the control of the outbreak.

The determining factor of the outbreak appears to have been hand hygiene since after the intervention measure techniques, the outbreak was controlled. Target of more than 90% hand hygiene compliance of the healthcare professionals has been set and training/practices are going on. Antimicrobial stewardship has been suggested as an important part of efforts to control multidrug resistant organisms.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

Disclosures

All procedures performed in studies were in accordance with the ethical standards of the institutional.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Authors' Contributions

SS, MP contributed to the writing, design, concept of the manuscript; SG analyzed bacterial culture reports; MP analyzed and interpreted the clinical data; RN analyzed the antimicrobial results and statistical analysis; all authors reviewed and approved the final manuscript.

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