Case series

Hypervirulent *Klebsiella pneumoniae*: A case series from tertiary care centre

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ABSTRACT

Considered the new public threat, hypervirulent *Klebsiella pneumoniae* (hvKp) has shown its prevalence in the Asia Pacific rim. It was first reported in Taiwan in 1986.Within the next few decades it became a cause of concern because of its pathogenicity and the panoptic nature of organs affected, and high mortality, especially in healthy individuals. The wide range of clinical picture includes hepatic abscess, distant metastases, pneumonia, necrotizing fasciitis, endophthalmitis, and meningitis. This case series aims to find such cases in Southern India and study the pattern, to provide an insight into hvKp and its prognosis and therapeutic strategies. It is a descriptive study performed in our medical college hospital where selective cases of microbiologically proven Hypervirulent *Klebsiella pneumoniae* were studied. An expert-validated structured proforma was used to obtain the information after obtaining permission from the authorities. It is imperative to identify risk factors, clinical features and management of hvKp cases globally, especially with the recent increase in its incidence. The emphasis should be mainly on the prevention of the infection in the community and healthcare facilities by actively working towards it.

Keywords: Aerobactin gene; antimicrobial resistance; hypervirulent *Klebsiella pneumoniae*; invasive infections; string test; virulence.

INTRODUCTION

Considered the new public threat, hypervirulent *Klebsiella pneumoniae* (hvKp) has shown its prevalence in the Asia Pacific rim was first reported in Taiwan in 1986 (1). Within the next few decades, it became a cause of concern because of its pathogenicity and the panoptic nature of organs affected, and high mortality, especially in healthy individuals (2). hvKp is causing menace as a healthcare and community acquired pathogen (3).

hvKp is characterized by hypermucoviscosity (gene *mag*A) on string test, increased capsular production with K1 and K2 serotype, presence of virulence factor aerobactin and genes *rmpA* and *rmp*A2 (4). The wide range of clinical picture includes hepatic abscess, distant metastases, pneumonia, necrotizing fasciitis, endophthalmitis, and meningitis (1). There is high lethality with over 29.5% within the first thirty days. The concomitant hepatobiliary disease has shown more predispositions to hvKp (5).

hvKp is a peril itself, but with the appearance of MDR -hvKp, it is far more difficult to predict the course. A case series done on XDR-hvKp causing neonatal sepsis in a tertiary care hospital in Northern India has shown a mortality rate of 100% in Carbapenem-resistant hvKp and 84.2% in Meropenem resistant hvKp (6). India, a developing Asian nation prone to infectious diseases cannot afford to have hvKp in any age group. It is crucial to study the hypervirulence of *Klebsiella pneumoniae* before further damage is done and higher drug resistance and complications are seen. This case series aims to find such cases in Southern India and study the pattern, to provide an insight into hvKp and its prognosis and therapeutic strategies. It is a descriptive study performed in our medical college hospital where selective cases of microbiologically proven hypervirulent *Klebsiella pneumoniae* were studied. An expert-validated structured proforma was used to obtain the information after obtaining permission from the authorities. The authors obtained ethical clearance for the study from Institutional Ethics Committee, Kasturba Medical College, Mangalore, approval number IECKMC MLR11/2021/ 350 dated 17/11/2021.

Case 1

A 75-year-old female, a known case of Type 2 diabetes mellitus, hypertension, COPD, and ischemic heart disease was brought to Emergency medicine with chest pain and sudden onset of breathlessness. On admission, the patient was afebrile with other vitals being normal. The systemic examination was done and crepitations were heard bilaterally in the basal area of the lung, and rhonchi were heard bilaterally in the posterior lung field. The Glasgow coma scale was assessed to be 8 out of 15. An echocardiogram was performed and the left ventricle was dilated, mild Mitral regurgitation was present with a 45% ejection fraction. The chest X-ray revealed bilateral lower lobe Pneumonia. Blood investigations revealed elevated total count (14400 cells/mm^3), HbA1C (9.8%), and decreased potassium (3.07 mm/L). The sputum sample showed growth of hypervirulent *Klebsiella pneumoniae*, sensitive to Carbapenem. The diagnosis was made as bilateral lower lobe pneumonia with hypokalemia, diabetes mellitus, and COPD. In the

ICU she was treated with intravenous steroids, diuretics, bronchodilators, and intravenous Carbapenem. She was shifted to the inpatient ward and was treated with Clarithromycin, Faropenem, and prophylactic Oseltamivir. Comorbidities were treated conservatively. The patient was discharged following medications.

Case 2

A 50-year-old male was brought to the emergency department with a sudden onset of cough with expectoration and dyspnoea associated with chest pain for 3 days. On admission, the vitals showed decreased spO_2 (86%). While the other systemic examinations were normal, the respiratory exam revealed the use of accessory muscles with bronchial breath sounds in the mammary and infra-axillary areas. A provisional diagnosis of right and left lower lobe pneumonia with hemoptysis under evaluation was made. The patient was intubated and Voriconazole as well as Inj. Teicoplanin was given along with other adjunct drugs. Mantoux test was negative. The culture report from the specimen obtained from the ET aspirate showed growth of Hypervirulent *Klebsiella pneumoniae*, sensitive to Carbapenem. Routine blood investigations revealed severe leukopenia (600 cells/mm^3) and thrombocytopenia (49,000 cells /mm^3). The CK-MB (53 U/L), LDH (449U/L), ESR (46mm/hr), AST (97 U/L), ALT (49 U/L) were elevated. The serum bicarbonate (13.8 mmol/L) was decreased. ABG showed decreased pO_2 (67.7). The patient was then administered IV Meropenem, Amikacin, and prophylactic Oseltamivir. However, the patient's condition kept deteriorating, and was shifted to ICU. He progressively had breathlessness and desaturated and was resuscitated with IV fluids. He was put on non-invasive ventilation and IV antibiotics were continued. He was arrested with bradycardia and asystole and CPR was given ACLS guidelines and could be recovered. The immediate cause of death was bilateral pneumonia due to septic shock and antecedent cause being neutropenia as a consequence of haemoptysis.

Case 3

A 27-year-old male agricultural worker with no previously known comorbidities presented to the internal medicine department with colicky abdominal pain associated with non-bilious vomiting for 2 days. The complaints were not associated with fever, headache, hematemesis, headache, or melena. The vitals on examination showed spO_2 value of 96%, blood pressure of 140/90 mm Hg, and respiratory rate of 20 cycles per minute. On systemic examination the abdomen was soft and there was epigastric tenderness. He was admitted for further management. On routine blood investigations serum creatinine was increased (1.7 mg/dl) along with ALT (121 U/L), AST (132 U/L), and ALP (448 IU/L). The blood culture showed growth of hypervirulent *Klebsiella pneumoniae*. He was initially started on empirical antibiotics and parenteral fluids. An ultrasound of the abdomen was done and it revealed chronic calcific pancreatitis, dilated common bile duct, hepatomegaly and calculi in CBD. CECT confirmed pancreatitis which was followed by MRCP. A diagnosis was made of acute onset of chronic pancreatitis with sepsis due to *Klebsiella* species. During the course of hospital stay, he was given IV Meropenem, IV Imipenem, Cefoperazone-sulbactam, Antihistamines, and pancreatic enzyme supplements. ERCP was performed. He was discharged following the above treatment and was symptomatically better.

Case 4

A 51-year-old female, a known case of carcinoma hypopharynx on palliative chemotherapy with Docetaxel, Carboplatin, and Cetuximab was brought to the emergency department with complaints of fever, breathlessness and loose stools for 2 days and she was drowsy. Her vitals on examination were blood pressure of 70/40 mm Hg, SpO_2 of 83%, pulse pressure of 110 beats per minute and respiratory rate of 28 cycles per minute. Bilateral crepitations were heard on systemic examination. She was stabilized with 4L O_2 and other resuscitation measures were taken with inotropes and IV antibiotics amikacin, fluconazole, olanzapine, ciprofloxacin, and dexamethasone in view of neutropenic sepsis. Her blood investigations revealed a decreased total count (500 cells/mm^3) hemoglobin (8 g/dl) and sodium (112 mEq/L). The ET aspirate blood revealed hyper-virulent *Klebsiella pneumoniae*, sensitive to Carbapenem. Her general condition worsened despite stabilizing and went into cardiac arrest and CPR was performed but could not be revived and she was declared dead. Her cause of death was sepsis due to septic shock with neutropenic shock as an antecedent cause.

DISCUSSION

Klebsiella pneumoniae, a Gram-negative bacterium that is one of the most prominent healthcare associated pathogens, is of two types; classical *Klebsiella pneumonia* (cKp) and hypervirulent *Klebsiella pneumonia* (7,8). Both of them are associated with hospital-acquired infections (68.8%), healthcare-associated, and community-acquired infections (31.2%; 9,10).

Initial reports of hvKp associated with pyogenic liver abscesses, meningitis, and endophthalmitis. hvKp showed the presence of mucosity-associated gene leading to hypermucoviscosity and positive string test more than 5mm (11). Further reports showed a strong relationship between *rmpA* and *hmv* gene (12).

The resistance of hvKp is seldom found compared to cKp. In recent times however, there has been an emergence of higher antibiotic resistance of hvKp. There are certain biomarkers associated with hvKp to

differentiate it from cKp. This included peg-344, iroB, iucA, rmpA, and rmpA2 and the strains also predominantly contain K1 and K2 capsules even though it is seen in cKp as well. With multiple factors playing a role in defining hvKp, the clinical picture also ends up playing an important role along with a positive string test in clinical practice (13).

Diabetes mellitus, malignancies, hypertension, and community-acquired infections were noted to be the associated risk factors for hvKp in some studies. In our patients we have seen patients having diabetes mellitus, hypertension, and carcinoma as comorbidities.

While studying differences between cKp and hvKp, healthy and non-immunocompromised populations were seemingly more affected by the latter (14,15). Two of our patients did not have any comorbidities while one amongst them was a young individual. This brings to the notice that colonization that leads to infection is therefore more often in hvKp. Colonization mostly occurs through dermal and mucosal surfaces along with perineum. The rates of colonization varied in different studies in different countries. In hospital settings, the transfer of organisms occurs using unsterilised equipment, improper handwashing among others. In the community, it appears to happen through person-to-person contact. Although the route of entry is still unclear, especially in community-acquired, studies have suggested few ways like high titre of bacteria in gut or interference with skin. The cause of concern here though would be cKp acquiring virulence plasmids of hvKp, which would be adversely increasing its incidence (16). In China, 22.8% of isolates of Kp have shown hypervirulence and 42.2 % in S. Korea (16). In India MICU study has shown 19.4% of such isolates.

The antimicrobial sensitivity of hvKp seems to be higher compared to cKp. In recent times the problem, however, arises from the emergence of carbapenem-resistant hvKp, XDR hvKp, and MDR hvKp . One of the patient samples has shown multi drug resistance.

The classical type and hvKp share similar clinical features that include fever, haemoptysis, pneumonia and abscesses where there is higher incidence of invasive infections, liver abscesses, abdominal infection, sepsis in hvKp, while it has lower incidence of urinary infections (14).

A study by Tang *et al.*, showed that there was 11.9% in hospital mortality rate. Another study done in China showed a 30-day mortality rate of 39.9%. 2 out of our 4 patients succumbed to the infection while both the causes being sepsis with septic shock (17).

Limitations

This is a case series based on selected cases and an extensive research study needs to be done to find multiple variables with significant findings.

CONCLUSION

It is imperative to identify risk factors, clinical features and management of hvKp cases globally, especially with the recent increase in its incidence but the emphasis should be mainly on the prevention of the infection in the community and healthcare associated infection by actively working towards it.

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CONFLICT OF INTEREST

We have no conflicts of interest to declare.

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