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Original Article

Mortality risk score for *Klebsiella pneumoniae* bacteraemia

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ABSTRACT

Background: Klebsiella pneumoniae bacteraemia (KPB) has been associated with multiple risk factors. However association of these risk factors with mortality secondary to KPB has been poorly documented.
Objectives: To assess underlying co-morbidities in patients with KPB and any associated presentations. These findings were then used to devise a score to estimate the risk of in-hospital mortality in patients with underlying KPB.
Methods: A retrospective analysis of all patients diagnosed with KPB between November 2007 and March 2012 at Mater Dei hospital in Malta was carried out. Using the odds ratios of risk factors for mortality associated with KPB, a mortality risk score was then prepared.
Results: 186 patients (mean age 62 years; mean hospital stay 22.6 days) were included. 51 patients died as inpatients. Being admitted to intensive care (Overall risk (OR): 9, $p < 0.0001$), having a solid organ tumour (OR 3, $p < 0.005$), and having an underlying pneumonia (OR 3, $p < 0.021$) were statistically significant risk factors associated with mortality. There were 0% mortality in patients with a score of 0, and progressively increasing mortalities with increasing scores up to a 100% mortality in patients with scores of >15. This translated into a validated risk score where an increasing score reflected an increasing mortality.
Conclusions: Klebsiella pneumoniae bacteraemia is associated with high in-patient mortality. ICU admission, underlying solid tumours, and co-existent pneumonias are among the factors used in our mortality risk score. This needs to be further validated in larger populations.

1. Introduction

Klebsiella pneumoniae is a gram-negative bacterium with rapidly emerging resistance that coincides with the extensive use of antibiotics. The increasing resistance of *Klebsiella pneumoniae* does not mirror the development of antibiotics against resistant gram-negative organisms. Infections with *Klebsiella pneumoniae* are usually hospital-acquired and occur primarily in patients with impaired host defenses [1].

Klebsiella pneumoniae bacteraemia (KPB) has been linked to a number of pathologies including solid tumours, haematological malignancies, liver cirrhosis, biliary tract infections, and diabetes mellitus. However the association between KPB and the mortality risk attributable to these pathologies has not been extensively documented.

2. Objectives

To assess underlying co-morbidities in patients diagnosed with *Klebsiella pneumoniae as* well as any associated presentations, antibiotics administered, and antibiotic sensitivities. These findings were then used to devise a score to estimate the risk of in-hospital mortality in patients with underlying KPB.

3. Materials & methods

The case notes of all patients known to have suffered from KPB between November 2007 and March 2012 at Mater Dei hospital (Malta) were reviewed. All patients with KPB were identified through the Pathology Department database and were included in this study. Demographic data, information on underlying co-morbidities, and any associated pneumonias, urinary tract infection, septic shock, and hepatobiliary infections were collected. Length of hospital stay and information on whether the patient needed intensive care unit management and whether the patient died during hospital stay were all noted. The type of antibiotic each patient received was recorded as well as antibiotic sensitivities of *Klebsiella pneumoniae* and the Extended Spectrum *B* Lactamase (ESBL) status. Statistics were worked out using SPSS version 19.

Odds Ratios for several risk factors (intensive care admission, solid malignancy, haematological malignancy, immunosuppression, multi-drug resistance, ESBL positivity, liver cirrhosis, age >60 years or newborn, septic shock, nosocomial infection, bacteraemia secondary to pneumonia, meningitis, or urinary tract infection) were calculated. Using these Odds ratios, a scoring system estimating the risk of death was devised. The score was then validated by calculating the

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percentage of patients who survived to discharge following KPB at each score.

4. Results

All 186 patients (97 male) who suffered from KPB between 2007 and 2012 at Mater Dei Hospital were included. Mean age at diagnosis was 62 years (Standard Deviation [SD] ±21.3) and mean length of hospital stay was 22.6 days (SD ± 26.6). KPB was commoner in the elderly group (Fig. 1). 51 patients (27.4%) died as in-patients following *Klebsiella pneumoniae* bacteraemia with most deaths occurring within the first 30 days of hospital stay (Fig. 2). Extended-spectrum β-lactamase (ESBL) producing bacteria were cultured in four (7.84%) of these patients. 18 patients (9.68%) required intensive care unit (ICU) admission.

14 patients (7.5%) tested *Klebsiella pneumoniae* ESBL positive, two (14.3%) of whom required ICU admission. There was no statistically significant difference ($p = 0.41$) between the mean age of patients who suffered from ESBL producing *Klebsiella pneumoniae* (mean age 64; SD ± 15.5) and those suffering from non-ESBL producing *Klebsiella pneumoniae* (mean age 62; SD ± 21.8). Four patients (28.6%) who had ESBL producing KPB died whilst being treated in hospital. ESBL positive patients had a significantly longer mean hospital stay ($p = 0.001$) (mean 44.5; SD ± 58.5) than ESBL negative patients (mean 19.0; SD ± 20.9).

4.1. Associated conditions

49 patients (26.3%) had underlying diabetes mellitus; nine (18.4%) of whom died as in-patients. 50 patients (26.9%) had underlying solid tumors which were mostly gastroenterological malignancies (colon, ten patients; oesophagus, one patient; pancreas, five patients) and urological malignancies (12 patients) (Table 1).

54 patients (29.0%) were immunosuppressed. (Table 2)

19 patients (38%) with underlying solid tumours died as in patients. 26 patients had ascites at the time of diagnosis but only ten patients were on prophylactic antibiotics (Table 3).

35 patients (18 · 8%) had been diagnosed with underlying haematological malignancies (Table 4), including two cases (5 · 71%) of ESBL producing *Klebsiella pneumoniae*. Seven of these patients (20%) died as in patients.

16 patients (8 · 60%) had documented liver cirrhosis (alcoholic liver disease, five; haemochromatosis, one; viral hepatitis, three; unknown cause, six; Non Alcoholic Steato Hepatitis (NASH), one). Carbapenem sensitive multi-drug resistant (MDR) *Klebsiella* pneumoniae was cultured in two of the patients (12,5%) with underlying cirrhosis. 21 patients had underlying hepatobiliary infections.

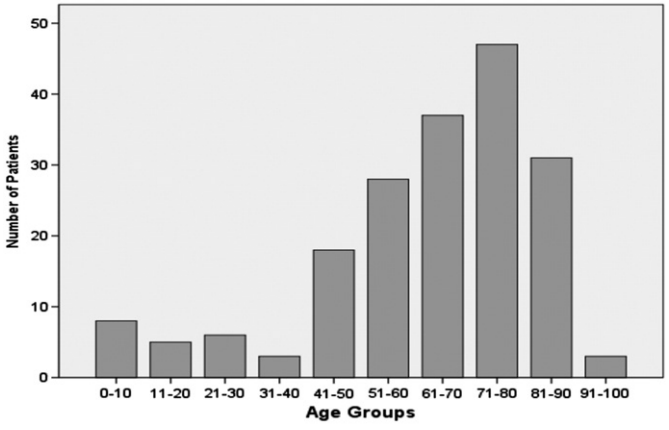

Fig. 1. Number of cases of *Klebsiella pneumoniae* within each age group.

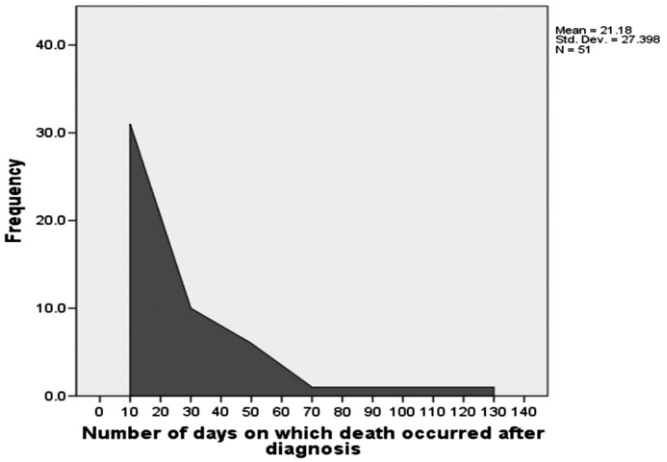

Fig. 2. Death following diagnosis of *Klebsiella pneumoniae*.

28 patients (15,1%) developed septic shock (defined as systolic blood pressure less than 90 mmHg [or a fall in systolic blood pressure of >40 mmHg], or a mean arterial pressure less than 65 mmHg after a crystalloid fluid challenge of 30 mL per kg body weight in a patient with severe sepsis) [2]. KPB was associated with underlying urinary tract infection (35 patients; 18.8%), pneumonia (28 patients; 15.1%), meningitis (two patients; 1.08%). The highest numbers of KPBs were noted in the years 2010 (58 patients) and 2011 (49 patients) (Fig. 3).

105 cases (56.1%) of KPB were diagnosed within the first three days of hospital admission (community-acquired). 76 patients (40.6%) were found to have KPB, three or more days following hospital admission (nosocomial). However there was no statistical significance between the numbers of reported MDR KP in both groups ($p = 0.617$).

4.2. Sensitivities

Most strains of *Klebsiella pneumoniae* were sensitive to Amikacin (99%) and Gentamicin (93%), Imipenem (98%), Co-amoxiclav (80%), Ceftazidime (90%), Ciprofloxacin (86%), Trimethoprim Sulfa (87%), Cefotaxime (85%), Cefazoin (83%), Cefepime (87%), Cefoxitin (83%), Pip/tazobactam (86%), Tobramycin (92%), and Cefotetan (100%). Highest resistances were reported for Ampicillin (97%) and Piperacillin (97%) (Table 5).

Six (3.24%) patients suffered from *Klebsiella pneumoniae* resistant to third generation cephalosporins, fluoroquinolones and aminoglycosides whereas two patients (1 · 08%) suffered from multi-drug resistant strains including resistance to Carbapenems. One of these three patients had underwent a right hemicolectomy due to neoplasm of the colon and was transferred to ICU due to anastomotic leakage. He was treated with Piperacillin / Tazobactam and Metronidazole. Another patient had been

Table 1
Types of underlying malignancies in patients with *Klebsiella pneumoniae* bacteraemia.

Type of Malignancy	Number of patients
Urological	12
Cholangiocarcinoma	11
Colon	10
Pancreas	5
Ovarian and uterine	5
Metastatic squamous cell malignancy of the tongue	2
Laryngeal	1
Lung	1
Thyroid	1
Oesophagus	1
Total number of patients	50