Outbreak of nosocomial sepsis in the Special Care Nursery at Port Moresby General Hospital due to multiresistant *Klebsiella pneumoniae*: high impact on mortality

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SUMMARY

We report an outbreak of nosocomial infection caused by *Klebsiella pneumoniae* in the Special Care Nursery of Port Moresby General Hospital. In the 13 months between October 2007 and October 2008, this organism was cultured from the blood of 57 neonates, of whom 23 died. 16 of the 20 organisms cultured in the first 3 months were cephalosporin sensitive, but during the next 10 months the proportion of sensitive organisms dropped dramatically to 10 of 37. Of the 31 multidrug-resistant organisms 6 were resistant to all the routinely available drugs. Response to the outbreak is discussed. The report highlights the urgent need for the implementation of improved infection control practices and the promotion of rational antibiotic policies.

Introduction

*Klebsiella* is an opportunistic pathogen that primarily targets immunocompromised and hospitalized individuals (1). Nosocomial infection with *Klebsiella pneumoniae* is an important cause of morbidity and mortality for neonates in high-risk nurseries (1). Recent reports of extended-spectrum β-lactamase (ESBL)-producing *Klebsiella pneumoniae* in nurseries have highlighted this problem to paediatricians (2).

The Port Moresby General Hospital (PMGH) is an 850-bed teaching hospital with a 24-bed nursery. There are approximately 11,000 deliveries per year with 1400 newborns admitted to the Special Care Nursery annually.

The Special Care Nursery is a small building located next to the maternity ward, adjacent to the main hospital. It was constructed in 1969 out of fibreboard and, except for a small extension in 1979, it has not been upgraded. It is extremely run-down and lacks basic amenities to accommodate its growing number of patients and their mothers.

A large number of cases of *Klebsiella pneumoniae* bloodstream infection occurred over 12 months from October 2007. The number of cases peaked in May 2008 with 8 multiresistant infections isolated in blood cultures. Of the 57 neonates from whom the organism was isolated, 23 died. The outbreak prompted analysis of the source and risk factors for infection, and implementation of control measures to contain the outbreak.

Methods

Confirmed cases of *Klebsiella pneumoniae* were identified during the period from October 2007 to October 2008 by review of blood culture results in the laboratory. Clinical and epidemiological data were recorded from clinical charts and data from the Nursery’s admission book.

Where possible, information including, but not limited to weight, gestational age, admission source, admission diagnosis, antibiotic therapy and mortality were obtained.

To define overcrowding and understaffing, the nurse-to-patient ratio and level of occupancy were obtained from nursing staff rosters and discussions with staff.

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Observations on infection control practices were made directly, as well as through discussions with the medical staff, trained nurses and community health workers who worked in the Nursery during this period.

Results

57 cases of infection with *Klebsiella pneumoniae* were identified in the 13-month period. Figure 1 shows the number of cases by month. The first positive blood culture for resistant *Klebsiella pneumoniae* was identified on 30 October 2007. During the last 3 months of 2007 there were a large number of patients with a blood culture positive for cephalosporin-sensitive *Klebsiella pneumoniae* (Figure 1). In December, 11 cases of *Klebsiella pneumoniae* were isolated in blood cultures. Only one was a multiresistant strain. There were no cases in January and February. One blood culture positive for multiresistant *Klebsiella pneumoniae* was identified in March. This was followed by an increase in the proportion and number of multiresistant organisms isolated from the Nursery, peaking in May, when there were 8 multiresistant *Klebsiella pneumoniae* bloodstream infections with 5 resistant to all antibiotics tested.

Comparison of the organisms isolated in 2007 with those in 2008 revealed an increasing proportion of multiresistant isolates in the later year. In 2007, 20% of *Klebsiella* isolates were multiresistant compared to 73% in 2008. 16% of the isolates in 2008 were resistant to all routinely available drugs leaving no treatment options (Figures 2 and 3). Over the whole period, of the 31 multiresistant organisms 6 were resistant to all the available drugs.

The median birthweight of neonates was 1750 g (interquartile range 1458-2730) and the median gestation was 35 weeks (IQR 32-39). The reason for admission documented in 55% of cases was for low birthweight/preterm, in 29% for respiratory distress and in 11% for birth asphyxia. The majority of cases (59%) were admitted directly from the labour ward, 19% from home, 17% from the operating theatre, 4% from a private clinic.

![Figure 1. Number of cases of multiresistant and cephalosporin-sensitive Klebsiella pneumoniae – October 2007-October 2008.](image-url)
Figure 2. Antibiotic sensitivity patterns of *Klebsiella* isolates, 2007: 16 cephalosporin-sensitive, 4 multiresistant.

Figure 3. Antibiotic sensitivity patterns of *Klebsiella* isolates, 2008: 10 cephalosporin-sensitive, 21 multiresistant, 6 resistant to all drugs.

Figure 4. Outcome of *Klebsiella pneumoniae* infection.
**TABLE 1**

**VARIABLES FOR KLEBSIELLA PNEUMONIAE BLOODSTREAM INFECTIONS IN THE SPECIAL CARE NURSERY**

**Variables**

**Continuous variables: median (IQR)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median birthweight, grams</td>
<td>1750 (1458-2730)</td>
</tr>
<tr>
<td>Median gestational age, weeks</td>
<td>35 (32-39)</td>
</tr>
<tr>
<td>Median day of admission when BC positive</td>
<td>8 (6-11)</td>
</tr>
<tr>
<td>Median day of admission when febrile or unwell</td>
<td>3 (1-5)</td>
</tr>
</tbody>
</table>

**Categorical variables: number (percentage)**

<table>
<thead>
<tr>
<th>Source</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labour ward</td>
<td>32</td>
<td>59.3%</td>
</tr>
<tr>
<td>Theatre</td>
<td>9</td>
<td>16.7%</td>
</tr>
<tr>
<td>Ward 11</td>
<td>1</td>
<td>1.9%</td>
</tr>
<tr>
<td>Private hospital/clinic</td>
<td>2</td>
<td>3.7%</td>
</tr>
<tr>
<td>Home</td>
<td>10</td>
<td>18.5%</td>
</tr>
</tbody>
</table>

Primary reason for admission:

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm/low birthweight</td>
<td>30</td>
<td>54.5%</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>16</td>
<td>29.1%</td>
</tr>
<tr>
<td>Birth asphyxia</td>
<td>6</td>
<td>10.9%</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>3</td>
<td>5.5%</td>
</tr>
<tr>
<td>Antibiotics on admission*</td>
<td>29</td>
<td>87.9%</td>
</tr>
<tr>
<td>Blood culture before antibiotics*</td>
<td>4</td>
<td>12.1%</td>
</tr>
<tr>
<td>Febrile on admission*#</td>
<td>8</td>
<td>24.2%</td>
</tr>
<tr>
<td>Deaths</td>
<td>23</td>
<td>40.4%</td>
</tr>
</tbody>
</table>

*only 33 of the 57 charts could be found for these variables
*or signs of sepsis
IQR = interquartile range
BC = blood culture
and 2% from Ward 11 (Table 1).

The majority of neonates were afebrile on admission to the Nursery (76%). However, most (88%) were commenced on amoxycillin and gentamicin in keeping with the local protocol. Reasons for starting antibiotic therapy included respiratory distress, maternal fever, prolonged rupture of membranes and use of contaminated instruments during home delivery. The median day of admission when the neonates showed signs of sepsis was day 3 (IQR 1-5) and the median day of sampling with a positive blood culture was day 8 (IQR 6-11).

Blood cultures were only taken in 4 patients before commencement of antibiotics and usually were not taken until empirical therapy had failed. Many patients were treated with one or more broad-spectrum antibiotics before directed treatment matching the antimicrobial sensitivity pattern of the Klebsiella isolate was given.

23 infected infants died (case fatality rate 40%). 29 neonates (51%) were discharged home; 2 (4%) remained unwell in the Nursery; and the outcome was unknown for 3 patients (5%) (Figure 4).

The current nursery was designed for 24 newborn infants. However, its occupancy varies from 30 to 40. On morning and afternoon shifts, there were 3 nurses for 30 to 40 neonates. There would usually be one registered nurse and two community health workers. This would equate to a nurse-to-patient ratio of 1:10 to 1:13. On a night shift, one registered nurse and one community health worker are rostered on, equating to a nurse-to-patient ratio of 1:15 to 1:20.

Hand washing was not routinely performed between handling of infants. Understaffing and overcrowding as well as lack of facilities, such as paper towels, were identified as barriers to frequent hand washing.

Infection control response

Following the rise in cases in May 2008, the front room of the Nursery, which is occupied by the very low birthweight and clinically unstable patients, was vacated for one day and cleaned by staff. Despite these measures, Klebsiella pneumoniae continued to be isolated in blood cultures. The infection control team took swabs from different sites within the Nursery. Multiresistant Klebsiella pneumoniae was identified from a thermometer container, the suction pump, a feeding tube, an intravenous catheter site, the sink and a baby cot as well as the hands of a nursing officer. The front room was then vacated for one week and fumigated. Other infection control responses included restricting the number of visitors to the Nursery.

In mid-October 2008 repeat swabs of multiple sites including the sink, oxygen outlet, intravenous sites and containers holding suction tubing grew multiresistant Klebsiella pneumoniae. Further fatal cases of multiresistant Klebsiella pneumoniae in September 2008 prompted plans to re-locate neonates to another site so that more extensive decontamination of the Nursery could occur.

A supply of imipenem was obtained at considerable expense to treat subsequent infected babies.

Discussion

The most common habitats of Klebsiella are the natural environment and the mucosal surfaces of mammals. Common sites for colonization in humans are the gastrointestinal tract, eyes, respiratory tract and genitourinary tract (1). Once it has been introduced, asymptomatic, colonized patients and/or the hospital environment serve as the reservoir for the organism and rapid spread to other patients can occur via the hands of health care workers.

A number of risk factors have been identified for infection with Klebsiella pneumoniae. These include prolonged hospital stay, low birthweight and low gestational age (3). These characteristics were all common in this review. Previous antibiotic therapy is significantly associated with Klebsiella infection (4) and local antibiotic policy is a major determinant of the colonization pattern (1). The emergence of ESBL-producing strains has been linked to the use of third-generation cephalosporins, which are used widely as empirical treatment for late-onset sepsis in nurseries (5).
private hospital. There were cases of multiresistant *K. pneumoniae* in neonates admitted from all of these sites. The presumed source of infection was an infected neonate who subsequently caused cross-infection and colonization of the Nursery environment. It is probable that a large proportion of the gastrointestinal tracts of infants in the Nursery were colonized with *K. pneumoniae*. Despite environmental decontamination procedures, the organism continued to spread between neonates via the contaminated hands of health workers.

Of note, there were many cases of cephalosporin-sensitive *Klebsiella pneumoniae* infection in late 2007, with the proportion of cases due to multiresistant *Klebsiella* increasing in 2008. It is possible that widespread use of broad-spectrum antimicrobials may have selected for emergence of the multiresistant strain. The dearth of cases seen between January and April 2008 may have been due to a decrease in the number of blood cultures taken, coinciding with loss of experienced staff.

In this review, almost all cases were commenced on antibiotics on admission and many infants were treated with multiple broad-spectrum antibiotics before the organism was isolated, commonly in the second week of admission. Blood cultures were not routinely taken on commencement of antibiotics.

Strategies to avoid the overuse of antibiotics in prophylaxis and empirical therapy are necessary. Where possible, blood cultures should be taken on admission before starting antibiotics and a septic screen should be performed when late-onset sepsis is suspected. This would enable clinicians to cease antibiotic therapy after 48 hours if the blood culture is negative and the patient had no signs of sepsis and guide directed antibiotic therapy based on organism susceptibility patterns.

Casolari et al. found a correlation between understaffing and overcrowding with clusters of *Klebsiella* infection (6). In the PMGH nursery, nurse-to-patient ratios have been as low as 1:20 on some shifts. In the United States, guidelines recommend a nurse-to-patient ratio of 1:1 for patients who are unstable and severely ill, 1:2 for patients who are stable but severely ill, and 1:4 for patients who are stable (6). Although these numbers may be unrealistic in the Papua New Guinean setting, some effort is necessary to address the severe understaffing of nurses and health care workers.

Overcrowding is a major issue. Cots are commonly lined up with no space between them and patients regularly overflow into the nurse’s work station area and isolation room. Bed occupancy is up to 170% of its originally designed capacity. From 1995 until 2007, the number of admissions to the Nursery per annum doubled from 700 to 1400. However, there has been no improvement in the quality or size of the facility.

Nursing staff do not routinely wash their hands between patients and have highlighted understaffing and overcrowding as barriers. The lack of adequate facilities is also a significant contributing factor. There are a total of 4 sinks in the Nursery, all with hand-operated taps. Soap dispensers are often empty and hands are usually dried by air or with hanging towels. There is no provision of paper towels or alcohol-based hand wash. In order to curb the spread of *Klebsiella pneumoniae* in the Nursery, there is an urgent need to re-emphasize infection control procedures, especially hand washing, and provide the necessary resources.

A number of studies have demonstrated containment of outbreaks of *K. pneumoniae* infection by cohorting colonized and infected infants (6,7). In Colombia, Richards et al. performed rectal cultures on all 175 infants in the nursery and cohorted patients who were colonized (7). They demonstrated a reduction in prevalence of colonized patients from 61% to 12% among patients admitted after the intervention. This strategy could be considered in our nursery.

**Conclusion**

*Klebsiella* are opportunistic pathogens that can spread rapidly and infect a large number of neonates causing significant morbidity and mortality. It is likely that the results of this review are an underestimate of the total number of cases and deaths. We continue to see cases of multidrug-resistant *Klebsiella pneumoniae*, a high proportion of which are resistant to all our routinely available antibiotics. Therefore there is an urgent need for infection control measures that counter the spread of this organism. The following recommendations are made:
• Improvement in nurse-to-patient ratios
• Provision of a new and larger neonatal unit with adequate hygiene facilities
• Improvement in infection control practices, particularly routine hand washing
• Development of an antibiotic policy that promotes rational use of antibiotics
• Implementation of surveillance cultures and cohorting to terminate an outbreak.

ACKNOWLEDGEMENTS

We thank Professor John Vince and Associate Professor Trevor Duke for reviewing the manuscript and Dr Dutta and staff from Port Moresby General Hospital Pathology for laboratory work.

REFERENCES