Hospital-acquired *Klebsiella pneumoniae* infections in a paediatric intensive care unit

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Background. Hospital-acquired infections (HAI) are a significant problem in the delivery of intensive care services. Each nosocomial infection prolongs an affected patient's stay in hospital by 5 - 10 days.
Methods. A retrospective case control chart review of children admitted to the paediatric intensive care unit (PICU) in Grey's Hospital between July 2003 and December 2010, who developed a hospital-acquired *Klebsiella pneumoniae* infection, was undertaken to describe the trend in HAI in a newly commissioned PICU and to identify any association with the patient demographics and modalities of care. Patients with a *K. pneumoniae* infection were identified through the PICU infection control surveillance system. Each case was matched to a control of the same age admitted during the same period, with a similar clinical diagnosis.
Results. During the 7.5-year period, 2 266 children <12 years of age were admitted to the PICU. Of these, 113 had *K. pneumoniae* cultured from a body fluid >48 h after admission, including 23 cultured from the blood. Clinical records were obtained for 14 of these patients and matched to control cases of similar age and gender who were admitted at the same time. The length of stay in both the PICU and hospital was longer in children with an HAI compared with the control group (3.7 v. 2.9 and 18.5 v. 9.14, respectively; p=0.04). There was no significant difference in the treatment modalities provided to the two groups, although most patients in the sample group required invasive treatment.
Conclusion. *K. pneumoniae* nosocomial infection was a significant problem encountered in Grey's Hospital paediatric intensive care. It has major cost implications, as it prolongs the length of stay in intensive care and hospital.

S Afr J CH 2014;8(4):125-128. DOI:10.7196/SAJCH.747

Hospital-acquired infections (HAI) are a significant problem in the delivery of intensive care services. Each nosocomial infection prolongs an affected patient's stay in the hospital by 5 - 10 days. This is an important preventable cause of increased cost, morbidity and mortality among hospitalised patients. The incidence of HAI increases with the use of invasive devices and with increased duration of hospitalisation.[1] Hospital-acquired *Klebsiella pneumoniae* in neonatal intensive care units (ICUs) has increased recently with numerous reports of outbreaks in neonatal ICUs throughout South Africa (SA).[2] Investigations into these outbreaks have identified an underlying context characterised by overcrowding, understaffing and a breakdown in infection control measures.

The incidence of HAI varies across ICUs and with different patient profiles.[3] Patients in facilities offering a higher level of care are at greater risk of developing HAI compared with those facililties offering a lower level of care.[4] Patient characteristics and treatment modalities play an important role in susceptibility to, and outcomes from, HAI. In multivariate analyses, modalities of care – specifically central venous catheters, arterial catheters and other procedures in the paediatric ICU (PICU) – as well as brief periods out of the PICU, were all associated with bloodstream infection.[5]

The PICU in Grey's Hospital, Pietermaritzburg, was established in 2003. It was commissioned as a 7-bed unit in July 2003 and increased to an 8-bed unit in 2006. It was closed for 9 months from November 2008 to July 2009 owing to lack of staff, and for 1 month in 2010 during a public sector strike. Since it was commissioned, surveillance systems have noted a low but rising incidence of *Klebsiella* nosocomial infections in the unit. This poses the question whether this is an independent variable or whether it is related to the spectrum of patients admitted to, or the modalities of care provided in, the unit. This study attempted to answer this question by:

- determining the rate of HAI
- identifying the contribution of *K. pneumoniae* to HAI
- describing the profile of patients, treatment modalities and the relationship between these and the incidence of *K. pneumoniae* HAI.

Methods

This was a retrospective case-control chart review of children admitted to the PICU in Grey's Hospital, Pietermaritzburg, over a 7.5-year period from July 2003 to December 2010.

Children of all ages admitted to the PICU and who developed a *K. pneumoniae* infection were eligible for enrolment. Only children with a positive blood culture obtained >48 h after admission to the PICU were considered for enrolment, while tracheal aspirates and urinary cultures were not considered in order to exclude colonisation of these sites. Patients with hospital-acquired *K. pneumoniae* were identified via an infection control surveillance system and were matched with children of the same age and gender who were admitted during the same period with a similar diagnosis.

Exclusion criteria included readmission to the PICU during a single hospital stay, positive blood cultures taken within 48 h of admission, positive cultures from sites other than blood and children admitted from another ICU.

Table 1. PICU statistics, 2003 - 2010

	Admissions	Bed occupancy (%)	ALOS (days)	+BC	All *Klebsiella* cultures	Positive *Klebsiella* BC	Incidence: *Klebsiella*/1 000 patients
2003	78	57.8	9.5	5	6	3	38.5
2004	423	77.5	5. 2	4	7	0	0
2005	324	77.7	7.4	13	11	3	9.5
2006	288	79.5	7.6	13	15	1	3.5
2007	331	79.9	7.8	14	29	4	12.1
2008	303	76.1	6.4	8	14	2	6.6
2009	139	72.7	8.8	13	7	4	28.8
2010	380	61.1	4.7	25	24	6	15.8

PICU = paediatric intensive care unit; ALOS = average length of stay; BC = blood culture.

Clinical records were retrieved from the medical registry and data extracted from the chart for analysis. The χ^2 test was applied for studying the significance of these risk factors in *K. pneumoniae* HAI. The probability value was obtained and considered significant if below 0.05.

Results

During the 7.5-year study period, 2 266 patients were admitted to the PICU at Grey's Hospital (Table 1). Of these, 113 had a positive culture for *K. pneumoniae*, although only 23 (20%) of these were positive blood cultures. Clinical records were retrieved for 14 of these children and matched with control cases identified as described above.

The average number of patients admitted to the PICU during the study period was 28.7 patients per month (median 27, range 13 - 35.3). This figure fluctuated between 27 and 34 patients per month from 2004, once the PICU was fully commissioned. This equates to an incidence of *K. pneumoniae* HAI of 10/1 000 patients. The average bed occupancy was 75.0%, ranging from 57.8% in 2003 to a peak of 79.9% in 2007. The lower rate seen from 2008 to 2010 was associated with the closure of the PICU and the public sector strike. The average length of stay ranged from 4.7 to 9.5 days, with an average of 7.6 days.

During the study period, there were 113 positive cultures for *K. pneumoniae*, including 23 blood cultures (20.4%). *K. pneumoniae* was grown in 24.2% of all positive blood cultures during this period.

The background data of the sample and control patients are presented in Table 2. The mean age of patients in the sample was younger than that of the control group (18.3 v. 26.3 months, respectively), although the range was similar in the two groups (1 - 145 v. 2 - 144 months, respectively). There were equal numbers of girls and boys in the study, but more girls in the control and more boys in the sample groups. The HIV status was unknown in 35.7% (5/14) of the sample and 21.4% (3/14) of the control group. Although more children in the control group were HIV-positive (28.6% v. 21.4% in the sample group), a higher proportion of children in the sample group had evidence of disease progression manifest by a World Health Organization stage of 2 or more (14.3% v. 7.1% in the control group). Almost twice as many children in the sample group were wasted compared with those in the control group. However, none of these differences was statistically significant.

Table 3 shows the treatment modalities received by children in this study. Although more children with *K. pneumoniae* nosocomial sepsis required nasotracheal intubation, second- or third-line antibiotics and steroids, these differences were not statistically significant.

Table 4 shows the outcome of children in this study. The duration of hospitalisation before a positive blood culture ranged from 2 to 14 days. Children in the sample group spent more time in hospital prior to admission to the PICU than those in the control group (3.7 v. 2.9 days, range 0 - 21 v. 0 - 26 days, respectively). The total period of hospitalisation of children in the sample group was double that of those in the control group (18.5 v. 9.1 days, range 5 - 60 v. 2 - 29 days, respectively), which was statistically significant (p=0.04).

Table 2. Background profile of cases

	Sample (N=14)	Control (N=14)	p-value
Age (months), mean (range)	18.3 (2 - 144)	26.3 (1 - 145)	0.57
Gender, *n* (%)			0.35
Female	6 (43)	8 (57)	
Male	8 (57)	6 (43)	
HIV status, *n* (%)			0.47
Positive	3 (21.4)	4 (28.6)	
Negative	6 (42.9)	7 (50)	
Unknown	5 (35.7)	3 (21.4)	
Clinical staging, *n* (%)			0.80
1	11 (78.6)	9 (64.3)	
2	1 (7.1)	0	
3	0	4 (28.6)	
4	2 (14.3)	1 (7.1)	
WHO nutrition, *n* (%)			0.14
Normal	7 (50)	10 (71.4)	
Wasted	7 (50)	4 (28.6)	
Internal referral, *n* (%)	7 (50)	9 (63.7)	0.16

WHO = World Health Organization.

Table 3. Treatment modalities employed in the patients

	Sample, *n* (%)	Control, *n* (%)	*p*-value
Intubation	10 (71.3)	7 (50.0)	0.26
Urinary catheter	13 (92.9)	12 (85.7)	0.55
Antibiotics			0.69
1st line	1 (7.1)	7 (50.0)	
2nd or more	13 (92.9)	7 (50.0)	
Steroids	5 (35.7)	3 (21.4)	0.42

Table 4. Outcome of children in the study

	Sample	Control	*p*-value
Length of stay prePICU (days), mean (range)	3.7 (0 - 24)	2. 9 (0 - 26)	0.78
Length of stay in hospital (days), mean (range)	18.5 (5 - 60)	9.14 (2 - 29)	0.04

PICU = paediatric intensive care unit.

Discussion

Incidence and trends of *K. pneumoniae* HAI

Yogaraj *et al.*[5] found that in their experience, in Washington DC, bloodstream infections accounted for 28% of HAI in the PICU, followed by ventilator-associated pneumonias, which accounted for a further 21%. Lakshmi *et al.*[6] reported on 116 episodes of bloodstream infection in 86 patients in India in 2006, with an incidence of 31.2 episodes/1 000 patient days. Marra *et al.*[7] found that *K. pneumoniae* ranked among the top ten pathogens causing bloodstream infection in the USA and Canada, and that it was the third most prevalent pathogen isolated in Latin America.

K. pneumoniae HAI is a significant problem in the delivery of intensive care services, and prolongs hospital stay. In this study, there was an incidence for *K. pneumoniae* HAI of 10/1 000 admissions, with a range of 0 - 28.8/1 000 patients per annum once the PICU was fully commissioned. Unfortunately, as this was a retrospective study, we were unable to access data on patient days, therefore a figure for comparison with international experience cannot be provided. There are no similar reports of *K. pneumoniae* HAI from SA, although outbreaks have been reported in RK Khan Hospital, Durban,[8] in 1992, Mahatma Ghandi Memorial Hospital, Durban,[2] in 2005 and Tygerberg Hospital, Cape Town, in 2001.[9]

Patient profiles

During the study period, 2 266 children aged 0 - 12 (average 2) years were admitted to the PICU in Grey's Hospital. Even though the number of patients with HIV infection was higher in the control compared with the sample group (28.6% v. 21.4%), more patients in the sample group were severely immunocompromised (14.3% v. 7.1%). Donowitz *et al.*[10] revealed that HIV-infected children and those with prolonged steroid treatment have a significantly reduced immunity which, in turn, is a major risk factor for the acquisition of nosocomial infections. Although not statistically significant, a similar trend was seen in this study, with a higher proportion of patients in the sample group receiving steroids.

Cell-mediated immunity is greatly suppressed in malnourished children, which predisposes these children to nosocomial infection. Isaack *et al.*[11] have reported a higher incidence of nosocomial infection among these children. The current study reveals a similar trend, with 50% of children in the sample group being wasted, compared with only 28.6% in the control group – although, once again, this was not statistically significant.

Impact of management on the incidence of *K. pneumoniae* HAI

As modalities of care increase, susceptibility of patients to nosocomial infection increases. The association between common invasive procedures, including intubation, urinary catheterisation and central venous lines, and *K. pneumoniae* HAI was studied in the current study. A higher rate of intubation and ventilation in the sample group (71.3%) compared with the control group (50.0%) was documented.

Tullu *et al.*[3] found an incidence of 27.54% for hospital-acquired pneumonia in patients with endotracheal intubation. This translated to 7.96/100 days of endotracheal intubation and 8.92/100 days of mechanical ventilation. The incidence of ventilator-associated pneumonia increased with the duration of ventilation; this has been reported previously.[12] In the current study, more patients were ventilated in the sample group, increasing the risk of nosocomial ventilator-associated pneumonia.

Although Darbyshire *et al.*[13] and Narendaran *et al.*[14] reported indwelling urinary catheters as a risk factor for HAI, this was not so in the current study, where there was little difference between the two groups; 92% of patients in sample group were catheterised as compared with 86% in control group.

Central venous catheters are often used in PICUs for vascular access, and Tacconelli *et al.*[15] and Kunin and McCormack.[16] have reported on the association between the duration of catheterisation and HAI. In the current study, there was no difference between both groups, since 42.8% in each group had central venous catheters. Yogaraj *et al.*[5] reported that PICUs have one of the highest central venous catheter-associated bloodstream infection rates, namely 7.7 infections per 1 000 central venous catheter days, surpassed only in burn units and neonatal ICUs. This study did not find a significant difference in the proportion of children in each group who had a central line.

In total, a higher proportion of children with HAI had one or other recognised risk factor, underlying immune status or modality of care, compared with those without HAI. However, unlike other published reports, this was not statistically significant for any individual risk factor, probably owing to the small sample size in this study.

The only statistically significant finding in this study was an increased duration of hospitalisation in children with an HAI (18.5 v. 9.14 days), which is similar to the findings of Deep *et al.*,[1] who reported that the duration of stay was longer in patients with nosocomial infections (9.8 v. 1.8 days), as was the mortality (30.5%) of the studied population. They reported common causes of HAI being *Klebsiella* and *Pseudomonas*. Mortality rate was not calculated in the current study.

Conclusion

K. pneumoniae HAI was a significant problem encountered in the PICU at Grey's Hospital. There was an association between HAI and recognised risk factors, as well as a doubling in the length of stay in hospital. This prolonged stay would not only be associated with an increased cost of care, but also with an ongoing increased risk of further HAI.

Further study is required to establish the broader consequences of these infections and, given the frequency of reported HAI outbreaks in neonatal nurseries, into the prevalence of such infections in other vulnerable groups.

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