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Major article

Extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* in the neonatal intensive care unit: Does vancomycin play a role?

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Background: Extended-spectrum β-lactamase (ESBL)-producing *Klebsiella* species cause worldwide problems in neonatal intensive care units (NICUs). This study aimed to determine possible risk factors for infection or colonization with ESBL-producing *Klebsiella pneumoniae* (ESBLKp) during an outbreak in the NICU.

Methods: A retrospective cohort study was conducted among neonates admitted to the NICU of a teaching hospital in Riyadh, Saudi Arabia, during an outbreak of ESBLKp from April to July 2008. The incidence density ratio was calculated to determine possible predictors of ESBLKp colonization or infection.

Results: During 2,265 person-days of follow-up of 118 neonates, 4 became infected, and 8 were colonized with ESBLKp. Univariate analyzes revealed that, among 14 neonates who were treated with vancomycin, 9 (64.3%) developed infection or colonization with ESBLKp, whereas, among 104 neonates who were not treated with vancomycin, 3 (2.9%) were affected, with an incidence density ratio of 4.22 (95% confidence interval: 1.47-5.15). Parenteral feeding and mechanical ventilation were found to be marginally significant risk factors.

Conclusion: Treatment with vancomycin appears to be a risk factor for infection or colonization with ESBLKp in the NICU setting.

Hospital-acquired infections by multidrug-resistant organisms are important causes of patient morbidity and mortality and cost health care systems between $4.5 and $5.7 billion annually in the United States.[1,2] A common mechanism for antibiotic resistance used by multiple organisms is the secretion of extended-spectrum β-lactamase (ESBL) enzymes that hydrolyze the amide bond of the β-lactam ring, inactivating antibiotics such as penicillins and cephalosporins. Some of these enzymes also are capable of hydrolyzing carbapenems, and therapeutic options to eradicate these strains are limited.[3,4]

Klebsiella pneumoniae is a gram-negative pathogen that can be responsible for outbreaks of nosocomial infections. ESBLs are heterogeneous (temoniera [TEM], sulfhydryl-variable [SHV], and others), and *Klebsiella* strains may carry multiple ESBLs.[5] Outbreaks may also be due to either the emergence of a clonal strain or the multiple strains circulating in a hospital.[6-9] The dynamic evolution of ESBLs requires tedious efforts to keep the medical community updated with the characterization and epidemiology of these organisms. This makes identification and treatment in the outbreak setting challenging for both microbiologists and clinicians.

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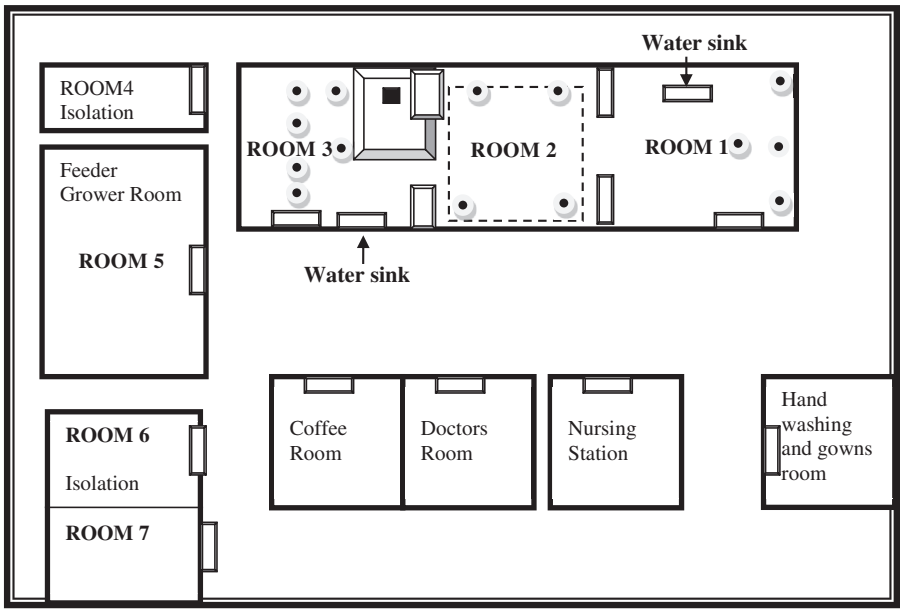

Fig 1. Neonatal intensive care unit (NICU) design at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia.

However, the current phenotypic and genotypic methods for the detection of ESBLs are neither sensitive nor specific for all ESBL types and therefore not routinely used in most clinical microbiology laboratories, further highlighting the difficulty in diagnosing, preventing, and controlling infections with the bacteria producing these enzymes.[10-12]

Hospitalized neonates are a particularly vulnerable population, and infectious outbreaks of ESBL-producing bacteria such as *Klebsiella pneumoniae* (ESBLKp) in neonatal intensive care units (NICUs) are well described.[1-5,13-17] Transmission of ESBLKp can occur from reservoirs of colonized patients during contact with health care workers (HCWs) or result from an environmental source within the health care environment.[13,18-20] Given the profound implications of these infections, much effort has gone into identifying risk factors for invasive disease and methods for outbreak control. These studies demonstrated variable colonization rates among patients and HCWs and identified a variety of risk factors for invasive diseases, suggesting that multiple risk factors are likely and further studies of outbreaks in NICUs can help delineate the importance of these different factors.[14,15,21,22]

The aim of this study was to describe the outbreak of ESBLKp in the NICU at King Khalid University Hospital (KKUH) using both epidemiologic and molecular methods and to determine the risk factors that predispose to the selection, spread, and clinical conditions associated with acquisition.

METHODS

Design

A retrospective cohort study was performed to determine possible risk factors for the acquisition of the outbreak strain of ESBLKp in the NICU at KKUH from April 10, 2008, to July 30, 2008.

Setting

The KKUH NICU is a level II nursery with a capacity of 27 beds within the main tertiary care teaching hospital in Riyadh, Saudi Arabia. This 850-bed hospital serves approximately 1.5 million people with 39,000 admissions and about 3,700 deliveries performed each year. The NICU has the following rooms: acute care rooms 1 and 2 have a maximum capacity of 10 neonates, acute care room 3 has a capacity for 6 beds, room 5 (the feeder and grower room) can house 8 patients, and rooms 4, 6, and 7 are isolation rooms (Fig 1). The nurse-to-patient ratio in these rooms is 1:1. There is a separate area for subacute care with a nurse-to-patient ratio of 1:2. There is 1 sink for every 3 to 4 patients. Medicated soap (4% chlorhexidine gluconate) and alcohol gel hand rub is available at each wash station and at every 2 incubators. Paper towels and gloves are also available in each room. Hand hygiene before and between each incident of patient contact is encouraged for both staff members and visiting parents with or without alcohol hand rub. When monitored over a 2-month period, the hand hygiene compliance rate in different intensive care units was 35.6% among physicians, 44.6% among nurses, 66.4% among technicians or therapists, and 34.9% among other allied health staff. The overall compliance rate in the NICU was 46.9%.[23] No screening program for multidrug-resistant gram-negative organisms was in place in the NICU prior to the outbreak. Approval was obtained from the hospital Ethics Committee to report on this outbreak.

Definitions

The outbreak period was from April 10, 2008, to July 30, 2008. A case of ESBLKp infection was defined as any NICU patient with symptoms or signs of sepsis that included any of the following: reduced activity, bradycardia, apnea, hemodynamic instability, hypoglycemia, and skin mottling, along with a positive culture for ESBLKp from either blood, urine, cerebrospinal fluid, bronchoalveolar lavage with quantitative culture, or aseptically obtained fluid or tissue from a surgical incision. Colonization was defined as the absence of clinical signs of active infection after the detection of ESBLKp from nonsterile sites.

All babies were born at KKUH, admitted to the NICU for the first time, and were not discharged from the NICU before this study; according to hospital policy, babies discharged from the NICU are readmitted in other pediatric units or the pediatric intensive care unit, if needed. Birth weight, gestational age, mode of delivery, and the following dates were recorded: NICU admission, discharge, initiation and conclusion of mechanical ventilation, use of central