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Original article

Carbapenem-resistant *Klebsiella pneumoniae* colonization in pediatric and neonatal intensive care units: risk factors for progression to infection☆

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ABSTRACT

Background: Little is known about factors associated with carbapenem-resistant *Klebsiella pneumoniae* infections in pediatric patients, who are initally colonized with carbapenem-resistant *Klebsiella pneumoniae*.

Materials and methods: A retrospective case–control study was conducted involving pediatric and neonatal intensive care units throughout a five-year period (January 2010–December 2014). Clinical and microbiological data were extracted from Hospital Infection Control Committee reports and patients' medical records. Risk factors were assessed in carbapenem-resistant *Klebsiella pneumoniae* colonized patients who developed subsequent systemic infection (cases) and compared to carbapenem-resistant *Klebsiella pneumoniae* colonized patients who did not develop infection (controls).

Results: Throughout the study period, 2.6% of patients admitted to neonatal intensive care units and 3.6% of patients admitted to pediatric intensive care units had become colonized with carbapenem-resistant *Klebsiella pneumoniae*. After a mean of 10.6 ± 1.9 days (median: 7 days, range: 2–38 days) following detection of colonization, 39.0% of the carbapenem-resistant *Klebsiella pneumoniae* colonized patients in pediatric intensive care units and 18.1% of carbapenem-resistant *Klebsiella pneumoniae* colonized patients in neonatal intensive care units developed systemic carbapenem-resistant *Klebsiella pneumoniae* infection. Types of systemic carbapenem-resistant *Klebsiella pneumoniae* infections included bacteremia ($n = 15$, 62.5%), ventilator-associated pneumonia ($n = 4$, 16.6%), ventriculitis ($n = 2$, 8.3%), intraabdominal infections ($n = 2$, 8.3%), and urinary tract infection ($n = 1$, 4.1%). A logistic regression model including parameters found

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significant in univariate analysis of carbapenem resistant *Klebsiella pneumoniae* colonization and carbapenem resistant *Klebsiella pneumoniae* infection groups revealed underlying metabolic disease (OR: 10.1; 95% CI: 2.7–37.2), previous carbapenem use (OR: 10.1; 95% CI: 2.2–40.1), neutropenia (OR: 13.8; 95% CI: 3.1–61.0) and previous surgical procedure (OR: 7.4; 95% CI: 1.9–28.5) as independent risk factors for carbapenem-resistant *Klebsiella pneumoniae* infection in patients colonized with carbapenem-resistant *Klebsiella pneumoniae*. Out of 24 patients with carbapenem resistant *Klebsiella pneumoniae* infection, 4 (16.6%) died of carbapenem-resistant *Klebsiella pneumoniae* sepsis.

Conclusion: Asymptomatic colonization with carbapenem-resistant *Klebsiella pneumoniae* in intensive care units of pediatric departments should alert health care providers about forthcoming carbapenem-resistant *Klebsiella pneumoniae* infection. Those carbapenem-resistant *Klebsiella pneumoniae* colonized patients at risk of developing infection due to carbapenem-resistant *Klebsiella pneumoniae* may be targeted for interventions to reduce subsequent infection occurence and also for timely initiation of empirical carbapenem-resistant *Klebsiella pneumoniae* active treatment, when necessary.

Introduction

Klebsiella pneumonia is a Gram negative rod belonging to *Enterobacteriaceae* family. Carbapenem resistance in *Klebsiella pneumonia* is mainly associated with *K. pneumoniae* carbapenemase.[1–3] It is a carbapenem hydrolizing beta-lactamase encoded by transmissible plasmids, which facilitate spread of the enzyme among bacterial species.[4] During the last decade, infections due to carbapenem resistant *Klebsiella pneumoniae* (CRKP) has been reported throughout the world, spreading from the United States in 2001.[2] Outbreaks of CRKP has been reported in several countries.[5,6] Rapid and global dissemination of CRKP is of great concern in health care facilities. It can cause diverse infections including primary bacteremia, urinary tract infections, pneumonia, intra-abdominal infections, and wound infections. Crude mortality rate of CRKP infections ranges from 30% to 44%.[7–9] It increases strikingly to 71.9%, when in the case of bacteremia.[10] CRKP strains have higher mortality rate compared to strains susceptible to carbapenem.[7,10]

Prompt initiation of appropriate antibiotic therapy for CRKP infections is crucial for patient survival.[8,11,12] However, appropriate antibiotics like colistin are not administered routinely to these patients until the cultures yield CRKP isolate. Knowing that a patient is colonized by CRKP may be beneficial in deciding to start empirical CRKP active treatment in suspicion of a Gram negative infection.

Risk factors for acquisition of CRKP colonization have been mainly assessed in studies involving adult patients and were identified as antibiotic exposure, especially carabapenem, intensive care unit stay, prolonged hospitalization, poor functional status, invasive devices.[7,8,13–15] CRKP colonization of the host is a major predisposing factor for developing subsequent CRKP infection.[7,16] The studies which evaluate the frequency and risk factors of CRKP infection occurrence in patients rectally colonized with CRKP are limited in the pediatric population. Therefore, the present study was planned to determine the frequency distribution and description of CRKP infections in rectally colonized patients, who were admitted in pediatric and neonatal intensive care units over five years, as well as to identify associated risk factors for developing subsequent CRKP infection.

Materials and methods

Hospital setting, data collection and study design

This report is a retrospective case–control study conducted in a tertiary university teaching hospital in Istanbul, Turkey. Since January 2010, infection control nurses assigned from the Hospital Infection Control Committee (HICC) have performed active surveillance of CRKP and vancomycin-resistant enterococci (VRE) rectal colonization in selective high risk wards, including pediatric and neonatal intensive care units (PICU and NICU, respectively). Rectal swabs of patients admitted to PICU or NICU were routinely screened once a week for the presence of CRKP and VRE. An infection control nurse prospectively tracked all health care associated infections occurring at the PICU and NICU, together with the results of rectal surveillance and reported these data monthly to the HICC. This database was reviewed to identify pediatric patients who were rectally colonized with CRKP and those who developed subsequent CRKP infection from January 2010 to December 2014.

Medical, microbiological and laboratory data were extracted from HICC reports and the patients' own medical records. The data collected from patients with CRKP colonization included demographics, hospital unit at the time of CRKP detection, underlying diseases, invasive procedures within previous four weeks, duration and types of antibiotics use, absolute neutrophil and lymphocyte count at the time of colonization, and type of CRKP infection. In order to identify risk factors for CRKP infection among colonized patients, a case–control study was performed comparing the characteristics of CRKP colonized patients who developed subsequent CRKP infection (cases) with CRKP colonized patients who did