

ABSTRACT

A PROSPECTIVE CASE CONTROL STUDY TO DETERMINE RISK FACTORS AND MORTALITY IN CHILDREN WITH CARBAPENEM RESISTANT ORGANISM SEPSIS

BACKGROUND: Sepsis due to carbapenem-resistant organisms (CRO) is now reported from all over the world, and children are especially vulnerable to these deadly organisms. Although there are numerous studies in adults and neonates about CRO sepsis, prospective studies from the pediatric population from the Indian subcontinent are lacking. This study was hence undertaken to study the risk factors and outcomes including mortality in pediatric CRO sepsis.

OBJECTIVES: Primary objective of the study was to compare mortality due to CRO sepsis with carbapenem-susceptible (CSO) sepsis. Secondary objectives were to look at risk factors for acquiring CRO sepsis and to compare severity of outcomes between these groups.

METHODS: This was a prospective case-control study of all children with gram-negative sepsis admitted to the pediatric wards and Pediatric ICU/HDU of the Christian Medical College, Vellore, from January 2015 to May 2016. Children with CRO sepsis were included as cases and those with CSO sepsis as controls, in a 1:2 case: control ratio. Neonates, children who were not admitted, duplicated and insignificant or contaminant cultures were excluded.

RESULTS: There were 224 children with gram-negative sepsis, of whom 89 had CRO sepsis and 135 had CSO sepsis.

Non-fermenting gram-negative bacteria (NFGNB) including *Acinetobacter* and *Pseudomonas* were more common than *Enterobacteriaceae* (63.4% vs. 34.3%). Children with CRO sepsis were significantly more likely to have been admitted to ICU and undergone procedures such as ventilation [OR 7.2, 95% CI 3.6 to 14.1], urinary catheterization [OR 2.6, 95% CI 1.5 to 4.5] and central venous line placement [OR 4, 95% CI 2.3 to 7.1]. Children with CRO sepsis had a significantly higher risk of developing ventilator-associated pneumonia [OR 4.2, 95% CI 2.1 to 8.5], septic shock requiring inotropic support and multi-organ dysfunction [OR 5.4, 95% CI 2.9 to 9.7]. All-cause mortality in the CRO group was 28%, as compared to CSO group with 8% [p< 0.0001]. Corrected mortality in the CRO group was also significantly higher [52.8% vs 18.5%, p<0.0001]. Resistance to Tigecycline in addition to carbapenems in CRO sepsis was associated with 70% mortality.

CONCLUSIONS: The high mortality in children with carbapenem-resistant sepsis even with appropriate antibiotic therapy, and the advent of pan-resistant gram-negative infections, leads to the conclusion that prevention of spread of these highly virulent organisms in the hospital and community should be a cornerstone of management of carbapenem resistance.