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Evaluating pattern of antibiotic therapy as a risk factor for multidrug resistance in Neonatal Intensive Care Unit at Alexandria University Children Hospital

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In

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ENGLISH ABSTRACT

Introduction: Sepsis in neonatal intensive care units remains one of the most significant causes of morbidity and mortality. Mortality due to sepsis caused by multidrug resistant pathogens is significantly higher. On admission of a neonate, the goal of initiating antibiotic therapy is to optimize management of suspected infection while minimizing risks. Misuse of antibiotics was recognized as a risk factor for multidrug resistant bacterial sepsis.

Aim: This study was conducted to evaluate pattern of antibiotic therapy (one line versus two or more lines) as regards: its role as a risk factor for developing multidrug resistance in neonates admitted to El-Shatby neonatal intensive care unit at Alexandria University Children Hospital and to identify neonates with highest risk, resistance pattern of main pathogens causing infection, and to estimate incidence and survival rates.

Methods: A retrospective medical record review cohort study was conducted on neonates admitted to neonatal intensive care unit at Alexandria University Children Hospital from December 2017 to December 2019. Resistance and susceptibility pattern of bacterial isolates were calculated. Logistic regression analysis was applied on significant variables from univariate analysis to detect factors that can predict the probability a neonate will develop multidrug resistant bacterial sepsis. Kaplan-Meier analysis was performed to estimate the probability of developing early and late onset multidrug resistant bacterial sepsis. Comparison of outcomes between neonates with versus without exposure to multiple lines of antibiotic therapy were made using Cox proportional hazards model.

Results: Incidence rates of early and late onset multidrug resistant bacterial sepsis were 27 per 1000 and 101 per 1000 birth lives, respectively. The risk of multidrug resistant bacterial sepsis among neonates who received two or more lines of antibiotic therapy, was 25% when developing late onset sepsis and 5% when developing early onset sepsis compared to 0% and1% among neonates who received one line of antibiotic therapy, respectively. Statistically significant risk factors for predicting multidrug resistant bacterial sepsis were Pattern of antibiotic therapy OR=13.64; 95% CI. [4.80 – 38.79]. Central venous catheter/Peripherally inserted central catheter OR=4.6; 95% CI. [2.72-7.8], Other tubes and catheters (Chest, gastrostomy, urinary & peritoneal dialysis) OR=4; 95% CI. [1.59–10.26], Mechanical ventilation OR=3.73; 95% CI. [1.06 -13.07], Gastric tube OR=2.5; 95% CI, [1.23–5.06] and Total parenteral nutrition OR=1.87; 95% CI. [1.04–3.37]. The overall risk for mortality related to multidrug resistance was 75% among late onset sepsis compared to 45% for early onset sepsis. *Klebsiella pneumoniae* and *Staphylococcus aureus* (90.3% of which Methicillin resistant) were the main isolated bacterial pathogens in both early and late onset sepsis. Alarming extensive and pan multidrug resistance were found among both *Enterococcus, Acinetobacter* and *Klebsiella pneumoniae*.

Conclusion: Initiating broad-spectrum antibiotics then switching between different lines of antibiotic therapy highly increased the risk of developing multidrug resistant bacterial sepsis. Antibiotic stewardship programs in NICUs should focus on initiating empiric antibiotic therapy targeting multidrug resistant *Klebsiella pneumoniae* and Methicillin resistant *Staphylococcus aureus*, avoiding switching to multiple lines of antibiotic therapy, early identification of microbial pathogen(s), de-escalation into appropriate narrow definitive culture-based antibiotic(s) and to reserve last resort antimicrobials by preauthorization and restriction of Colistin, Linezolid and Carbapenems.

Key Words: "Pattern of antibiotic therapy", "Risk factors", "Multidrug resistance", "NICU"