19. Risk Profile, Clinical Presentation and Immediate Outcomes in Neonates with Fluconazole-Resistant Candidal Sepsis and Their Response to Voriconazole: A Retro-Prospective Case Series

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BACKGROUND: Neonatal candidal sepsis remains a significant cause of morbidity and mortality in neonatal intensive care units (NICUs). Rising rates of fluconazole resistance among Candida isolates pose increasing therapeutic challenges, necessitating the evaluation of alternative antifungal agents such as voriconazole. Data on the use of Voriconazole in this population are scarce, especially in Fluconazole-resistant candidemia. This case series describes the clinical characteristics, risk factors, microbiological spectrum, and treatment outcomes of neonates with fluconazole-resistant candidal sepsis treated with voriconazole in real-world tertiary NICU setting. It contributes a unique, practice-oriented evidence on voriconazole-based therapy in this high-risk population and that voriconazole may achieve microbiological clearance with acceptable safety, while also highlighting the growing predominance of non-albicans Candida species and the urgent need for species-directed antifungal stewardship in neonatal care. **METHODS:** This retro-prospective case series was conducted in a tertiary-care NICU over a period of 3 years (March 2022–March 2026). Neonates with culture-confirmed candidal bloodstream infection demonstrating in vitro or clinical resistance to Fluconazole were included. Demographic variables, risk factors and clinical presentations were recorded. Cultures were processed using the BacT/ALERT system (bioMérieux, France), identification and antifungal susceptibility testing was performed using the VITEK® 2 Compact system (bioMérieux, France) according to CLSI M60 guidelines. All eligible neonates received Voriconazole and repeat blood cultures were obtained after 5–7 days of initiation of antifungal therapy. Antifungal therapy was continued for 14 days following sterile blood cultures. All neonates with candidemia underwent systematic end-organ screening to evaluate for disseminated fungal infection. Patients were followed up until discharge or death and clinical outcomes were documented. Primary outcomes included survival and microbiological clearance; secondary outcomes included duration of antifungal therapy, length of NICU stay, end-organ dissemination, species distribution, antifungal susceptibility profile and associated neonatal risk factors. **RESULTS:** Twenty-six neonates with culture-proven candidemia were included, predominantly preterm (Mean gestational age 34.3 ± 5.1 weeks) and low birth weight (1.78 ± 0.96 kg). Most were male (16, 61.5%) and delivered by C-section (18, 69.2%). Common maternal risk factors included pregnancy-induced hypertension and PPROM. Central vascular access and respiratory support were frequent NICU interventions. Thrombocytopenia was the most frequent clinical manifestation (13, 50%). End-organ dissemination occurred in 9% of neonates. Non-albicans Candida species predominated, with Candida tropicalis (6, 23.1%) being the most common isolate, followed by Candida albicans and Candida krusei (5, 19.2% each). All isolates demonstrated 100% susceptibility to Micafungin, Caspofungin, Amphotericin B and Voriconazole, whereas Fluconazole susceptibility was variable and lowest among Candida glabrata and Candida krusei. The Mean duration of antifungal therapy was 24.5 ± 9.8 days, with blood culture sterilization achieved in 10.17 ± 5.15 days. Survival to discharge was 69.2% (18), while mortality was 30.8% (8). Hepatotoxicity was observed in 15.3 **CONCLUSION:** Fluconazole-resistant neonatal candidemia predominantly affected preterm, low-birth-weight infants and was largely caused by non-albicans Candida species. Voriconazole-based therapy achieved timely microbiological clearance with acceptable safety and survival rate. Species-directed antifungal therapy and antifungal stewardship remain essential and larger multicentre studies are needed to optimize management and long-term outcomes in this high-risk population.

Key Words: Neonate; Fluconazole resistance; Voriconazole; NICU; Candidemia

Figure 1. Composite summary of risk profile, microbiological spectrum, clinical presentation, and treatment outcomes in neonates with Fluconazole-resistant candidemia treated with Voriconazole (n=26).