



## EXPERIENCE WITH ANTI-FUNGALS IN OUR NICU

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**ABSTRACT**

Primary objectives of this study is to know indications of starting antifungal. Secondary objectives to know Incidence of using antifungal in NICU and outcome of neonates in whom antifungals used. Prophylactic antifungal drugs have been shown to reduce fungal colonisation and infection rates in randomised trials in VLBW babies<sup>4</sup>. In this review we discuss the potential benefits and risks of fungal prophylaxis in VLBW babies. The medical case records of all Babies admitted in NICU during the study period were thoroughly analysed for antifungal therapies, indication and day of life when started. The outcome was measured as mortality or discharge. Results- Out of total 14 VLBW babies 86% (12) discharged and 14 % ( 2) died ,out of 4 ELBW babies 50% discharged and 50% died and total 3 post-operative babies 33% discharged and 67% died. Conclusion-Prophylactic antifungal therapy does not affect the mortality in ELBW's and Post Operated groups.

**KEYWORDS** : Invasive fungal infection, very low birth weight, extremely low birth weight, Prophylactic antifungal drugs, mortality.

**INTRODUCTION**

Invasive fungal infection is an important cause of mortality and morbidity in very low birth weight (VLBW) infants. Extremely preterm and extremely low birth weight infants are at highest risk because of the intensive and invasive nature of the care that these infants receive. Additional specific risk factors include prolonged use of parenteral nutrition and exposure to broad-spectrum antibiotics and babies on ventilator. Diagnosis is difficult and often delayed, and this may contribute to the high levels of deep-organ dissemination and associated mortality and morbidity. The most commonly used antifungal agents are amphotericin B and fluconazole. Recent research has assessed the value of early empirical and prophylactic treatment. However, although systemic antifungal prophylaxis reduces the incidence of invasive fungal infection, there is no evidence of effect on mortality. Concern exists about the impact that widespread use of prophylaxis may have on the emergence of antifungal resistance. Survival of extremely preterm babies is increasing and fungal infection is an emerging problem in this vulnerable population. Invasive fungal infection is defined as positive fungal cultures from blood, cerebrospinal fluid or urine (collected by suprapubic aspiration or bladder catheterisation). Early diagnosis of fungal infection can be difficult as it often has a similar presentation to bacterial infection. Babies may present insidiously with poor colour, elevated C reactive protein and falling platelets in the absence of positive bacterial cultures. It is therefore important to maintain a high index of suspicion and to consider screening specifically for fungal infection in at-risk babies when signs of sepsis are present and they are not responding to antibiotics in the usual way. Invasive fungal infection is usually nosocomially acquired. It accounts for approximately 10% of all first episodes of late onset sepsis in very low birthweight (VLBW) babies<sup>1</sup>. *Candida albicans* is the most commonly cultured fungal organism and the third most frequent cause of late-onset sepsis in the VLBW baby<sup>1</sup> The diagnostic sensitivity of blood culture for invasive fungal infection is low at approximately 50%, and therefore the true incidence may be under-represented<sup>2</sup> Preterm, VLBW babies are at greatest risk of invasive fungal infection. If fungal infection is suspected in this population, fungal cultures should be sent and in addition to this other investigations such as renal ultrasound, echocardiography, and ophthalmic assessment should be considered as they may reveal evidence of disseminated candidaemia.

Prophylactic antifungal drugs have been shown to reduce fungal colonisation and infection rates in randomised trials in VLBW babies<sup>4</sup>. However these studies collectively do not show convincing reductions in mortality and appear to take place in units with very high rates of invasive fungal infection in the placebo arm of the trials. There are concerns about widespread use of antifungals because of the potential for toxic side effects and drug resistance. Clinicians remain in equipoise regarding universal fungal prophylaxis<sup>5-7</sup>. Some centres have adopted routine prophylaxis. Others have attempted to limit exposure to prophylactic antifungals by selecting babies with additional risk factors for fungal sepsis, such as exposure to cephalosporins, and they too report reductions in fungal infection rates. In this review we discuss the potential benefits and risks of fungal prophylaxis in VLBW babies. Primary objectives of this study is to know indications of starting antifungal. Secondary objectives to know Incidence of using antifungal in NICU and outcome of neonates in whom antifungals used.

**MATERIALS AND METHODS**

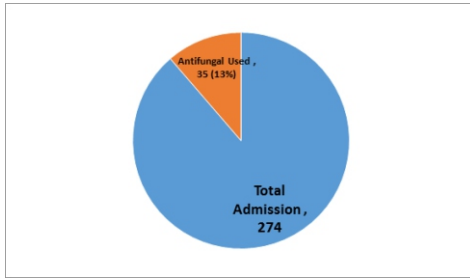
- **STUDY DESIGN:** Medical record based retrospective study
- **STUDY SETTING:** Tertiary care hospital.
- **SAMPLE SIZE:** 35
- **INCLUSION CRITERIA:** Any baby admitted in NICU started on antifungals.
- **EXCLUSION CRITERIA:** Babies not given antifungal therapy

**METHODOLOGY:** The medical case records of all Babies admitted in NICU during the above said period were thoroughly analysed for antifungal therapies, indication for starting and day of life when antifungals were started. Details of indication for which antifungal therapy was started were noted and results were evaluated by means of discharge or death.

**STATISTICAL ANALYSIS:** Data collected was analyzed for statistics in terms of percentage discharged and percentage died during NICU stay.

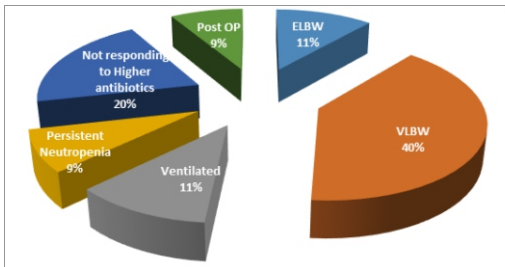
**OBSERVATIONS & RESULTS:**

**Figure 1:1-** Total sample size and Percentage who received antifungals



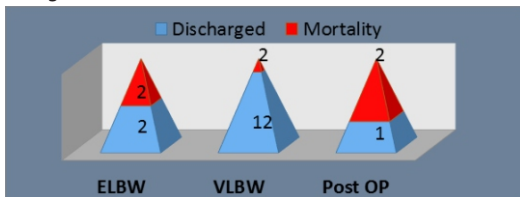
% percentage

Figure 1:2- Indications (percentage) to start antifungals



% percentage, VLBW- Very Low Birth Weight, ELBW- Extremely Low Birth Weight, POST OP- Post-Operative

Figure 1:3- Results in terms of Percentage Discharged and Percentage Deaths



ELBW: Extremely Low Birth Weight, VLBW-Very Low Birth Weight, POSTOP- Post-Operative

**DISCUSSION:**

Major concerns with Fluconazole prophylaxis in preterm infants is emergence of resistance by 2 Mechanisms:

1. Increase MICs (Minimum Inhibition Concentration)
2. Emergence of species with an intrinsic resistance to this azole.

According to the Cochrane Library 2015, the conclusion of “prophylactic systemic antifungal use and reduction of incidence in very preterm or VLBW” should be interpreted and applied cautiously as Meta-analysis does not demonstrate a statistically significant effect on mortality.

According to some study published among ELBW babies(8), fluconazole prophylaxis compared with placebo did not result in a lower incidence of the composite of death or invasive candidiasis and findings do not support the universal use of prophylactic fluconazole in extremely low-birth-weight infants.

In our study Total neonates (n = 274) were admitted out of which 13% (35) were started on antifungals. Average day of life when antifungals were started was on DOL 9 in VLBW, on DOL 1 in ELBW and Immediately after operation in post-operative neonates. Different indications for starting antifungals are Extremely Low Birth Weight Babies , Very Low Birth Weight Babies ,Not Responding To Higher Antibiotics ,Persistent Neutropenia , Babies On Ventilator ,Post Operated babies .Out of total 14 VLBW babies 86% (12)discharged and 14%(2) died ,out of 4 ELBW babies 50% discharged and 50%(2) died and total 3 post-operative babies 33% discharged and 67% died .

**CONCLUSION:**

To Conclude Finally

1) Prophylactic antifungal therapy does not affect the mortality in ELBW's and Post Operated groups

**LIMITATIONS OF STUDY**

- Limited sample size
- Purposive sampling methods
- Areas based research
- Not all babies' suspected fungal sepsis showed fungal growth in blood culture.

**TAKE HOME MESSAGE**

1. Prophylactic antifungal therapy does not affect the mortality in ELBW and Post Operated groups
2. In this era of resistant strains : Are we proceeding ahead in developing resistant Invasive fungal strains “A SERIOUS THOUGHT TO BETHOUGHT OF ”

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