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FREQUENCY OF FUNGAL INFECTIONS IN NEONATES: A RETROSPECTIVE STUDY CONDUCTED IN A TERTIARY CARE HOSPITAL OF NORTH-EAST PUNJAB

Sidra Ameen[1], Muhammad Faheem Afzal[2], Maryam Ameen[3], Afifa Munir Ahmad[4], Aleena Hussain[5], Arshia Tabassum[6]

[1]PGR Paediatrics department, Lahore General Hospital, Lahore. drsidraameen01@gmail.com
[2]Professor, Paediatrics department, PGMI/AMC/Lahore General Hospital, Lahore, Email mfaheem169@yahoo.com
[3]MPhil Student Epidemiology and Public Health, University of Agriculture Faisalabad Pakistan, Email: maryamameen97@gmail.com
[4]Senior Registrar, Paediatrics department, Queens Medical College Kasur, afifa_munir1993@hotmail.com
[5]Senior Registrar, Paediatrics department, Avicenna Medical College, Email. aleenahussain@gmail.com
[6]Senior Registrar, Paediatrics department, Avicenna Medical College, Email: arshiatabassum79@gmail.com

ABSTRACT:
Background: Invasive fungal infections mainly of candida species are of prime importance because of its high morbidity and mortality in neonates. This issue is of great public health concern. However, insufficient epidemiological information is available in low and middle income countries like Pakistan. The **objective** of the present study was to determine the frequency of fungal infection among the neonates between May – December 2023.**Methodology:** A retrospective descriptive study was conducted in department of pediatrics, Lahore General Hospital Lahore. A total of 272 neonates admitted to NICU were included in this study to determine the frequency of fungal infection among the study population. Categorical variables were presented in the form of percentages and numbers. Presence and absence of fungal infection was determined by following the available clinical and microbiological record of the under study population. Data of the understudy neonates were recorded in Microsoft Excel sheet from the hospital medical record. **Results:** Candida species were found in under study neonates, p-value for birth weight and gestational age were found significant and among risk factors p-value of prematurity, mechanical ventilation and prolonged hospital stay were found significant. **Conclusion:** Frequency of neonatal fungal infection was 8.45% and among the risk factors prolonged hospital stay, prematurity, mechanical ventilation were found significant while use of broad spectrum antibiotic and umbilical catheterization were found non significant.

KEYWORDS: Neonatal fungal infection, Candida infection, risk factors

INTRODUCTION:

The term "invasive fungal infection" (IFI) describes conditions where fungus enter the body and spread, resulting in tissue damage and inflammatory responses. IFI has emerged as the primary cause of infections in premature infants in NICUs due to a number of factors including the rise in high-risk children admitted to NICUs, the increasing use of broad-spectrum antibiotics, the rise in invasive procedures, and the use of sophisticated life support systems. Currently, Candida is the leading cause of fungal infections in new-borns (Engbers et al., 2022).

Candida albicans is the most prevalent pathogenic species, but non-albicans species such as Candida tropicalis and Candida parapsilosis are also common, and regional variations in pathogenic species have been reported (Fly et al., 2022). Candida infections can manifest as invasive candidiasis that resembles sepsis, oral thrush, or Candida diaper dermatitis (Talapko et al., 2021). Clinical Indicators of invasive candidiasis are Lethargy, temperature instability, food intolerance, apnea, hypotension, respiratory distress, abdominal distension, and thrombocytopenia (Charoo et al., 2019).

Candida species that cause NIC can be acquired horizontally from the neonatal intensive care unit (NICU) setting or vertically from a colonized mother upon vaginal delivery (Kilpatrick et al., 2022).The latter situation, where inadequate hospital practices may result in intermittent outbreaks of NIC, is commonly documented from low- and middle-income settings. Both geographical regions and different centers within the same region have varied rates of NIC. According to epidemiological research, the most frequent species causing NIC in high-income countries (HICs) are Candida albicans and Candida parapsilosis (Warris et al., 2019). Studies exploring the epidemiology of candidiasis in developing country hospitals are rare

METHODOLOGY:

A retrospective descriptive study was conducted between May -December 2023 in NICU of pediatric department of Lahore general hospital Lahore to determine the frequency of fungal infection in neonates admitted to NICU. All the eligible neonates admitted to the selected NICU during the specified period of time which were 272 included in the present study by using census sampling technique. Hospital medical and microbiological record was reviewed retrospectively.

The inclusion criteria was

- Neonates with age of 28 days at the time of admission
- Neonates admitted to NICU during the specified period of time
- Neonates with microbiological and medical record available

And the exclusion criteria was

- Neonates having records with missing necessary information
- Individuals admitted after 28 days of birth
- Neonates with unconfirmed microbiological record

Operational Definition:

Fungal Infection: In the present study, fungal infection was defined as the documented neonatal fungal infection in the clinical and microbiological records of the hospital

Data Collection:

After approval from the ethical committee of the hospital the data of the neonates admitted to the NICU during the specified period of time was identified from the hospital medical and microbiological record system. All the identified record was screened and the demographic information, microbiological information and the relevant clinical information was recorded in Microsoft Excel based data sheet. Frequency of the fungal infection was measured using standard frequency measuring formula.

Data Analysis: The data were analyzed using SPSS version 26 and recorded in the form of percentages and frequency.

RESULTS:

Among the positive cultures (23/272), *Candida albicans* were 15 (65.2%) and other species were 8(34.8%). Demographic information showed that males were more in number as compare to females. Out of 272 under study neonates 163 were with birth weight ≤ 2499g and premature neonates were 162 in number (Table 1.1)

Table 1.1: Demographic distribution

SR.NO.	Characteristics	Distribution	N=272	Results in %
1	Gender	Male	156	(57.35)
		Female	116	(42.64)
2	Birth Weight	≤ 2499g	163	(59.92)
		>2499g	109	(40.07)
3	Gestational Age	≤ 36 weeks	162	(59.55)
		>36 weeks	110	(40.44)

Among perinatal characteristics 117 were out born and 155were inborn in study population and antenatal care was given to 191 neonates. In study population 158 neonates were delivered by CS and 114 were through SVD (Table 1.2)

Table1.2: Perinatal Characteristics

SR.NO.	Perinatal Characteristics	Category	N=272	Percentages %
1	Place of Birth	Inborn	155	(56.98%)
		Out born	117	(43.01%)
2	Antenatal Care	Received	191	(70.22%)
		Not Received	81	(29.77%)
3	Mode of Delivery	CS	158	(58.08%)
		SVD	114	(41.91%)

In the present study neonates with prematurity were 162, umbilical catheterization was observed in 11 neonates, Neonates with prolonged hospital stays (> 7 days) were, mechanical ventilation and broad spectrum antibiotics exposure were 104, 89, and 245 respectively. Percentage values of the study risk factors are mentioned in the figure 1.1

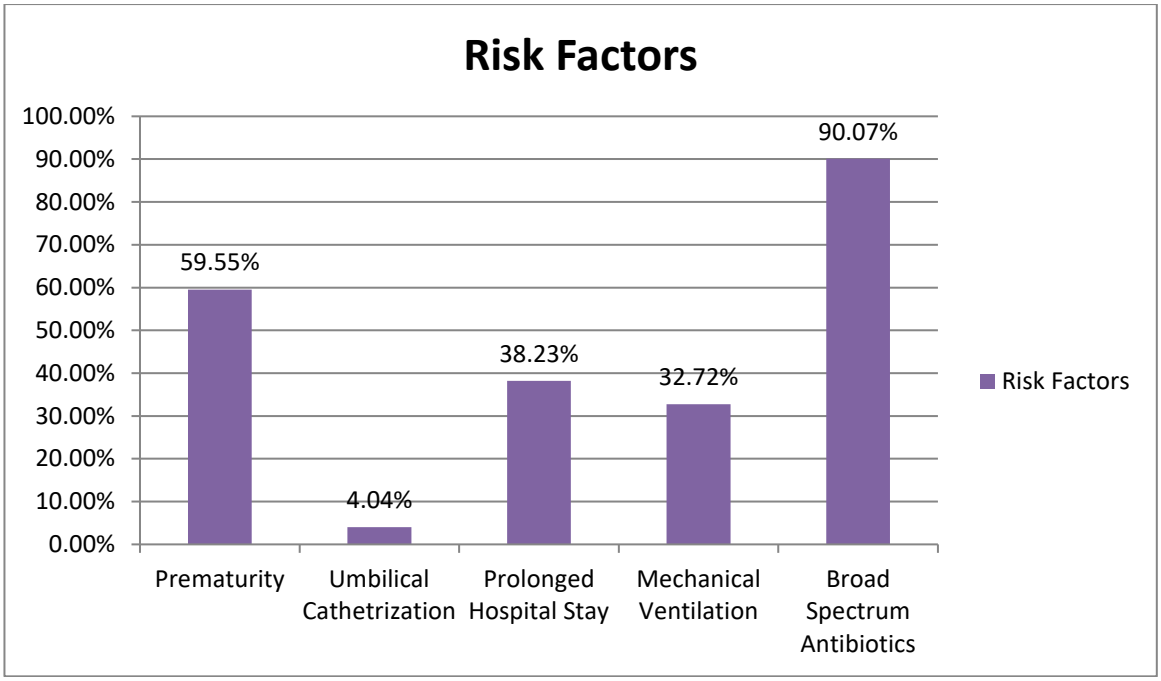


Figure 1.1: Graphical Presentation of Presence of Risk Factors

On the basis of microbiological considerations 23 neonates were found with fungal culture positive and most common microorganism was *candida albicans* and was observed in 15 neonates and remaining 8 were observed with other *candida* species. In males 14(8.97%) and in females 9(7.75%) developed fungal infection. P-value for birth weight and gestational age were found significant (Table1.3). Frequency of fungal infection with respect to risk factors were also measured (Table 1.4). Chi-square and Fisher Exact test were used to find the association of fungal infection with risk factors. For risk factors broad spectrum antibiotics and umbilical catheterization p-value was calculated by Fisher's exact test and for all other factors and variables Chi-square test was used. P-values of birth weight and gestational age were found significant (P-value less than 0.05 was considered as significant).

Table 1.3: Frequency of fungal infection on the basis of demographic and perinatal characteristics

SR. NO.	Characteristics	Distribution	Frequency	Percentage	P-value
1	**Gender**	Male	14	(8.97%)	0.74
		Female	9	(7.75%)	
2	**Birth Weight**	≤ 2499g	19	(11.65%)	0.019 *
		>2499g	4	(3.66%)	
3	**Gestational Age**	≤ 36 weeks	19	(11.72%)	0.019*
		>36 weeks	4	(3.63%)	
4	**Place of Birth**	Inborn	11	(7.09%)	0.36
		Out born	12	(10.2%)	
5	**Antenatal Care**	Received	14	(7.32%)	0.34
		Not Received	9	(11.11%)	
6	**Mode of Delivery**	CS	14	(8.86%)	0.78
		SVD	9	(7.89%)	

* P-value less than 0.05 were Significant.

Table1.4: Frequency of fungal infection on the basis of risk factors

Sr. No.	Risk Factor	Total	Frequency	Percentage %	P-value
1	**Prematurity**	162	19	11.72	0.019*
2	**Broad Spectrum antibiotics**	245	23	9.38	0.12
3	**Umbilical catheterization**	11	1	9.09	1
4	**Mechanical ventilation**	89	15	16.85	0.003*
5	**Prolonged Hospital stay**	104	14	13.46	0.024*

DISCUSSION:

The present study showed that out of total under study neonatal population (272) 23 were found with fungal culture positive (8.45%). On microbiological basis 15(65.2%) were *Candida albicans* and 8(34.8%) were found with other species comparable with the results of study conducted by (Tunc et al., 2023). There are limited reported studies available from Punjab Pakistan related to the frequency of fungal infections in neonates. A study conducted in Pakistan reported fungal infection 10.2% (Afzal et al., 2020) which is higher than 8.45% of our study. If we compare our result with the cross border countries like china a study conducted in china showed the results of fungal infection as 1.3%(Chen et al., 2016) and are comparable to our study.

The present study indicates that fungal infection was more prevalent in neonates with birth weight ≤ 2499g and gestational age ≤ 36 weeks which was 11.65% and 11.72% respectively. Among total identified fungal infections *Candida albicans* infection were more common which is 65.2%. High morbidity and mortality rates in newborns are linked to systemic fungal infections, particularly in extremely low birth weight preterm infants. Due to frequent antibiotic treatments, prolonged parenteral nutrition, and immunological deficiencies brought on by infancy, preterm newborns are susceptible to fungal infections. The reported early neonatal sepsis due to candida were 1.4% while 16.7% in late-onset sepsis in extremely low birth weight neonates (Gülaşı and Çelik, 2016).

In a single-center study of nosocomial infections, they found 61.9% Gram-positive bacteria, 30.9% Gram-negative bacteria and 7.2% fungi (Tunc et al., 2023).Studies in Europe have reported this rate as varying between 1.1 and 1.3% Caggiano et al., 2017). Another study reported the candida infections which is 9% (Benjamin et al., 2010) and is higher than 8.4% recorded in our study. In the present study percentage of fungal infection developed is more neonates born via C-section which is 14(8.86%) comparable with the results of the study conducted by (Auriti et al., 2022).

Obstetric tears are thought to be related to this enhanced colonization of *candida albicans*. Adherence to vaginal epithelial cells is the first stage of fungal infection. By generating cytokines and inflammatory mediators, the vaginal epithelial cells try to reduce fungal infection. The stimulation of endocytosis and active penetration mediate the binding of Candida albicans. Protease synthesis promotes vaginal epithelium degradation by breaking the strong epithelial protein connections, and hyphal development is engaged in the active penetration process between vaginal epithelial cells. Both endocytosis and penetration, which result in necrosis and apoptosis, are responsible for this damage to the vaginal epithelium (Moyes et al., 2015).

Among the total under study neonates, neonates with ≤ 36 weeks of gestational age and mode of delivery CS was most common similar to the results of the study conducted by (Butt et al., 2024). In the present study fungal infection was more common in males (8.97%) as compare to the females similar to the results of the study conducted by (Hsu et al., 2018).

The ability of Candida species to adhere to foreign materials (such as invasive and indwelling devices) and form biofilms, which may be linked to high virulence, is well known. These biofilms act as a biological barrier that keeps antifungal agents from penetrating and shields the fungal cells from host immune responses. This information may help to explain why indwelling and invasive medical devices have been linked to a higher risk of candidaemia (Zhang et al., 2012).

Among the under study risk factors prematurity, prolonged hospital stay and mechanical ventilation were found significant similar to the results of the studies conducted by (Chen et al., 2016). While broad spectrum antibiotic use and umbilical catheterization were found non-significant similar to the results of the study conducted by (Afzal et al., 2020).

The study has certain limitations. The study's statistical power may have been impacted by the single center design. There were no sophisticated microbiology facilities available for species identification. It was not possible to determine the incidence of candidaemia with rising antibiotic use. Since the facility's nursery does not routinely use central line catheters, this could not be identified as a risk factor. Despite these limitations, this study might be regarded as contributing important information to the literature. The authors were able to exclude possible confounders and include all patients with positive fungal sepsis who fit the case description. The results of this study support the need for local recommendations for the empirical and preventive treatment of candidaemia a public health issue, especially in extremely preterm infants in the intensive care unit who are at risk for Necrotizing Enterocolitis**.**

CONCLUSION:

The study concluded that the frequency of fungal infection was 8.45%. Among the understudy risk factors prematurity, mechanical ventilation and prolonged hospital stay were found significant. Neonatal fungal infection is an important public health issue and requires great attention to cope with the situation.

Conflict of Interest: Authors showed no conflict of interest.

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