Original Research Article

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20173803

Clinical profile of Candidiasis in neonates

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Received: 12 July 2017 Accepted: 05 August 2017

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ABSTRACT

Background: Opportunistic infections are increasing in Neonatal Intensive Care Unit (NICU). Neonates often have compromised skin integrity, gastrointestinal tract disease, chronic malnutrition, central venous catheters, long term endotracheal intubation and other factors that lead to increased risk of acquiring such infections. Infections with fungi (candida) and with coagulase-negative staphylococci (CoNS) are especially prevalent. The need of study is to know the clinical profile of candidiasis in neonates in our setup and to determine associated risk factors of candidiasis.

Methods: The present study was undertaken by Dept of paediatrics, SSIMS and RC Davangere among 296 neonates of which 96 babies admitted in NICU and 200 were in PNC ward to study clinical profile of candidiasis in neonates and risk factors associated with them. Parents of 296 babies were interviewed using preformed study proforma. Clinical examination was done and investigations included KOH examination of oral swab, Gram stain of the swab and blood culture of suspected sepsis babies. There are several factors associated with development of neonatal candidiosis. Of them, prematurity, LBW, perinatal birth asphyxia, long term antibiotics, central venous catheters, mechanical ventilation, septicemia, played a major role in development of candidosis.

Results: In the present study, incidence of candidiasis in neonates revealed 13.8% of babies admitted in NICU. Male babies out numbered the female babies in incidence of candidiasis in neonates. Males formed 69% and females 31% of positive cases. Most of neonates admitted in NICU (96) were of low birth weight between 1.5kg to 2.5 kg. Out of which most of cases positive for candidiasis/candidemia were belonged to 1.0-1.5 kg. In present study, 13 babies were positive for candidiasis, of which 5 babies (38.3%) were of birth weight between 1-1.5kg. Birth asphyxia alone or with mechanical ventilation played an important risk factor in development of candidiasis in neonates. In present study, birth asphyxia and mechanical ventilation per se had played a significant role in development of candidiasis in neonates admitted in NICU.

Conclusions: The present study revealed the clinical profile of candidiasis in neonates associated with various risk factors. Study shows that low birth weight, birth asphyxia and mechanical ventilation were significant risk factors for candidiasis in neonates. Blood cultures were positive in babies without mucosal lesions suggesting the importance of diagnosing fungal sepsis.

Keywords: Birth asphyxia, Candidiameia, Oral candidiasis

INTRODUCTION

Opportunistic infections are increasing in Neonatal Intensive Care Unit (NICU). Neonates often have compromised skin integrity, gastrointestinal tract disease, long duration of antibiotic therapy, central venous catheters, long term endotracheal intubation and others factors that lead to increased risk of acquiring such infections.¹ Infections with fungi (candida) and with

coagulase-negative staphylococci (CoNS) are especially prevalent.¹

Candidiasis refers to fungal infections with fungi of genus *candida*. Candidemia is presence of *candida* fungi in the blood. Most of neonatal infections are caused by candida albicans or candida parapsilosis. Preterm infants are predisposed to candida infections because of immaturity of their immune system. Transmission of candida may be vertical (from maternal vaginal infection) or nosocomial.

Approximately 10% full term infants become colonised in gastrointestinal tract and respiratory tracts in first 5 days of life. Colonization of health worker is as high as 30%. Initial site of colonization is gastrointestinal tract.² Skin colonisation is common after 2 weeks of age.³ Invasive fungal infection occurs in approximately 6% to 7% of all infants admitted to the neonatal intensive care unit (NICU), but the incidence is inversely correlated with birth weight: the lower the birth weight, the greater the risk of invasive fungal infection.⁴

Host factors that contribute to the susceptibility of the NICU infant to fungal infection include birth weight of less than 1500 g, 5-minute Apgar scores of less than 5, disruption of cutaneous barriers by percutaneous catheters and relative immunocompromise ascribable to reduced numbers of T cells, impaired neutrophil number and function, and reduced levels of complement.

Concomitants of nursery care that are thought to increase the risk of fungal infections include prolonged use of antimicrobials (especially third-generation cephalosporins), indwelling central venous catheters, abdominal surgery; parenteral nutrition, parenteral lipid formulations, histamine H_2 receptor antagonists, endotracheal intubation and length of stay more than 1 week.⁴

Risk factors include: a) very low birth weight (<1500gms); b) use of broad spectrum and or multiple antibiotics; c) use of central venous catheters; d) parenteral alimentation and intravenous fat emulsion; e) colonization of candida and or previous episode of mucocutaneous candidiasis; f) prolonged urinary catheterization.²

The need of study is to know the clinical profile of candidiasis in neonates in our setup and to determine associated risk factors of candidiasis.

Candida is a common cause of oral mucous membrane infection and perineal skin infections in newborn infants. Disseminated candidiasis and candidemia have become a frequent problem in NICU.⁵

Over the last 2 decades, yeasts have become important nosocomial pathogen, *Candida*species being the most frequent isolate. This rise is largely attributed to extensive use of broad-spectrum antibiotics and advances in medical field, which contri-bute towards the large pool of susceptible population available for these opportunistic pathogens.⁶

Importance of Candida species in nursery and intensive care units (ICUs) is increasingly being recognized. Candida species account for 9-13% of all blood isolates in neonatal intensive care units (NICUs) Although C. albicans has historically been the most frequently isolated species, infections caused by the nonalbicans Candida have been diagnosed with increasing frequency in recent years, notably *C. tropicalis, C. glabrata*, and *C. parapsilosis*. Common use of broad-spectrum antibiotics, low birth weight (LBW), prematurity, and intravenous catheter, etc. makes neonates prone to candidemia.⁶

The incidence and associated mortality due to candidemia can be influenced by several factors including characteristic of the population at risk, standard of the health care facilities available, distribution of *Candida* species, and prevalence of antifungal resistance. These factors may vary from one geographical region to other. The increased isolation rates of nonalbicans *Candida* species and a gradual shift in the antifungal susceptibility profile have underlined the need to monitor laboratory data for possible emergence of resistance and to select most appropriate antifungal agent for therapy.⁷

Recently, non-albicans *Candida* have emerged as important opportunistic pathogen, notably *C. tropicalis, C. glabrata* and *C. parapsilosis*. This could be because of selection of lesser susceptible non-albicans species due to frequent use of fluconazole. The need of study is to know the clinical profile of candidiasis in neonates in our setup and to determine associated risk factors of candidiasis.

METHODS

It is a prospective study to ascertain clinical profile of fungal infections and its incidence in neonates admitted in SSIMS and RC; Davangere. Duration of study was 1st November 2014 to 31st October 2015. After taking written informed consent from the parents and fulfilling inclusion and exclusion criteria of neonates will be included in the study.

Method of study

Neonates hospitalized for more than three days will be serially studied until discharge from the neonatal intensive care unit. Detailed physical examination will be undertaken to look for mucocutaneous candidiasis in newborns. Scrapings from oral thrush, diaper rash, and skin rash will be examined for presence of candida species by Gram Stain and KOH preparation. Gram staining will be done to identify fungi.

KOH mounting will be done to see the fungus clearly. Blood culture to diagnose systemic candidiasis will be done in babies positive for mucocutaneous candidiasis. Blood culture for candidiasis will also be done in babies presenting with septicemia. Newborns with mucocutaneous candidiasis will be started with local antifungal application and will be monitored for response. Babies showing positive blood culture will be started on systemic antifungal drugs.

Laboratory evaluation

- Scrapings from oral thrush, diaper rash, and skin rash will be examined for presence of candida species by Gram Stain and KOH preparation.
- Gram staining will be done to identify fungi.
- KOH mounting will be done to see the fungus clearly.
- Blood culture to diagnose systemic candidiasis will be done in babies positive for mucocutaneous candidiasis.
- Blood culture for candidiasis will also be done in babies presenting with septicemia.
- Species identification will be done using biochemical tests.

Inclusion criteria

All neonates admitted in the Neonatal intensive care unit and post natal wards of SSIMS and RC, Davangere, India.

Exclusion criteria

Neonates already on antifungal drugs for suspected candidiasis. Neonates which died within 48hrs of admission because of obvious causes like severe birth asphyxia and fatal congenital anomalies.

RESULTS

Incidence

296 babies were admitted in NICU and PNC had been evaluated for candidiasis in neonates.

Among 296, 96 babies admitted in NICU, rest of them were admitted in PNC. 13 babies (13.8%) were positive for candidiasis including both gram stain and culture for candidiasis admitted in NICU. None of babies admitted in PNC were positive for candidasis.

Table 1: Incidence of neonatal candidiasis in NICUand PNC.

Cases	Positive	%	Negative	%	Total
NICU	13	13.8	83	86.2	96
PNC	0	0	200	100	200
	13		283		296

Sex distribution

Out of 296 babies, 96 were admitted in NICU and evaluated for candidiasis.

Remaining 200 babies were screened for candidiasis admitted in PNC and OBG ward. Among babies admitted in NICU have equal sex distribution, compare to babies screened for candidiasis in PNC ward.

Table 2: Sex distribution in NICU and PNC.

Sex	NICU	Positive	PNC	Positive
Male	48	9 (75%)	119	0
Female	48	4 (25%)	81	0
Total	96	13	200	0

Birth weight and positivity of gram stain and culture

Among 296 babies evaluated for candidiasis, 96 babies were admitted in NICU.

Maxmimum number of babies were between 1.5 to 2.5kg (n=47). Babies more than 2.5kg were 38.

Out of 13 babies positive for both gram stain and blood culture, maximum number of babies were between 1 to 1.5kg (5 out of 13) 38.3%, p<0.0313 in NICU.

Table 3: Birth weight distribution in NICU, PNC and OBG.

Birth weight (BW)	NICU	Positive gram stain and culture for candidosis.	%	PNC	Positive gram stain and culture for candidosis	%
< 1 kg	1	1	100	0	0	0
1.0-1.5 kg	10	5	50	1	0	0
1.5-2.5 kg	47	4	8.5	51	0	0
>2.5 kg	38	3	7.8	148	0	0
Total	96	13	13.5	200	0	0

Risk factors of candidiasis in neonates: birth asphyxia

Among 296 babies, 96 neonates were admitted in NICU, of which 19 had birth asphyxia. 5 neonates of which

developed oral candidiasis (P<0.004, CI-0.079) and were positive with gram stain and 3 babies had developed candidemia (P<0.004). Babies born in PNC and OBG ward had no significant relation to birth asphyxia.

Table 4: Distribution of cases in relation to birth asphyxia in NICU and PNC (gram stain for candidosis).

	Gram stain			PNC		Total
	Positive	Negative		Positive	Negative	
Yes	5 (55%)	14	19	Nill	Nill	
No	4 (44%)	73	77	Nill	200	
	9	87	96		200	296

Table 5: Distribution of cases in relation to birthasphyxia in NICU (blood culture for candidosis).

Birth asphyxia	Blood culture		
	Positive	Negative	Total
Yes	3 (75%)	16	19
No	1 (25%)	76	77
	4	92	96

Mechanical ventilation

96 neonates were admitted in NICU, of which 19 had birth asphyxia. Among 19 babies, 13 babies needed mechanical ventilation support of which, 5 of neonates developed oral candidiasis and were positive with gram stain (p<0.0001, CI-0.067).

Table 6: Distribution of cases (gram stain for candidosis) in relation to mechanical ventilation in NICU.

Mechanical ventilation	Gram stain		
	Positive	Negative	Total
Y	5 (55%)	8	13
N	4 (44%)	79	83
	9	87	96

Hematological profile

96 babies admitted in NICU underwent septic screening like total leucocyte count, CRP, blood culture.

Table 7: Distribution of cases (gram stain and culture)in relation to total leucocyte count in NICU.

ТС	Cases	Positive cases	%
<10000	19	3	15
10000-20000	56	5	8.9
20000-30000	21	5	23
>30000	0	0	

Out of 96 babies, 56 cases has increased total counts compare to other groups (p<0.8). Among 13 positive

cases, most of neonates had total counts between 10000 to 30000.

C-reactive protein

Among 96 babies admitted in NICU, 74 babies had CRP positive with 5 cases positive for gram stain (p<0.9) and three for blood culture of candidemia (p<0.3).

Table 8: Distribution of cases (gram stain) in relationto CRP in NICU.

CRP	GS		
	Positive	Negative	Total
Positive	5	69	74
Negative	4	18	22
	9	87	96

Maternal risk factors

The various maternal risk factors like, premature of membrane (PROM), meconium stain amnioitic fluid (MSAF), fetal distress, preeclampsia, pregnancy induced hypertension (PIH) clinically associated with candidiasis of neonates.

Table 9: Distribution of cases in relation to maternalrisk factors in NICU.

Risk factors	No of cases in NICU	Positive cases
PIH	33	5
PROM	13	3
MSAF	19	4
Polyhydramnios	1	1
APH	2	0
No risk factors	28	0

DISCUSSION

Neonatal candidosis has a various presentation and this study reveals clinical profile of these babies admitted in NICU. In order to decrease the morbidity of these neonates suffering from candidosis, early detection and management of candidosis is required.

Table 10: Distribution of cases in relation to maternalrisk factors in PNC and OBG.

Risk factors	No of cases in PNC and OBG
PIH	26
PROM	34
MSAF	30
Polyhydramnios	0
APH	4
No risk factors	106

Hence the present study has made an attempt to evaluate the various risk factors and their significance in the development of candidosis. In the present study babies admitted in PNC wards had not developed candidosis since babies got discharged within 3-5 days and for colonization a minimum period of 10 days is required.

296 babies were evaluated in study and reveals the incidence of candidiasis is 13.8% among babies admitted in NICU of 96 babies. The present study had more prevalence among babies admitted in NICU compared to PNC and these results are comparable to study conducted by Martin and Stephen (10%).³

Among babies admitted in NICU, male sex has a predominant role in development of candidiasis in neonates. Among 96 babies, 13 neonates had candidiasis, of which 9 are male babies (75%) compare to females. In present study, male sex has more predominance over females to develop candidiasis and these results are comparable to study conducted by the Gupta (80%).⁷

96 neonates admitted in NICU were of birth weight between 1.0kg to 2.5 kg. Out of which most of cases were positive for candidiasis/candidemia were belong to 1.0-1.5 kg. In present study, 13 babies were positive for candidiasis, of which 5 babies (38.3%) of birth weight between 1-1.5kg (P=0.0313) has developed candidiasis compared to 19% of cases as studied by el-mohandes and coworkers and 40% 0f cases by Ritu agarwal study.^{9,10} As the birth weight decreases, the incidence of candidiasis in neonates increases as revealed by the present study.

Birth asphyxia is an important risk factor for the development of candidiasis in neonates. In the present study, birth asphyxia has a significant association in development of candidiasis in neonates admitted in NICU as compared to other studis by Jyostna (p<0.03) and Gupta et al study (p<0.0226).^{6,7}

Mechanical ventilation is an important risk factor for development of candidiasis in neonates. In the present study, mechanical ventilation has a significant association in development of candidiasis in neonates admitted in NICU as compared to other studies by Kumar A.¹¹

Others risk factors like maternal risk factors were studied in relation to candidiasis in neonates. But study revealed no significant association to develop neonatal candidiasis to support the association.

Laboratory parameters like CRP and total leucocyte count were studied in babies with candidiasis. But study revealed that no significant association exists between CRP posititivity (p<0.9) and total leucocyte count (p<0.8).

CONCLUSION

The observations made both in clinical and laboratory parameters in present study was comparable with the other studies. The present study had made an attempt to study the clinical profile and various risk factors of neonatal candidiasis. Low birth weight, birth asphyxia and mechanical ventilation were the risk factors played a significant role in the development of neonatal candidiasis as it is revealed by the present study.

ACKNOWLEDGEMENTS

Authors would like to thank faculty, residents, junior doctors and other staff of the Department of Pediatrics, SSIMS and RC Davanagere for their valuable support and contribution in the completion of this study.

Funding: No funding sources

Conflict of interest: None declared Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Latha GS, Veeresh Babu DV, Thejraj HK. Clinical profile of Candidiasis in neonates. Int J Contemp Pediatr 2017;4:1875-80.