

## Original Research Article

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## Study of Epidemiology, Risk Factors and Clinical Spectrum for Neonatal Candidemia at Tertiary Care Hospital in North India

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### ABSTRACT

#### Keywords

*Candida*, Neonates, Candidemia, Risk factors

#### Article Info

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*Candida* colonization is a significant cause of neonatal morbidity and mortality. The aim of our study was to evaluate isolation rate, risk factors and clinical spectrum for neonatal candidemia. A descriptive study was conducted between March 2016 and August 2017. During this period, a total of 426 blood cultures were received from NICU. Out of which, 44 isolates showed the growth of *Candida* spp. In our study previous use of antibiotics and intravenous catheterization was reported in 100% cases. Among the maternal risk factors-vaginal delivery and intrapartum use of antibiotics were found to be the major risk factors for neonatal candidemia. *Candida* spp. are increasing in nosocomial infections day by day, so preventive measures such as appropriate use of multiple invasive medical devices and a restrictive policy of antibiotic use should be followed to decrease *Candida* colonization rates.

### Introduction

Neonatal sepsis is acquired from the mother (vertical transmission) or nosocomially (horizontal transmission). Neonatal sepsis is divided into early onset sepsis (defined as onset of sepsis in the first three days of life) and late onset sepsis (after day three of life)<sup>[1,2]</sup>. Candidemia refers to presence of fungi in blood and it associated with high morbidity and mortality. Candidemia in neonates is a serious problem and a common cause of late onset sepsis. Due to immature immune system, neonates are more vulnerable to invasive *Candida* infection<sup>[3,4]</sup>. Colonisation of hands of health care workers, skin and gastrointestinal tract of neonates is

the first step in pathogenesis of candidemia. Various risk factors have previously identified in acquisition of neonatal candidemia, including prematurity, low birth weight, total parenteral nutrition, prolonged hospitalization, prolonged antibiotic therapy, intensive care unit (ICU) admission and invasive interventions<sup>[5,6]</sup>.

Now a days, candidemia has become a major cause of mortality in neonates in health care system due to presence of non specific signs and symptoms. Therefore the aim of present study was to evaluate incidence and epidemiology and to know about risk factors and clinical profile of candidemia in neonates.

## Materials and Methods

This descriptive study was conducted in the departments of Microbiology and Pediatrics of Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India on neonates who were admitted in neonatal intensive care unit (NICU) with clinical suspicion of sepsis for a period of one and half year from March 2016 to August 2017. The study was approved by institutional research committee and institutional ethics committee. A total of 44 neonates with culture proven candidemia were admitted in NICU during the study period and were included in the study.

Information regarding name and central record number was recorded. Cases were analysed for presence of various risk factors for candidemia like gender, age at admission, birth weight, gestation age, prior use of antibiotics and antifungals, duration of hospital stay, intravenous catheterization, mechanical ventilation, any surgical intervention and referred from other places. Along with neonatal risk factors, maternal risk factors like mode of delivery, h/o intrapartum use of antibiotics, h/o foul smelling liquor, h/o prolonged rupture of membranes, h/o maternal fever, h/o prolonged fever and h/o assisted delivery were also recorded. The clinical features like feed intolerance, poor cry, convulsions, apnea, temperature instability, irritability/lethargic were noted. Along with these all factors laboratory findings were also recorded and whole data was analysed.

## Statistical analysis

Data was entered in Microsoft Excel and statistical analysis was done

## Results and Discussion

During study period, total 426 consecutive blood cultures were received from NICU of

Guru Gobind Singh Medical College and Hospital, from clinically suspected cases of neonatal septicaemia. Out of these 426 blood cultures, 44 showed the growth of *Candida*. So we obtained isolation rate of *Candida* as 10.33% (44/426). We found that all the 44 species of *Candida* were non albicans. Out of these non albicans *Candida spp.*, 40.91% were *C. tropicalis*, 34.09% were *C. pelliculosa* and 25% were *C. krusei*.

Out of these 44 neonates, 36.4% (16/44) had early onset and 63.6% (28/44) had late onset sepsis (Table 1). The difference between two was statistically significant ( $p=0.109$ ). Out of 44 newborns selected for study, 70.5% were male neonates (Fig. 1).

At the time of admission, 56.8% (25) of neonates were having age between 0-7 days, 29.5% (13) were having age between 8-14 days, 11.4% (05) were having age between 15-21 day and only 2.3% (01) neonate having age >21 days (Fig. 2).

33 (75%) babies were have gestational age <37 weeks. There were 08 neonates with birth weight >2.5kg (18.2%), 18 (41%) belonged to 1.5-2.5kg group, 12 (27%) belonged to group 1-1.5kg and only 06 (13%) neonates were under 1kg (Table 2).

Among the potential risk factors (Table 2) studied for neonatal candidemia- prior use of antibiotics and intravenous catheterization were most common (100%), followed by referred from other places (47.72%), prior antifungal use (29.5%), mechanical ventilation (22.7%), hospital stay >15 days (20.4%) and any surgical intervention (4.5%).

Of the various maternal risk factors observed, vaginal delivery was the most common (52.2%), followed by h/o intrapartum use of antibiotics (29.5%), h/o foul smelling liquor (18.2%), h/o prolonged rupture of membranes (9.1%) and h/o prolonged labour (4.5%).

While h/o assisted delivery and h/o maternal fever not found even in single case of neonatal candidemia (Fig. 3).

23 out of 44 newborns (52.2%) had apnea during NICU stay and had cessation of respiration >20 seconds (Table 3).

Feed intolerance was observed in 35 out of 44 newborns (79.5%), out of which 29 (82.9%) neonates developed abdominal distension (Table 4). It was assessed by measuring abdominal girth.

Other clinical features observed in these 44 neonates were- lethargic 66% (29) and irritable 34% (15), presence of poor cry in

43.2% (19) newborns and 13.6% (06) babies develop convulsions during hospital stay.

Normal temperature of a neonates ranges from 36.5°C-37.4°C. In our study, recorded temperature was <36.5°C in 10 (22.7%) neonates and >37.4°C in 12 (27.3%) neonates.

Thrombocytopenia was observed in 28 out of 44 neonates (63.6%). Thrombocytopenia was defined as platelet count less than 1.5 lakh (Table 5).

Out of 44 neonates with candidemia, 28 neonates survived. So, overall survival of neonates was 63.6% in our study (Fig. 4).

**Table.1** Distribution of neonates with candidemia according to the time of onset of sepsis (n=44)

Time of onset of sepsis	Number	Percentage
Early onset sepsis (EOS) <sup>a</sup>	16	36.36%
Late onset sepsis (LOS) <sup>b</sup>	28	63.64%
<b>Total</b>	<b>44</b>	<b>100.00%</b>

p value between a & b=.0109 (Statistically significant)

**Table.2** Potential risk factors of neonates with candidemia (n=44)

Risk factor	Number	Percentage
<b>Birth weight</b>		
Normal Birth Weight (>2.5 kg)	08	18.18%
Low Birth Weight (LBW<2.5 kg)	36	81.82%
<b>Gestation period</b>		
Preterm(<37weeks)	33	75.00%
Term (37 weeks)	11	25.00%
<b>Prior use of antibiotics</b>	44	100.00%
<b>Intravenous catheterization</b>	44	100.00%
<b>Mechanical ventilation</b>	10	22.72%
<b>Any surgical intervention</b>	02	4.54%
<b>Prior antifungal use</b>	13	29.50%
<b>Referred from other places</b>	21	47.72%
<b>Duration of hospital stay &gt;15 days</b>	09	20.45%

**Table.3** Distribution of neonates on the basis of presence/absence of apnea (n=44)

Presence of apnea	Number	Percentage
Yes	23	52.2%
No	21	47.8%

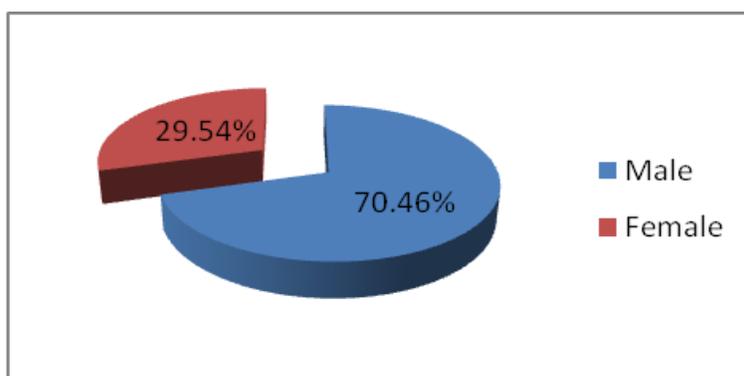
**Table.4** Distribution of neonates on the basis of feed intolerance (n=44)

Presence of feed intolerance	Number	Percentage
Yes	35	79.5%
No	09	20.5%

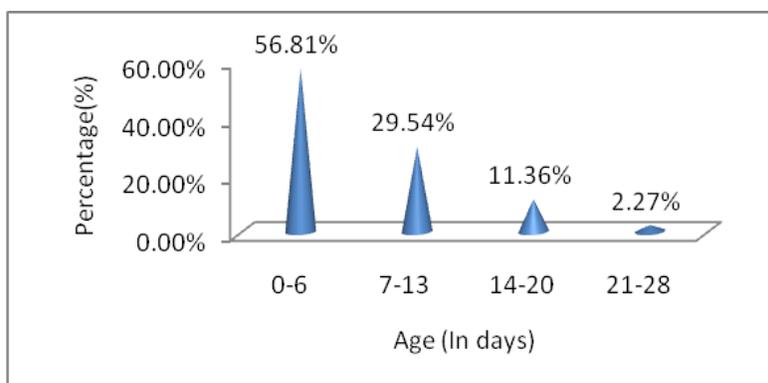
**Table.5** Distribution of neonates on the basis of thrombocytopenia (n=44)

Presence of thrombocytopenia	Number	Percentage
Yes	28	63.6%
No	16	36.4%

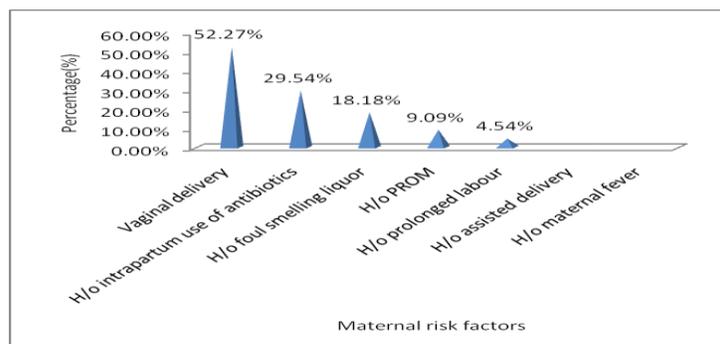
**Fig.1** Sex distribution of neonates with candidemia



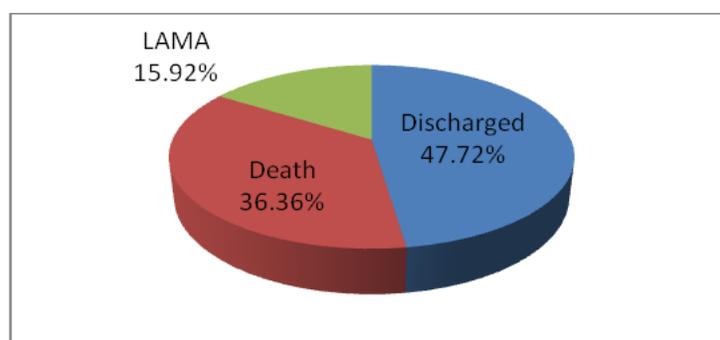
**Fig.2** Age distribution of neonates with candidemia



**Fig.3** Maternal risk factors



**Fig.4** Final outcome of neonates with NAC spp. infection



In NICU, infection with rare organisms is increasing day by day. In today's practice, due to advances in medical and surgical management, there is increase in rate of nosocomial fungal infection. Rate of neonatal candidemia has increased drastically during the past time, due to increase in rate of survival of low birth weight babies.

The isolation rate of neonatal candidemia varies from institution to institution and in the same institution it varies from time to time. In the present study, candidemia was found to be responsible for 10.33% cases of neonatal septicaemia which is consistent with the observations of Goel *et al.*,<sup>[7]</sup> and Benjamin *et al.*<sup>[5]</sup>. However some authors have observed lower rates (1.5-4%) of neonatal candidemia<sup>(8,9)</sup>. This variation in isolation rate of *Candida* could be because of variability in the various risk factors in the study population. Of the 44 neonates with

candidemia in the present study, majority 28 (63.64%) presented with late onset sepsis and only 16 (36.36%) had early onset sepsis, which is consistent with the findings of Caggiano *et al.*,<sup>[10]</sup> and Benjamin *et al.*,<sup>[5]</sup>, they also reported candidemia as a third most common cause of late onset sepsis in NICU patients accounting for 9-13% of blood stream infection in neonates.

The reported mean age of onset of candidemia ranged between 15 to 33 days in earlier studies.<sup>[11,12]</sup> In the present study, it was observed as early as 7.5 days of life. In our study, males were more affected than females and the male to female ratio was 2.38:1. The difference between the affected males and females was also statistically highly significant ( $p=.00013$ ).

The major risk factors identified in the present study were prior use of antibiotics (100%),

intravenous catheterization (100%), low birth weight (81.82%) and prematurity (75%). Other associated risk factors were referred cases from outside (47.72%), prior prophylactic antifungal use (29.50%), mechanical ventilation (22.72%) and surgical interventions (4.54%). These findings are consistent with many other studies from different regions of India.<sup>[4,7,13,14]</sup> The hands of health care workers (HCWs) and environmental surfaces have also been recognised as reservoirs for nosocomial *Candida* infection. Prolonged use of antibiotics may suppress the bacterial flora and also result in development of refractory candidemia. Use of multiple indwelling devices (catheters, endotracheal tube) may cause break in skin/ mucosal integrity and predispose these sites for colonization/ infection by *Candida* spp. *Candida* spp. are very egreious to their capacity to attach with foreign materials and result in biofilm formation, that may be associated with higher rate of candidemia.

Among the maternal risk factors, vaginal delivery (52.27%) was found to be most important risk factor, followed by H/o intrapartum use of antibiotics, H/o foul smelling liquor, H/o prolonged rupture of membranes and H/o prolonged labour. This is consistent with findings of Chen *et al.*,<sup>[15]</sup> Wadile *et al.*<sup>[4]</sup> and Hammoud *et al.*,<sup>[16]</sup> Vaginal delivery may contribute to neonatal candidemia due to vertical transmission from maternal vaginal flora and also due to hands of healthcare workers.

Thrombocytopenia may be a specific marker for fungal sepsis. In our study, it was found in 63.6% neonates, that is comparable to Ariff *et al.*<sup>[17]</sup> However Yunas *et al* reported 80% incidence of thrombocytopenia in their study.<sup>[18]</sup>

The crude mortality rate in our study due was 36.36%, (Table 5) which was lower than the

observation of Femitha P *et al.*<sup>[19]</sup>

In conclusion the since, *Candida* spp. are assuming an increasingly important role in nosocomial infections in neonates, preventive measures such as appropriate use of multiple invasive medical devices and a strict policy of antibiotic use should be implemented to decrease *Candida* colonization/infection rates. Meticulous attention should be paid to hand hygiene practices, use of sterile alcohol swabs and intensive housekeeping routine to ensure proper asepsis.

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