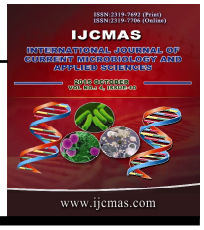
Int.J.Curr.Microbiol.App.Sci (2015) 4(10): 368-373

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 4 Number 10 (2015) pp. 368-373**
http://www.ijcmas.com



Original Research Article

Candida colonization and Candidaemia in a Neonatal Intensive Care Unit

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Keywords

Candida, Colonization, Neonates

A B S T R A C T

Candidaemia in the neonates is associated with high mortality. In recent years non albicans candida are being reported with increasing frequency. Colonization is the first step to develop invasive infection. Objectives of the study are to find the incidence of oral colonisation and subsequent candidaemia, to identify the risk factors for colonization with candida, and to speciate the candida isolates. 120 neonates admitted to NICU were included, oral swabs were collected and processed and identified as per standard protocol. 71.66% were colonized with *Candida*, low birth weight was the significant risk factor for colonization. Although *C. albicans* was the predominant species 35.41%, Non albicans candida together were 64.59%. Candidaemia was seen in 5% of those colonized. Non albicans candida is on the rise, routine surveillance of colonization and risk factors to identify those at risk helps to formulate the policies for prophylaxis. Complete identification of *Candida* species is indicated.

Introduction

Invasive fungal infection is associated with substantial morbidity and mortality in the preterm infants (Kaufman *et al.,* 2001). In recent years Non albicans candida (NAC) are being increasingly reported. Colonisation with *Candida* species is an important risk factor for subsequent infections (Kicklighter *et al.,* 2001). Several authors have evaluated the role of fluconazole prophylaxis to minimise colonisation and subsequent invasive infections (Kaufman *et al.,* 2001; Kicklighter *et al.,* 2001; Tushar *et al.,* 2007). The high mortality associated with fungaemia highlights the need for effective strategies to prevent invasive fungal infections. The present study aimed at evaluating the incidence and the risk factors for oral colonisation of *Candida* and subsequent candidaemia in the colonised neonates. In view of rise in NAC with emerging resistance to fluconazole, the study also focussed on the species identification.

Material and Methods

The prospective study was done during

December 2009 to November 2010. A total of 120 neonates constituted the study group.

Inclusion criteria: all neonates admitted to the neonatal intensive care unit irrespective of host characters and clinical diagnosis.

Exclusion criteria: As the study was focussed on colonisation, neonates with obvious oropharyngeal candidiasis were excluded.

A questionnaire and review of medical records was used to obtain following information viz: gender, place of birth, mode of delivery, prolonged rupture of membranes (PROM), gestational age, birth weight, invasive procedures, antibiotics received.

Sterile swabs moistened with distilled water were rolled over in the oral cavity and transported to the laboratory and processed without delay. Swabs were cultured on Sabouraud's dextrose agar and incubated at room temperature for 48 hours. Species identification was done by germ tube test, urease test, clamydospore formation on corn meal agar and sugar assimilation tests by standard methods (Jagadish Chander, 2009). Blood cultures were collected in brain heart infusion broth by sterile precaution and the same was processed as per standard protocol.

Results and Discussion

Oral colonisation of *Candida* species was observed in 86(71.66%) neonates. Colonisation in LBW was significantly higher than that of normal weight babies with a p value of <0.05. Although not statistically significant, colonisation was observed to be more in neonates born in hospital 72.03% and pre terms 73.03%. Contrary to our expectation colonisation was more often observed in babies born by LSCS 85.71% in comparison to babies born by vaginal delivery 69.81% (Table 1).

96 isolates were obtained from 86 colonised neonates. Ten cases (11.62%) had two isolates. *C. albicans* with *C. tropicalis* were found in 6(60%) of these cases. Overall, *C. albicans* 34 (35.41%) was the predominant isolate. NAC constituted 64.59%, predominant among them was *C. tropicalis* 24 (38.70%) (Table 2).

Of the 120 blood cultures, 41 showed growth of pathogens of which predictably a majority were gram negative bacteria 34(28.33). One gram positive cocci was isolated. Candida species were isolated only in 6(5.0%) cases. Four of these six isolates were *C. tropicalis* 66.66%, the other 2 isolates were *C. albicans* 33.33%.

Over the last 2 decades, yeasts have become important nosocomial pathogens (Jyotsna *et al.,* 2004). *Candida* is known to cause easy to treat mucocutaneous infection to the most serious candidaemia. The incidence of candidaemia has risen dramatically, and this increase has been accompanied by a shift in the infecting pathogen away from *Candida albicans* to treatment resistant NAC species (David, 2003). Fungal colonization represents a significant risk for cutaneous or systemic candidiasis in the low birth weight infants (Baley *et al.,* 1986).

An alarmingly high rate of oral colonisation by *Candida* 86(71.66%) was observed in our study. There is a considerable variation in the reported rates of yeast carriage. For instance, one Indian study has reported 71.4% (Singh *et al.,* 1999), in contrast to another that reported 30% (Tushar *et al.,* 2007). Western studies have reported carriage rates as low as 26.7% to as high as 60% (Baley *et al.,* 1986; Kaufman *et al.,* 2001). The overall *Candida* carriage rates in our study agreed with that of Singh *et al.*

(1999) and Baley *et al.* (1986). The wide ranging differences in various studies indicate that a broad observation cannot be made as geographical variations are known to occur. Besides the management protocols and host variables are likely to influence the carriage rates in various studies.

Reported risk factors for colonisation are LBW, gestational age, male sex, prolonged PROM, administration of steroids and antibiotics and vaginal colonisation of the mothers (Mendiratta *et al.*, 2006). We found that LBW had a statistically significant risk of *Candida* carriage as against normal weight babies. Although not statistically significant, a strong association was observed between administration of antibiotics, PROM, babies delivered in hospital, preterms and colonisation. Contrary to our expectation babies delivered by LSCS showed a higher colonisation rates 85.71% compared to those delivered vaginally 69.81% (Table 1). The likely reason for this could be the post operative environmental factors which influence colonisation in the hospital.

Although *C. albicans* is the most commonly isolated species in the colonised or infected infants, in the past decade infection and colonisation with other species of *Candida* has risen dramatically (Mendiratta *et al.*, 2006). By and large *C. albicans* is reported to be the predominant species by several authors 43.5%, 62%, 19%, 95% (Baley *et al.*, 1986; Singh *et al.*, 1999; Narang *et al.*, 1996). We too found that *C. albicans* was the most predominant of all the species isolated. Other species such as *C. glabrata*, *C. krusei*, *C tropicalis* are emerging as important pathogens and this transition has had a significant clinical impact due to decreased susceptibility of these non albicans yeasts to antifungal agents (Abi-Said *et al.*, 1997). NAC have been reported to cause 56% colonization (Tushar *et al.*, 2007). Similarly we found that overall the NAC were 64.59% which was higher than *C. albicans* alone 35.41%. Of these *C. tropicalis* was the predominant species followed by *C. glabrata*. It could be inferred that these species are now slowly replacing *C. albicans*. A growing body of evidence supports the still controversial contention that the increasing use of azole antifungals is at least partially responsible for the proliferation of treatment resistant NAC, especially *C. glabrata* (David, 2003). In the present study too, we found that *C. glabrata* 18.8% was the second most common non albicans candida species, second only to *C. tropicalis* 26.59%.

Six (5%) cases were blood culture positive for *Candida*. Much higher rates of 25.8% (Tushar *et al.*, 2007) and 20% (Kaufman *et al.*, 2001) have been reported by other authors. As regards to species responsible for candidaemia, four of the six cases i.e., 66.66% were due to *C. tropicalis*. The proportion of NAC species among *Candida* species is increasing: over the two decades to 1990, NAC represented 10–40% of all candidaemias. In contrast, in 1991–1998, they represented 35–65% of all candidaemias. These findings are in context with general population (Krcmery and Barnes, 2002). Some authors have reported that 96.8% of the isolates causing invasive candidiasis were NAC (Tushar *et al.*, 2007), others have reported 50% (Kaufman *et al.*, 2001). Narang *et al.* (1996) have reported *C. albicans* 43.5%, *C. tropicalis* 21.7%, *C. guillermondi* 13%, *C. parapsilosis* 13%, and *C. krusei* 8.7% as causative agents of invasive candidiasis. *C. krusei* has more recently emerged as a notable pathogen with clinical manifestations such as fungaemia, endopthalmitis, arthritis and endocarditis which usually occur in compromised patient groups in nosocomial settings (Yuthica and Samaranayake, 1994). The high incidence of NAC species causing cnadidaemia is of

concern as many of them are known to be resistant to fluconazole. Although we did not find any invasive candidiasis cases caused by *C. glabrata* and *C. krusei* (which are more likely to be drug resistant), the shift towards NAC is clearly evident.

When we analysed the association of colonisation and subsequent candidaemia, we found that colonisation preceded candidaemia in all the 6 cases. It is note worthy to mention that none of the non colonised babies had candidaemia.

Table.1 Distribution of *Candida* species

Isolates	No	%
Candida albicans	34	35.41%
Candida tropicalis	24	25.0 %
Candida glabrata	11	11.45 %
Candida krusei	08	8.33 %
Candida dubliniensis	06	6.25 %
Candida guilliermondii	05	5.20 %
Candida kefyr	04	4.16 %
Candida parapsilosis	04	4.16 %
Total	96	100 %

Table.2 Host factors influencing colonization

Host factors	No.colonised	No.not colonised	Total
Hosp.delivery	85(72.03%)	33(27.96%)	118(98.33%)
Home delivery	01(50%)	01(50%)	02 (1.66%)
Vaginal delivery	74(69.81%)	32(30.18%)	106(88.33%)
LSCS delivery	12(85.71%)	02(14.28%)	14(11.66%)
Preterm delivery	65(73.03%)	24(26.96%)	89(74.16%)
Term delivery	21(67.74%)	10(32.25%)	31(25.83%)
LBW	77(76.23%)	24(23.76%)	101(84.16%)
Normal weight	09(47.36%)	10(52.63%)	19(15.83%)
With PROM	04(100%)	0	04(3.33%)
Without PROM	82(70.68%)	34(29.31%)	116(96.66%)
Antibiotics received	83 (67.5%)	29(24.16%)	112(93.33%)
Antibiotics not received	03(2.5%)	05(4.16%)	08(6.66%)
Inv procedures	84(72.41%)	32(27.58%)	116 (96.66%)
No inv procedures	02(50%)	02(50%)	04(3.33%)

Candidaemia has been associated with an attributable mortality rate of almost 40% (David, 2003). We observed a crude mortality of 66.66%. Of these 50% were associated with *C. tropicalis* sepsis and 16.66% with *C. albicans*. Mortality due to NAC species is reported to be similar to *C. albicans*, ranging from 15 to 35% (Krcmery and Barnes, 2002).

In view of the high mortality rates, several authors have evaluated the role of fluconazole prophylaxis in the high risk. It is reported that *Candida* colonisation is reduced from 46% to 15% after fluconazole therapy (Kicklighter *et al.,* 2001) and from 23% to 4.9% (Kaufman *et al.*, 2001). The authors concluded that prophylactic administration of fluconazole during the first six weeks of life is effective in preventing fungal colonization and invasive infection in infants with birth weights of less than 1000g. Conversely, another study (Tushar *et al.*, 2007) did not find fluconozole prophylaxis to be effective in preventing invasive fungal infections in neonates.

Although the overall percentage of candidaemia among the colonised cases in our study was low, we observed that mortality was quite high 66.66%, thus posing a dilemma as to the rationale of fluconozole prophylaxis to may minimise the development of invasive fungal infection especially those at risk. Some authors have raised concern that the increased use of antifungals may cause a shift in the prevalence of candida species towards difficult to treat pathogens particularly *C. glabrata* and *C. krusei* (David, 2003). Thus a cautious approach appears to be prudent.

In conclusion, Non albicans candida has been increasingly reported and may eventually replace *C. albicans*. LBW was a significant risk factor for *Candida* carriage. Routine surveillance of colonization and the risk factors is important to target the prophylaxis to those in need as indiscriminate use of antifungals is unjustified. Conflicting data regarding the use of antifungal prophylaxis highlights the need for intervention studies on a larger scale to impact the prescription policies in the hospitals. Furthermore, in view of an increase in NAC species, the need for culture and complete identification of the species is highlighted.

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