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ORIGINAL ARTICLE/ARTICLE ORIGINAL

# Oral colonization: A possible source for candidemia in low-weight neonates

## *Colonisation orale : une source possible pour la candidémie chez les nouveaux-nés de faible poids*

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**KEYWORDS**
*Candida*;
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Oral colonization;
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**Summary**
*Objective.* — To check the oral colonization in neonates at high-risk and to associate these cases with candidemia.
*Subjects and methods.* — This study was conducted in the NICU. For six months, 125 high-risk neonates were investigated for oral colonization and septicemia by yeasts. From this total, 19 neonates had yeasts on the oral mucosae and 12 neonates developed fungemia. All of the 12 neonates with fungemia were included in the amount of 19 who have presented oral colonization by yeasts.
*Results.* — There was a species concordance between the yeasts of the oral mucosae and the blood in 6 neonates (50%) among the 12 neonates with oral colonization and septicemia at the same time. The yeasts isolated in these 6 cases regarding the species concordance were *Candida albicans* (5 cases, 83.4%) and *Candida parapsilosis* (1 case, 16.6%). All of the cases involving an association were confirmed by PFGE. All of the strains of yeasts involved in oral colonization and also blood presented the same karyotype. A total of 66.6% of the patients with strains in agreement progressed to death.
*Conclusion.* — The results indicate the relevance of monitoring the oral microbiota, as a possible source of fungal infection, and assisting to develop appropriate therapeutic strategy.


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**MOTS CLÉS**
*Candida* ;
Candidemia ;
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Nouveau-nés

**Résumé**
*Objectif*. — Vérifier la colonisation orale des nouveau-nés à haut risque et à associer ces cas avec une candidémie.
*Sujets et méthodes*. — Cette étude a été réalisée à l'USIN. Pendant six mois, 125 nouveau-nés à haut risque ont été étudiés pour la colonisation de levures dans la cavité buccale et l'existence d'une levurémie. De ce total, 19 nouveau-nés ont la levure dans la muqueuse buccale et 12 nouveau-nés ont développé une fongémie. Tous les 12 nouveau-nés avec fongémie ont été inclus dans le montant de 19 qui ont présenté colonisation orale par les levures.
*Résultats*. — Il y avait une concordance entre les espèces de levures de la muqueuse buccale et du sang chez 6 nouveau-nés (50 %) parmi les 12 nouveau-nés avec colonisation orale et septicémie simultanées. Les levures isolées dans ces 6 cas étaient *Candida albicans* (5 cas, 83,4 %) et *Candida parapsilosis* (1 cas, 16,6 %). Tous les cas impliquant une association ont été confirmés par PFGE. Toutes les souches de levures dans la colonisation orale et l'hémoculture présentaient le même caryotype. Soixante-six pour cent des patients avec la même espèce (cavité buccale et sang) sont décédés.
*Conclusion*. — Les résultats montrent la pertinence du suivi de la flore buccale, comme une source possible d'infection fongique, et comme aide à élaborer une stratégie thérapeutique appropriée.


## Introduction

In most neonatal intensive care units (NICUs), yeasts infections are the third-most frequent cause of nosocomial infection [25,29]. The observed incidence of infection has varied from 2.2% to 12.9% among low-weight (< 1500 g) neonates [12].

Yeasts of the genus *Candida* have been recognized as important pathogens in this context [7]. The incidence of systemic candidiasis in hospitalized patients has been increasing for more than two decades, particularly in neonates with a birth weight lower than 1500 grams [1,10,28,32]. The incidence of infections caused by *Candida* ranges from 1.6% to 16%, followed by a mortality rate from 25% to 60% [9].

Neonates in a NICU are at high-risk for developing fungal infections due to various factors, including low birth weight and the use of wide-spectrum antibiotic [8,27]. However, colonization by yeasts especially by *Candida* has been identified as the most significant predisposing factor regarding systemic yeast infection. Approximately 3/4 of the neonates admitted to NICUs have their oral mucosa already colonized within their first month of life and many of them developed systemic infection after being colonized [18,23,24]. From 100 hospitalized neonates of a study by Baley et al. [2], 26% of them were colonized by yeasts and 7% developed sepsis. Although various studies have been published concerning colonization as the main predisposing factor for infection few of these have supported this association based on molecular biology and the importance of monitoring the oral microbiota.

Due to its excellent discriminating power and its reproducibility, pulsed field gel electrophoresis (PFGE) is one of the most commonly used method in epidemiological analyses concerning *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, and other species [4,30,31,33,34]. The PFGE is a technique of electrophoresis in agarose gel that permits the separation of large DNA molecules, including chromosomes, which vary in size in different isolates. Each sample is characterized by a karyotype [3]. This technique is very useful to monitoring isolates from the same patient during the course of an infection and may be used to monitoring therapeutic efficacy.

Therefore, considering the seriousness of this fungal disease, its high mortality among neonates and that the first colonization is the oral colonization, we decided to check the oral colonization in neonates at high-risk and to associate these cases with candidemia.

## Patients

The neonates in this study were hospitalized in the NICU of a Public Hospital in São Paulo, Brazil. The length of this study was 6 months (October 2006 to March 2007). Neonates were included in this study if they had the low birth weight (< 1500 g) as a risk factor. According to the regulations of the hospital, where this study has been performed, is important to note that neonates who presented oral colonization were not treated with antifungal drugs. Ethical clearance was obtained from the Ethical Committee of the University of São Paulo, and has been conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki. The legal guardians of the patients were recruited and agreed to participate by signing an informed consent form.

## Material and methods

### Oral mucosa

The strains were collected from 125 hospitalized neonates at the moment of birth, 24 hours postpartum, and then at weekly intervals until being discharged from the hospital. The material was collected using sterile swabs (Cefar, São Paulo, Brazil) and seeded in Petri dishes containing Sabouraud dextrose agar (Difco, Massachusetts, USA) and in Petri dishes containing CHROmagar culture medium (Difco, Massachusetts, USA).