

Candida Colonization among Neonates with Low Birth Weight: There Is Much More to Explore

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Abstract

Background and Objectives: Candida colonization in neonates with low birth weight is reported to be the first step for invasive candidiasis. This study was designed to describe the patterns of *Candida* spp. colonizing neonates with low birth weight in Mwanza, Tanzania to provide baseline information for future studies in this field. **Methodology:** The hospital based cross sectional study was conducted between January 2019 and April 2019 among neonates with low birth weight. Clinical and social demographic data were collected using interview guide questionnaire. Oral and umbilical rectal swabs were collected on the first and seventh day of life to assess *Candida* spp. colonization status. Data were analyzed using STATA version 13 following the study objectives. **Results:** A total of 320 neonates with median body weight of 1600 [IQR 1000 - 2000] grams were enrolled. Prevalence of *Candida* spp. colonization on either oral, umbilical or rectum was 16.2% (52/320). A total of 34 (10.6%) and 41 (12.8%) neonates were colonized by *Candida* spp. on the first day and seventh day of life, respectively. Of 34 neonates colonized on the first day of life, 23 (67.7%) were still being colonized on the seventh day. *Candida albicans* 38 (73.1%), was the predominant species detected followed by *Candida glabrata* 10 (19.2%). **Conclusion:** The prevalence of *Candida* spp. colonization among neonates with low birth weight is within the reported range and is mainly due to *Candida albicans*. Future studies are highly needed to explore the role of colonization and subsequent *Candida* spp. infections.

Keywords

Candida Colonization, *C. albicans*, *C. glabrata*, Oral

1. Introduction

Globally the leading cause of neonatal deaths is infection with 10% reported to be due to *Candida* spp. [1] [2]. The mortality due to neonatal-candidiasis is estimated to range between 30% and 73% [2] [3]. *Candida* colonization in neonates with low birth weight is reported to be the first step for invasive candidiasis [2] [4]. Studies have shown 7% - 25% of low birth weight neonates are colonized by *Candida* spp. and are at high risk of developing invasive candidiasis [5] [6]. Among neonates with very low birth weight admitted in intensive care unit, *Candida* spp. is reported to be the third leading causative agent of sepsis [1] [7].

Neonatal *Candida* spp. colonization is reported to commonly occur in the first weeks of life whereby up to 10% - 64% of neonates can be colonized [8]. The neonatal *Candida* spp. colonization was reported in a study conducted in India to be significantly more in neonates with low birth weight < 1500 gram with prevalence of 33.3% compared to the prevalence of 10% among neonates with birth weight > 1500 gram [9].

Risk factors for *Candida* spp. colonization include: use of broad spectrum antibiotics, resuscitation after birth and per vaginal deliver with colonized mother [9] [10]. Furthermore, *Candida* spp. colonization has been pronounced more in premature neonates regardless of their birth weight [11]. Studies have documented 7% - 28.3% of *Candida* spp. colonized premature neonates developed blood candidiasis [9] [11] [12]. Invasive procedures like mechanical ventilation, cannulation, central catheterization and parenteral nutrition have been documented as factors associated with invasive *Candida* spp. infection among colonized neonates with low birth weight [10] [13] [14].

Despite having 40% - 50% admissions of neonates with low birth weight at Bugando Medical Centre neonatal intensive care unit (BMC NICU), there is paucity of data on the magnitude and patterns of *Candida* spp. colonization in this and other centers in the developing countries. Here, we report the prevalence of *Candida* spp. and their distribution among recruited neonates from intensive care unit of the Bugando Medical Centre (BMC), Sekou Toure Regional Referral Hospital (SRRH) and Sengerema District Designated Hospital (SDDH).

2. Material and Methods

The descriptive cross sectional hospital based study was conducted from January 2019 to April 2019. The study recruited neonate with low birth weight below 2500 grams on their first day of life admitted in neonatal intensive care units and premature units of BMC, SRRH and SDDH. The neonatal admission per month at BMC ranges from 100 - 200 with about 40% - 50% having low birth weight. At

SRRH and SDDH the admissions due to low birth weight range from 40 - 50 and 150 - 200, respectively. The study excluded all neonates with abdominal wall malformations such as gastroschisis, omphalocele and genital urinary tract like bladder exstrophy. The sample size was obtained by the use of Kish Leslie formula [15] using the prevalence of *Candida* spp. colonization obtained from a study conducted in Uganda [11].

Screening of the neonatal gestation age and maturity was done using Ballard score [16]. Parents with neonates fulfilling inclusion criteria were interviewed to obtain social demographic and clinical data like age, sex, residence mode of delivery, serological HIV status and history of premature rupture of membrane (PROM). Clinical examination to assess temperature, respiratory rate, presence or absence of cyanosis, jaundice, umbilical redness, convulsions, reduced movements and inability to feed was done by qualified pediatrician. Oral and umbilical-rectal swabs were taken on day 1 and day 7. All swabs were transported to microbiology laboratory in the Stuart transport media (HiMedia-Mumbai, India) within two hours of collection for processing. All swabs were cultured on Sabouraud's dextrose agar (SDA) supplemented with 50 µg/ml gentamicin and 50 µg/ml chloramphenicol (HiMedia-Mumbai, India) as previously described [17]. Colonial morphology, germ tube test and reaction on the chromogenic agar (Brilliance *Candida* agar, Oxoid-UK) were used for identification of *Candida* spp.

Data were entered on excel spread sheet for consistent check and cleaning then transferred to STATA version 13 for analysis. Categorical data were summarized using proportions while continuous data were summarized using median and interquartile range. The protocol of this study was ethically approved by the joint CUHAS/BMC research ethics and review committee (CREC) with certificate number CREC /333/2019. Parents were informed about the purpose, procedures, risks and benefits of the participation, prior to obtain written informed consent.

3. Results

3.1. Social Demographic and Clinical Data of 320 Studied Neonates

A total of 227 (70.8%), 57 (17.8) and 36 (11.4%) neonates were recruited from BMC, SRRH and SDDH, respectively. Their median body weight was 1600 [IQR 1000 - 2000] grams and median gestation age at delivery being 33 [30 - 35] weeks. Nearly half of neonates were admitted in the neonatal intensive care unit 165 (51.6%). The majority 208 (65.0%) of studied neonates were spontaneous vaginal delivery. A total 231 (72.2%) of parents resided in urban areas and the slightly majority of studied neonates were female 182 (56.8%) (Table 1).

The majority of neonates were delivered in the health care facilities 302 (94.4%) and 192 (60.0%) were resuscitated at birth. A total of 210 (65%) neonates had poor feeding and 194 (65.6%) had IV cannulation. Antibiotics use was

Table 1. Socio-demographic distribution and other characteristics of 320 neonates with low birth weight.

Characteristics	Number (n)/Median	Percent (%) /IQR
Body weight (gram)	1600	1000 - 2000
GANBS (weeks)	33	30 - 35
Gender		
Male	138	43.2
Female	182	56.8
Ward		
Premature	155	48.4
NICU	165	51.6
Antibiotic use		
Yes	126	39.4
No	194	60.4
Location		
Urban	231	72.2
Rural	89	27.8
Education level of the mother		
No formal education	72	22.5
Primary	135	42.2
Secondary	98	30.6
University/college	15	4.7
Work of the mother		
Employed	47	14.7
Self employed	192	60.0
Student	4	1.2
Unemployed	77	24.1
Frequency of antenatal visit		
None	7	2.2
Once	68	21.2
Twice	100	31.2
Thrice	84	26.3
Fourth and above	61	19.1
Trimester during antenatal booking		
First trimester	92	28.8
Second trimester	216	67.5
Third trimester	12	3.7
Mode of delivery		
C/section	109	34.1
SVD	208	65.0
Ass. Vagina delivery	3	0.9

GANBS is gestation age at delivery by new Ballard score, SVD is spontaneous vertex delivery.

recorded in about one third of the neonates 126 (39.4%). Fever (axillary temperature above 37.5°C) was observed in 40 (12.5%) neonates.

3.2. *Candida* Spp. Colonization

A total of 52 (16.3%) neonates were colonized by *Candida* spp. on both day 1 and 7. A total of 34 (10.6%) and 41 (12.8%) neonates were colonized by *Candida* spp. on first day and seventh day of life, respectively. Of these, 28 (82.4%) were orally and 6 (17.6%) were colonized on the umbilicus/rectum. Of 34 neonates colonized on the first day of life, 23 (67.7%) were still being colonized on the seventh day. The majority of neonates were colonized by *Candida albicans* 38 (73.1%). Of 14 non-*albicans Candida* spp. detected 10 (19.2%) were *Candida glabrata*, **Figure 1**.

Of 28 orally colonized neonates, 20 (71.4%) had *Candida albicans*. For the second swab taken on day 7, a total of 41 neonates were colonized and of them 31 (75.6%) were orally colonized. Of 31 neonates colonized orally by *Candida* spp. 25 (80.6%) had *Candida albicans*.

4. Discussion

Candida colonization in neonates has been documented as a major predisposing factor to invasive candidiasis [18] [19] [20]. In the current study the prevalence of neonatal *Candida* colonization on either oral, umbilicus or rectum was found to be 16.3%. This prevalence is within the range of 12.4% - 18% previously reported in Jordanian, Brazil and India [9] [19] [20] [21]. Horizontal transmission from the nursing mother, overcrowd and sharing of incubators are among risk factors which have previously documented to influence *Candida* spp. colonization among neonates with low birth weight [9] [10] [11] [13] [14] [22].

The prevalence reported in the current study is significantly lower ($p = 0.022$) than the prevalence reported from Uganda 23.3% [11]. The study in Uganda recruited much younger neonates with low birth weight than the current study, age and birth weight have been found to increase risk of *Candida* spp. colonization [11]. In the current study the median gestation age and birth weight was 33 [30 - 35] weeks and 1600 [100 - 200] grams, respectively.

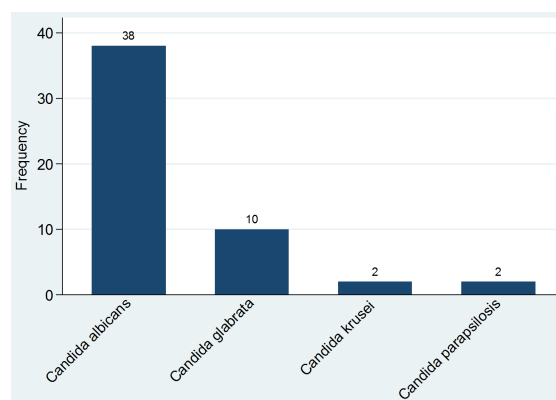


Figure 1. *Candida* species colonizing low birth weight neonates.

As in previous studies, [11] [19] [23] *Candida albicans* was the predominant specie detected. The ability of *C. albicans* to maintain synergistic relationship with other bacteria flora of the skin and buccal cavity can explain the findings [24] [25]. Non-albicans *Candida* spp. were detected to colonize 26.9% of colonized neonates with low birth weight. *Candida* colonization by non-albicans *Candida* spp. have also been observed in different population from our previous studies [17] [23]. This has also been reported in other studies worldwide in the past decade [26] [27] and is highly associated with increased rate of candida infections due to non-albicans *Candida* spp.

Candida glabrata has been noted as one of the leading non-albicans *Candida* spp. colonizing and causing infections in different population [17] [27]. This has also been observed in the current study whereby *Candida glabrata* was the most frequently non-albicans *Candida* spp. isolated. The isolation of *Candida glabrata* is of public health concern due to its variable susceptibility to fluconazole the most frequently used antifungal agents [28]. *Candida glabrata* has also been reported as emerging health threat causing neonatal sepsis [27].

5. Conclusion

The prevalence of candida colonization among neonates with low birth weight is within the reported range of other studies from Africa, and is mainly due to *Candida albicans*. Future studies are highly needed to explore the role of colonization and subsequent *Candida* spp. infections.

6. Limitation

The patterns of *Candida* spp. colonizing these neonates might not reflect the true picture due to low discriminatory index of the techniques used to speciate the isolated *Candida* spp.

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Ethics Approval and Consent to Participate

The protocol of this study was ethically approved by the joint CUHAS/BMC research ethics and review committee (CREC) with certificate number CREC/333/2019. All parents of the neonates were requested to sign the written informed consent before recruitment was done. All data were treated as confidential

Consent for Publication

None applicable.

Availability of Data and Materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Conflicts of Interest

None declared.

Authors' Contributions

WM and MFM designed the work. WM, FM & AH recruited patients, BM, VS and MFM performed laboratory investigations and results interpretations. MFM and WM analyzed and interpreted the data. MFM wrote the first draft of the manuscript which was critically reviewed by all authors. All authors read and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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