Sudan Journal of Medical Sciences
Volume 12, Issue no. 3, DOI 10.18502/sjms.v12i3.934
Production and Hosting by Knowledge E

Research Article

Candida albicans and Napkin Dermatitis: Relationship and Lesion Severity Correlation

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Abstract

Introduction: Napkin Dermatitis (ND) is a common problem in infancy that affects almost every child during the early months and years of their lifetime. It is a skin disease that becomes a challenge for both parents and physicians because of its frequency and difficulty in eliminating all of the causative factors in diapered infants. Usually Napkin dermatitis is self-limiting but when associated with *Candida albicans* (*C. albicans*) seems to be moderate to severe. **Aim:** The aim of the present study was to determine the colonization of *C. albicans* in children with Napkin dermatitis and to correlate between intensity of *C. albicans* colonization and the severity of napkin rash. **Patients and Methods:** This case-controlled study was conducted at Qassim University pediatric outpatient clinics, during the period from August 2014 to July 2015. Sixty patients with diaper dermatitis and 33 healthy controls were enrolled to this study. Sociodemographic and clinical data were obtained from the parents of each participant using questionnaires Paired (stool and skin) samples were collected from all cases and healthy control children. The samples were cultured on differential and selective chromogenic medium for isolation and initial identification of *candida species*. Identification confirmation of the isolates was determined by the Vitek 2 compact automated system. **Results:** Diaper dermatitis shows significant outcome to washing diaper area (per day) ($P = 0.001$), History of diarrhea last 7 Days ($P < 0.001$), skin lab results (+/-) for *Candida albicans*, ($P < 0.001$), skin colony count, ($P < 0.001$), However, there is no correlation to age ($P = 0.828$), gender ($P = 0.368$) and feeding style ($P = 0.401$). **Conclusion:** The severity score of napkin dermatitis was significantly observed among cases with diaper dermatitis (p-value < 0.001) and control children (p-value < 0.001) respectively.

Keywords: *Candida albicans*, Napkin dermatitis, Diaper dermatitis, Vitek 2 compact system, Qassim

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Received: 15 June 2017
Accepted: 1 July 2017
Published: 4 July 2017

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Editor-in-Chief:
Prof. Mohammad A. M. Ibnouf

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1. Introduction

Napkin dermatitis (ND), also called diaper dermatitis (DD), diaper rash, and nappy rash. ND is one of the most common skin diseases during infancy and in toddlers [1]. Prevalence of diaper dermatitis varying under the conditions of each country and the most commonly used diaper. The prevalence for children has been reported in the Japan, USA, UK, and Italy 87%, 75%, 25%, and 15% respectively [2]. Diaper dermatitis was the reason for 20% of all visits to the dermatologist of children, usually starts within the age of the third and 12th weeks and the peak of its incidence is the age of 6-12 months [3–5], up to the age of 5 years [6]. The highest incidence in infants is between 9 and 12 months of age [3–5].

Conditions of DD were first noticed in the 1940s, but diapers were initially considered to be luxury items. Thereafter, diapers began to be used on a mass scale by 1960s [7, 8]. By then diapers were ready-made containing many layers of cellulose, which made them more absorbent and resistant. [7, 8]. The cellulose layers can also cause acute DD and diaper rash, especially, when it is contaminated with urine and stool substances. Most cases of DD clear up spontaneously in a day without treatment [7, 8], exacerbation of persistent cases (that last in 3 days or more) may be associated with different infections, especially Candida yeasts infections [8–10].

There are, however, many causes of DD, Irritant diaper dermatitis (IDD) it is a type of irritant contact (eczema) regarded as a localized form of contact dermatitis caused by several factors including warmth, prolonged contact with urine and feces, and over-hydration of the upper portion of the skin (stratum cornueum) [1, 11]. Diaper dermatitis affecting predominantly the convex surfaces in closest contact with wet or soiled diapers. The buttocks, genitalia, lower abdomen, and upper thighs are usually the most severely affected, but the distribution depends on the position in which the infant is allowed to lie. The flexures are spared, particularly in the obese child. In the mildest forms there is only erythema, but with increasing severity, papules, vesicles, small erosions, and larger ulcers may occur. In chronic forms scaling is combined with glazed erythema. Scaling may be conspicuous manifest particularly in the healing stages. Diaper dermatitis may be graded according to severity into: (i) grade 1: slight erythema, perhaps with scaling; (ii) grade 2: moderate to severe erythema, perhaps with scaling; or few papules and some edema (iii) grade 3: moderate to severe erythema, perhaps with scaling, moderate to severe edema and papules, or early ulceration; and (iv) grade 4: severe erythema, perhaps with scaling, or severe edema, papules, and ulceration [12]. There is a challenge is Candida a causative factor or it is a secondary contaminant that flourishes in the moist warmth environment [13]. Many experts believe that the presence of Candida infection plays a primary as well as a secondary role in the development of this frequently and sometimes painful eruptions [11, 14]. Candidiasis

and Candida diaper dermatitis often complicates non infectious diaper dermatitis and occurs as an adverse effect of oral antibiotic treatment [15].

In general, Candida exists in 3 morphological forms one of them is the yeast cells. The dimorphic yeasts of the genus Candida are ubiquitous in the environment, however, *Candida albicans* causes Candidiasis in children and although it is not part of the indigenous skin flora, but it is a frequent transient on skin and may colonize the human alimentary tract and vaginal as a saprophytic organism [16]. Certain environmental conditions notably elevated temperature and humidity are associated with increased frequency of isolation of *C. albicans* from skin. Many bacterial species inhibit the growth of *C. albicans* and the use of antibiotics, conversely, alter the normal flora and may promote over growth of the yeast [17]. some apparently healthy infants, although, may reveal culture positive for Candida and other organisms without exhibiting any symptoms [14], there seems to be a positive correlation between the severity of the diaper rash noted and the likelihood of secondary involvement [14, 18]. *C. albicans* was recovered from patients with diaper dermatitis more than from normal healthy control groups in many researches [19–21]. Gastrointestinal carriage of *C. albicans* assists on its isolation from stool, skin and rectum of patients with contact dermatitis [22, 23]. It has also been demonstrated that bacterial infection does not play a substantial part in the development of DD [11], however, can act in synergy with bacteria such as *Escherichia coli* [8, 24] and *S. aureus* [8, 18].

This study aimed to determine the colonization of *C. albicans* in children with napkin dermatitis and to correlate between intensity of *C. albicans* colonization and the severity of napkin rash. The role of *C. albicans* in diaper dermatitis has been studied in many countries but correspondingly this issue, to the best of our knowledge, was not studied in this country and particularly in Qassim area.

2. Subjects and Methods

A case-control study was conducted at Qassim University pediatric outpatient clinics, during the period from August 2014 to July 2015. Institutional review board approval was obtained from the Research and Ethical Committee of the College of Medicine and the Deanship of Scientific Research, Qassim University, Saudi Arabia. Informed consent was obtained from all participants.

The inclusion criteria were included erythema with or without papules, vesicles, bulla, scales, fissures or erosions only in napkin area. Severity grades was assigned for all patients as mild, moderate or severe [12]. The exclusion criteria were excluded all children with immune suppression and those who had exposure to local treatment in the anogenital area in the past 7 days. The control group was selected from children attending for their routine and scheduled vaccination. Stool samples and skin swab

scrapping swabs has been collected from all individuals. Sociodemographic and clinical data were obtained from the parents of each participant using structured pre-tested questionnaires.

2.1. Collection and Processing Specimens

Paired specimen of stool and skin swabs were collected from each participant and directly transferred to the laboratory. In the medical laboratory, all samples were processed for wet preparation for microscopic exam, gram stain. Samples were then cultured on selective and differential media and incubated for 24-72 hours. The identification of isolates was done according to several laboratory techniques.

2.2. Laboratory Diagnosis

2.2.1. Processing of Stool Specimens

Stool samples were collected from all cases and controls directly or using a rectal swab (swab is inserted into the rectum and rotated gently) and then withdrawn (replaced in its container), carefully labeled and transferred to the laboratory within 30 minutes of collection or refrigerated (4°C) until the time of analysis (within 12 hrs). Initially, a 0.1 ml of stool or 0.1 gm of formed stools was diluted in 0.9 ml of sterile distilled water and serial dilutions were prepared (10^3 up to 108). A volume of 0.1 ml of each dilution was spread on SDA supplemented with (0.05mg/1ml) chloramphenicol (Oxoid UK, Code: CM0041) and incubated at 37°C for 24-48 hrs. Suspected colonies were streaked on CHROMagar (Watin-Biolife Cat#2020, Riyadh, Saudi Arabia) to obtain pure colonies of *C. albicans* and calculated in form of CFU/gm or CFU/ml. *C. albicans* overgrowth was defined as growth of $\geq 10^5$ CFU/ml or gram of stool. All faecal specimens were also examined macroscopically for morphology, consistency, colour, pH, and microscopically for pus cells, red blood cells, and presence of parasitic infections (as worm, ova, trophozoites and cysts).

2.2.2. Processing of Skin Swab Specimens

Samples were carefully scraped from the skin region covered by the diaper for all controls (normal skin area) and cases (from lesion rash area) by using a swab moistened with sterile distilled water. The skin swabs were collected from the affected (inguinal/peri-anal) area, replaced in its container, carefully labeled and transferred to the laboratory along with the stool swab. In the medical lab, the skin swabs were cultured on to SDA supplemented with (0.05mg/1ml) chloramphenicol and incubated at

37°C for 24-72 hrs. The subcultures were seeded into CHROMagar media and incubated at 35°C for 48 hrs for presumptive identification and differentiation of *Candida species* and to perform colony count in a form of CFU/ml.

2.2.3. Isolation and Identification of C. albicans

The Isolation and Identification (ID) of *C. albicans* was done based on a combination of morphological characteristics and automation technique. The morphological characteristics were including gram stain, colonial morphology (shape, size, texture, etc.) and yeast structures (shape, size, budding pattern, germ tube) [5, 7, 8]. The automation technique was done by using the fully automated VITEK-2 Compact System. Prior application of Vitek system, clinically significant isolates were sub-cultured for purity on SDA plates and incubated aerobically at 35-37°C in 5% CO.2. Isolated yeasts were differentiated according to their colonial morphology and the colour produced on CHROMagar [25] in addition to gram stain. Then colonies were used to prepare a standardized saline inoculum for the appropriate VITEK ID card. Special ID and sensitivity (AST) cards (BioMérieux, France) were used for identification of yeasts (YST). The automation methods were conducted as described by the manufacturers' manual and techniques also described elsewhere [26]. The VITEK-2 ID and AST cards were logged and loaded into the VITEK-2 Compact system. The VITEK-2 Compact system automatically reported the results through software 06.01

The study has been approved by the ethics committees of the College of Medicine Research Ethics Review Board at Qassim University and informed consent was obtained from parents/caregiver of children.

3. Statistics

SPSS for window (version 16) was used for analyses. Students' t-test and Chi-Square (χ^2) were used to compare continuous (normally distributed) data and proportions between the cases and controls, respectively. When data were not normally distributed the Nonparametric (χ^2 and 2-independent samples) tests were used. Binary logistic regression was performed where the Candidiasis was the dependent variables and clinical parameters were the independent variables. Odds ratio and 95% CI were calculated. P-values ($P < 0.05$) was considered statistically significant.

4. Results

Out of 123 children with diaper dermatitis, 28 (22.7%) had been excluded because they had incomplete data, or, not enough samples. A total of 95 children were enrolled in

Variables		Control (n = 35)	Cases (n = 60)	p
Gender	Male	21(60)	38 (63.3)	0.828
Feeding Style	Breast Feeding	6 (17.1%)	13 (21.7%)	0.401
	Bottle Feeding	31 (88.6%)	49 (81.7%)	
Diaper changing practices	3 times/day	13 (37.1%)	22 (63.9%)	0.460
	4 times/day	27 (45%)	33 (55%)	
Washing diaper area (per day)	1 time/day	3 (8.6%)	4 (6.7%)	
	2 time/day	9 (25.7%)	22 (36.7%)	0.001
	More Than 2 time/day	23 (65.7%)	34 (56.7%)	
History of Diarrhea	Last 7 Days	20 (33.3%)	0 (0.0%)	0.001
The presence of oral thrush		2 (5.7%)	9 (15%)	0.172
Personal history of dermatologic conditions		1 (2.9%)	7 (11.7%)	0.136
Family history of dermatologic conditions		4 (11.4%)	17 (28.3%)	0.055

Table 1: Comparing N(%) of control children and cases with napkin dermatitis.

Candida species		Cases (n = 60)	Controls (n = 35)	p
Skin	No Candida	23 (38.3%)	28 (80%)	<0.001
	C. albicans	21 (35%)	6 (17.1%)	
	Other species of candidiasis	16 (26.7%)	1 (2.9%)	
Stool	No Candida	25 (41.7%)	24 (68.6%)	<0.001
	C. albicans	23 (38.3%)	9 (25.7%)	
	Other species of candidiasis	12 (20%)	2 (5.7%)	

Table 2: Distribution of *C. albicans* and other species of isolated from stool and skin of children with napkin dermatitis and control participants.

the study. The cases were 60 (63.2%) children of which 38 (40%) were males, where is 35 (38.8%) were apparently healthy counterparts as controls. There was no significant difference between the case and controls in the mean (SD) of the age 7.31 (5.144) vs. 7.28 (5.636), (P < 0.828), gender, feeding style, diaper changing practice and feeding practice. In comparison to the controls high number of cases had less times of changing diaper area and had family history of dermatological lesion, table 1 and figure 1.

Significantly a higher number of candidiasis was detected in skin in the cases than in the controls. There were 21 (35%) vs 6 (17.1%), 16 (26.7%) vs. 1 (2.9%) P < 0.001 of *C. albicans* and other species of candidiasis in the cases and controls, respectively, table 2.

Variables	Skin Candidiasis			Stool Candidiasis		
	OR	95, CI	P	OR	95, CI	P
Age	1.037	0.93–1.14	0.485	1.01	0.91–1.11	0.824
Male gender	2.409	0.94–6.15	0.066	1.53	0.60–3.92	0.368
Feeding practice	0.862	0.53–1.39	0.543	0.77	0.47–1.25	0.297
Diaper changing practice	1.028	0.42–2.48	0.951	0.76	0.31–1.85	0.546
Washing diaper area	1.245	0.58–2.66	0.572	0.93	0.41–2.07	0.865
Oral thrush	1.190	0.23–6.09	0.835	0.45	0.07–2.72	0.388
Personal history of skin lesion	8.431	0.79–62.1	0.087	9.19	0.78–39.5	0.078
Family history of skin lesion	0.446	0.12–1.62	0.220	0.32	0.08–1.29	0.111
Recent history of diarrhoea	2.470	0.82–7.42	0.107	1.89	0.63–5.64	0.251
Cases vs. controls	7.86	2.51–24.8	<0.001	3.75	1.19–7.56	0.022

Table 3: Binary regression for the risk factors for skin and stool candidiasis in children with napkin dermatitis.

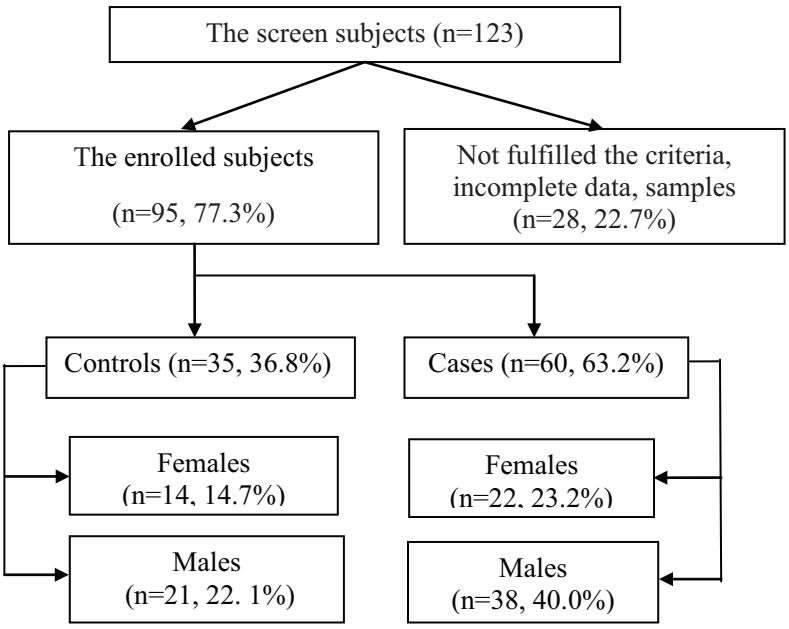

Figure 1: Schematic diagram of the study design.

Likewise, there were 23 (38.3%) vs. 9 (25.7%) and 12 (20%) vs. 2 (5.7%), P < 0.001 C. albicans and other species of candidiasis in the stool of cases and controls, respectively, table 2.

In binary regression, while age, gender, feeding style, diaper changing practice, feeding practice were not associated with skin or stool candidiasis, the cases were significantly associated with skin (OR = 7.8) and stool candidiasis (3.75), table 3.

5. Discussion

The main findings of the current study were; *C. albicans* colonization was detected in the stool and skin in the diaper area of both healthy children and cases with diaper dermatitis. Skin colonization by *C. albicans* among cases and control was 37 (61.7) and six (17.1%) respectively.

This finding support the hypothesis that Candida, are not generally considered to be primary colonizers, and colonization of the diaper with *Candida species* occurs secondarily as skin damage squally [27]. Similarly, the study by D. Forbes 2001 found that, *Candida species* was predominantly isolates yeast, which were identified in the stools of 43 children (39%) with diarrhea and 26 (36%) without diarrhea. The concentration of *Candida species* was positively associated with recent antibiotic use and with the presence of another enteric pathogen, but not with patient age, nutritional status, feeding style or duration of diarrhea.

Our findings are in concurrence with recent reports [4, 8, 9] as well as with a study done by Martins N., et al 2014, the main predisposing factors for ND from the diaper area including *C. albicans* which has been isolated most frequently, regardless of the underlying condition of the skin [3]..

Although, *C. albicans*, has been widely implicated and account (80-90 %) in moderate-to-severe ND [3, 9, 28], in contrast, other organisms are not considered causative factors for ND [3]. Similarly, Bilal J et al 2013, the study of atopic dermatitis (AD) has recovered various bacterial flora from the skin of infants, *S. aureus* colonization was the most frequently isolated bacteria of skin lesions and non-lesional skin of 37.5% to 15% respectively [29].

Based on the clinical findings, a ND of primary reaction to acute irritation (in 1-2 days) was diagnosed in 20 (33.3%) of cases and candidiasis was found in 12 (60%) of them ($P \leq 0.001$). Klunk C., and his colleagues reported that, materials that made the diapers can cause a primary reaction to irritation acute DD (diaper rash), especially, when become contaminated with urine and stool substances, however, most of cases clear up spontaneously in a day without treatment [7, 8], exacerbation of persistent cases (that last in 3 days or more) may be associated with different infections, especially Candida yeasts infections [8].

6. Conclusion

According to the findings of this study, comparing to the control group, the severity of napkin dermatitis score was significantly observed among children cases with diaper dermatitis. washing diaper area per day, personal history of dermatologic conditions history of diarrhea last seven days were more vulnerable to candidiasis and Napkin dermatitis. However, there were no relation to age, gender, family history of dermatologic conditions, the presence of oral thrush, and feeding style mode.

7. List of abbreviations

DD: Diaper dermatitis, IDD: Irritant diaper dermatitis, hr: hour, SDA: Sabouraud Dextrose Agar, CHROMagar: differential and selective chromogenic medium, ID card: identification card, YST card: Yeast card, AST card: Antimicrobial susceptibility cards, vs.: versus,

8. Declarations

8.1. Ethics Approval and Consent to Participate

Institutional review board approval was obtained from the Deanship of Scientific Research, Qassim University, Saudi Arabia. Informed consent was obtained from all subjects.

8.2. Consent for Publication

Not applicable.

8.3. Availability of Data and Materials

All the data supporting our findings are contained within this work.

8.4. Competing Interests

The authors declare that they have no competing interests.

8.5. Funding

This study was supported by grants from the Deanship of Scientific Research, Qassim University, Saudi Arabia.

8.6. Authors' Contributions

Amani H. Karsani, Abdullateef A. Alzolibani, Yasser Farouq and Khalid zedan carried out the study and participated in drafting the manuscript. Mohamed ElOtaiby and Ghada Bin Saif participated in designing the study and participated in drafting the manuscript. IH Babikir coordinated and participated in designing the study, statistical analysis and drafting the manuscript. IH Babikir carried out the laboratory work. All the authors read and approved the final version.

8.7. Acknowledgements

This study was funded by the Research Deanship of Qassim University, Saudi Arabia. We would like to thank the Deanship of Scientific Research, Qassim University, for

approving and funding this study. The authors are very grateful to all children and their families for their contribution and participation in the study.

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