Superficial Mycoses Associated with Diaper Dermatitis

Alexandro Bonifaz · Rubí Rojas · Andrés Tirado-Sánchez · Dinora Chávez-López · Carlos Mena · Luz Calderón · Ponce-Olivera Rosa María

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Abstract Diapers create particular conditions of moisture and friction, and with urine and feces come increased pH and irritating enzymes (lipases and proteases). Fungi can take advantage of all these factors. Candida yeasts, especially C. albicans, are responsible for the most frequent secondary infections and are isolated in more than 80 % of cases. Correct diagnosis is important for ensuring the correct prescription of topical antifungicals. Nystatin, imidazoles and ciclopirox are effective. It is important to realize there are resistant strains. Dermatophytes can infect the diaper area, with the most common agent being Epidermophyton floccosum. The clinical characteristics of dermatophytosis are different from those of candidiasis, and it can be diagnosed and treated simply. Malassezia yeasts can aggravate conditions affecting the diaper area, such as seborrheic dermatitis, atopic dermatitis, and inverse psoriasis. Additional treatment is recommended in this case, because they usually involve complement activation and increased specific IgE levels. Erythrasma is a pseudomycosis that is indistinguishable from candidiasis and may also occur in large skin folds. It is treated with topical antibacterial products and some antifungicals.

Keywords Diaper dermatitis · Candida albicans · Dermatophytosis · Epidermophyton floccosum · Malassezia spp.

Introduction

Disposable diapers were first produced in the 1940s, but were initially considered to be luxury items. It was not until the 1960s that they began to be used on a mass scale. By then, diapers were made with layers of cellulose, which made them more absorbent and resistant. [1–3]. However, they can also cause diaper dermatitis (DD), also known as diaper rash, which can be associated with different infections, especially Candida infections [3]. Other superficial mycotic conditions commonly found in the diaper area are dermatophytosis or tinea infections, exacerbation of seborrhic dermatitis by Malassezia yeasts and some pseudomycotic conditions like erythrasma [4–6]. Since diapers are mainly used for babies, most complications occur among this age group, but it must be remembered that some elderly people also use diapers for some reasons.

Our main objective in this study is to review superficial mycoses of the diaper area and their...
clinical, epidemiological, and diagnostic characteris-
tics and treatment.

Candidiasis Associated with Diaper Dermatitis

Epidemiological, Pathogenic and Clinical Forms

DD is a common condition, especially among new-
borns and infants. It is an irritating and inflammatory
acute dermatitis in the perineal and perianal areas
resulting from occlusion and irritation caused by
diapers. Most cases clear up in a day without
 treatment, but cases that last 3 days or more are more
complicated and may be associated with infections [1–
3]. Prevalence and incidence are high, varying under
the conditions of each country and the most commonly
used diaper. DD prevalence is estimated at 7–35 %,
and incidence is highest in infants between 9 and
12 months of age [3, 6–9]. In a recent study conducted
in the UK [10], for example, the prevalence of diaper
rash was 25 % in the first month after birth, contrasting
with the first studies carried out in the 1980s, which
revealed a prevalence of almost 70 % [1–3, 6, 8, 11].

The first studies inferred the main triggering factor
was increased pH caused by microflora [3, 6, 8, 9].
Although this is normally an important factor, we now
know that DD development is much more complex
and multifactorial, involving a series of orchestrated
processes [12–22], all of these are summarized in
Table 1.

The most common infections associated with DD
are caused by Candida yeasts, especially Candida
albicans, which has been reported in more than 80 %
[3, 6, 7, 17, 18]. These yeasts also cause secondary
infections. Normally the number of Candida yeasts
in the diaper area without dermatitis is low and such
yeasts have been isolated in <4 % of cases [18, 19],
while they are present between 70 and 92 % of
children with DD [8, 9, 20]. The origin of these yeasts
is directly related to the intestinal flora, and they have
been isolated in children with oral and esophageal
candidiasis (thrush). The clinical symptoms in these
cases are more severe because the yeasts are excreted
in the feces. [7–9, 21, 22].

A series of factors favor Candida infection in the
diaper area. They are mostly acidophilic yeasts that
thrive at skin pH, which is around 5.5, or 6.0 in
newborns (owing to vernix caseosa and amniotic
fluid), tending to normalize in a few days [1, 3, 17, 18,
22]. C. albicans and other yeasts provide examples of
perfect adaptation to pH changes, which is controlled
by two genes: PHR2, which is activated in acidic
environments and is deactivated when pH increases,
and PHR1, which does the opposite, i.e. is activated
at a high pH (neutral and basic levels) [23]. Another
proven factor in developing fungi (yeasts and der-
matophytes) is CO2 levels, which are higher in the
occlusive environment of standard disposable diapers
and barely detectable in breathable diapers [16, 24,
25].

Candida albicans, settle infection, causing
increased yeast numbers and a micromorphological
change from blastoconidia to hyphae and pseudohy-
phae, which penetrate the superficial parts of the
stratum corneum and epidermis [18, 19, 25]. In
general, secondary Candida yeast infections are the
most common complication of DD, occurring in more
than 80 % of cases. It has been demonstrated that these
infections can act in synergy with bacteria such as
Escherichia coli to increase the cellular adhesion of
the yeasts [3, 26]. Most reports point out the main
infectious agent is C. albicans (80–90 %). [4, 22, 27].
Other species have been found in lesser proportions:
Candida tropicalis [28], Candida parapsilosis [17]
and Candida glabrata [27]. It is important to take this
into account, because some of these species do not
have the same sensitivity to the various antimycotics.
C. glabrata is especially significant since it does not
form pseudohyphae or hyphae, meaning its infection
is only regulated by an increase in the number of
blandoconidia, and it is more resistant to antimycotics,
especially fluconazole.

With the development of new disposable diapers,
the incidence and severity of DD have greatly
decreased. New technology has allowed superab-
sorbent polymers such as sodium polyacrylate to be
incorporated into the diaper core. These polymers
form a gel when they come into contact with urine,
reducing skin dampness and friction and helping to
normalize skin pH. They can absorb 50–80 times their
weight in fluid [11, 16]. The second type of diapers is
called breathable diapers [25]. These are made of
microporous membranes that enable evaporation
while preventing leaks. This reduces the occlusion
caused by standard diapers. In some studies, children
wearing these diapers had 50 % fewer episodes of DD
[16, 19]. Akin et al. [25] conducted a study to assess
Candida infections in breathable and non-breathable diapers. Adult volunteers were inoculated with \textit{C. albicans} at a concentration of $10^6$–$10^7$ colony-forming units (CFUs), and yeast survival was demonstrated to be 62\% lower in the breathable diapers. This suggested the “breathing” mechanism has a direct effect on the presence of yeast.

Clinically, dermatitis appears in the region covered by the diaper, affecting the gluteal, perineal and inguinal areas, and occasionally part of the genitals. In more severe cases, it can spread to other regions [1–3, 8, 9]. Early irritant dermatitis is characterized by erythema, mild maceration and edema, while \textit{Candida} diaper dermatitis (CDD) is characterized by erythematous and scaly plaques with maceration and edema, sometimes with satellite pustules or papules, the latter being the most characteristic feature of \textit{Candida} infection. Erosion and ulceration can occur in severe cases. Their symptoms are burning and itching, but these are hard to assess since the condition affects small children [1–3, 7, 9, 11] (Fig. 1).

Disposable diapers are also used in elderly patients who are bedridden or who suffer from any of various conditions: urinary incontinence, mental disorders (Alzheimer’s disease, etc. [27–29]). The clinical characteristics of CDD in the elderly are similar to those found in infants and most patients complain of burning and itching. Foureur et al. [28] conducted a prospective study to evaluate the etiology of DD in bedridden elderly patients. They enrolled 46 patients with an average age of 85 years. The most common cause was candidiasis (by \textit{C. albicans}), which affected 63\% of patients, followed by irritant dermatitis (16\%), eczema and psoriasis (11\% each). This study highlighted the high prevalence of candidiasis and the need for prophylactic use of topical antimycotics [28] (Fig. 2).

Differential diagnoses of CDD include: contact dermatitis, inverse psoriasis, seborrheic dermatitis, atopic dermatitis, dermatophytosis, acrodermatitis enteropathica, impetigo, Langerhans Cell Histiocytosis (formerly: Letterer–Siwe disease), and congenital syphilis [1, 3, 11, 19, 30].

Laboratory Diagnosis

The diagnosis of DD should be clinical, but mycological cultures are required to confirm CDD. Direct

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### Table 1 Main predisposing factors for DD and their mechanisms of action

| Predisposing factor | Mechanism of action |
|---------------------|---------------------|
| Moisture [1, 3, 12]  | Increased relative moisture of the skin  |
|                      | Damage to the skin barrier              |
| Friction [3, 10, 11]| Friction between diaper and damp skin increases skin damage (convex regions) |
| Urine [1, 3, 9]      | Presence of urea causes irritation and is the base product for conversion to ammonia |
| Feces [1, 3, 9, 13, 20]| The presence of lipases and proteases causes skin damage with filaggrin proteolysis and increased NMF$^a$ and TWEL$^b$ |
| Ammonia and increased pH [1, 3, 12, 13]| Conversion of urea to ammonium hydroxide by bacterial flora (main responsible, \textit{Bacillus ammoniagenes}) Increase in pH from 5.5 to 6.8–7.15 |
| Microorganisms [1, 3, 12, 13, 16–19, 21, 22]| Bacteria \textit{Staphylococcus aureus} (isolated most frequently) Other: (β-hemolytic) \textit{Streptococcus} sp., \textit{E. coli} and \textit{Bacteroides} sp. More than 80\% \textit{C. albicans} (80–90\%) Other: \textit{C. tropicalis}, \textit{C. parapsilosis}, \textit{C. glabrata} |
| Use of antibiotics [1, 3, 9, 21, 22]| Use of broad-spectrum antibiotics causes increased \textit{Candida} spp. |
| Association with other conditions [1, 3, 11]| Seborrheic dermatitis, inverse psoriasis, epidermolysis bullosa, granuloma gluteale infantum and acrodermatitis enteropathica |

$^a$ NMF natural moisturizing factor
$^b$ TWEL transepidermal water loss
examination with KOH (10 %) should reveal pseudo-
hyphae and blastoconidia, pointing to Candida sp.
infection; generous collections of blastoconidia are
only found in C. glabrata infection. When there is
important maceration, it is possible to take samples for
staining (Giemsa, PAS, Wright) [3, 6, 11, 31]. Samples
are normally taken with swabs and can be placed in
Sabouraud dextrose agar (SDA), and preferably chro-
mogenic media (CHROMcandida®) since the etiolog-
cal agent can usually be determined with
primoisolation. The yeasts obtained can be identified
through biochemical testing (zymograms), molecular
testing (PCR) and proteomic testing (MALDI-TOF).
Biopsies are normally more invasive but are also
useful, especially in cases where other diagnoses are
possible. Infection is usually seen on the surface
(stratum corneum) and in the dermis, with multiple
pseudo hyphae and blastoconidia [3, 28, 31].

Fig. 1 Candidiasis associated with diaper dermatitis. a In an infant. b In an elderly female patient. c Candidosis + dermatophytosis in the diaper area. d Tinea in diaper zone

Treatment

For early DD, the most important thing is to reduce
occlusive exposure to urine and feces. This is why
frequent diaper changes are recommended. Barrier
creams or simple emollients should be used with each
diaper change; the best ingredients are zinc oxide,
petrolatum, cod liver oil and lanolin [1–3, 6, 7, 11, 19,
30, 31]. The first two ingredients are the most often
used. It is important to realize that if there is a Candida
infection, they are normally counterproductive [19].

Corticosteroids can be used, but only for a short
time, i.e., 1–2 weeks at most. They should only be
used to treat moderate to severe DD, with intense
erthema and irritation, and preferably only if the DD
has not responded to inert products [2, 11, 19, 20, 31].
It is better to use low-strength steroids such as
hydrocortisone. Although there are medium-to-high-
strength steroids on the market with higher anti-inflammatory activity, these are not recommended, as they can cause serious side effects like tachyphylaxis, skin atrophy, striae, granuloma gluteale infantum; also may be systematically absorbed, causing Cushing’s syndrome or hypothalamus–pituitary–adrenal axis suppression [9, 19, 32]. Many of the symptoms associated with steroids may be made much worse by candidiasis [9, 19].

Antimycotics: Since most cases are caused by C. albicans, they usually respond well to the various topical antimycotics available. Nystatin is still commonly used [1–3, 11, 19, 31, 33], but is less active than imidazole derivatives. Therefore, if the infection does not respond in 1–3 days of nystatin treatment, switching to azoles is recommended. The most widely used azoles are clotrimazole [1, 3, 6, 11, 19, 33], ketoconazole [11, 19], and bifonazole [28]. They are normally applied twice a day for 7–10 days and generally have high cure rates, ranging from 50 to 68 %.

In an in vitro evaluation study [34] (CLSI M44A method) of strains of Candida isolated from candidiasis and CDD, 149 strains were obtained and divided into two groups: C. albicans (64.4 %) and Candida non-albicans (35.6 %). In short, regardless of the species of Candida, clotrimazole had around 20 % resistance and ketoconazole had around 35 % resistance, while nystatin was 100 % sensitive to the C. albicans strains and only showed 11 % resistance to non-albicans strains. These latter data are interesting since they show that although the old treatments are effective, they can display resistance of 10–35 % [34].

Fig. 2 a Candidiasis, pseudohyphae and blastoconidia (KOH 10 %, ×40). b Dermatophytoses, hyphae (KOH 10 %, ×40). Malassezia sp., blastoconidia (Gram. ×100). Epidermophyton floccosum: macroaleurioconidia (Cotton blue, ×40)
Ciclopirox is one of two new antimycotics that have been used to treat CDD. Gallup et al. [35] conducted an open-label, non-comparative study using a ciclopirox suspension (0.77%) applied twice daily for 7 days and assessed after 14 days. They obtained good results in total success scores ($p < 0.047$), as significantly decreased signs and symptoms and mycological cure were found on evaluation.

Sertaconazole nitrate is a broad-spectrum third-generation [36]. It is a fungicide with long skin perdurability (up to 72 h), which is one of the properties that makes it different from other imidazoles. Bonifaz et al. [37] conducted a study on CDD and obtained the following results: Sertaconazole cream (2%) was applied twice daily for 14 days, causing a decrease of more than 50% in clinical signs after 7 days of treatment, with 88.8% clinical and mycological cure. It was particularly effective against non-albicans species and caused only one side effect (3.7%), namely dermal irritation. We consider this drug to be a new alternative to treat CDD since it has a good efficacy–safety ratio [37].

The use of oral antimycotics is only restricted in severe cases and cases associated with other types of candidiasis (oral and gastrointestinal). Nystatin suspension has been administered at a dose of 1 ml 3–4 times daily (100,000 IU), as has fluconazole at a dose of 3–6 mg/kg/day [11, 19, 31].

**Dermatophytosis in the Diaper Area**

**Epidemiological, Pathogenic and Clinical Forms**

Dermatophytosis or tinea infections can affect the diaper area. This is called dermatophyte diaper dermatitis and has been studied for many years. It occurs much less often than CDD [4, 38–42]. The most frequently isolated etiological agent is *Epidermophyton floccosum*, found in around 80% of isolations, followed by *Trichophyton rubrum*. There are also some isolated cases of *Trichophyton interdigitale* (*T. mentagrophytes* var. *interdigitale*) and *Trichophyton verrucosum* [38–42].

The most reports are from the 1980s. Though few cases are published nowadays, they undoubtedly still occur [38–42]. This condition develops differently from CDD since dermatophytes, unlike yeasts, are not found among normal flora; external infection is required. Most cases reported had some relation to the parents or caregivers of the children. Almost all patients had tinea pedis (most often by *E. floccosum*) [38, 40, 42], and some had onychomycosis (*T. rubrum*) [4, 39, 42], which suggests the dermatophyte spores were transmitted from hands or fomites and benefitted from the moist conditions and high CO2 concentrations, which are known to stimulate dermatophyte growth [24, 25].

Dermatophytosis has the following clinical characteristics: it appears in the whole area covered by the diaper, affecting the lower abdomen, gluteal and inguinal regions, and upper third of the thighs, and can spread to the waist. The genitals are not affected unless the condition is associated with steroids that are high in strength and/or used over a long period of time. Morphologically, the condition presents erythematous, scaly dry plaques with active vesicles and borders and no satellite lesions, with satellite papules only occurring in exceptional cases, when there is a mixed infection (dermatophyte + *Candida* sp.) (Fig. 1). The condition is related to corticosteroid treatment [38–42]. The most common symptom is itching. There have been few comparable reports in the literature on elderly patients who use disposable diapers, but there are more cases since adults more often have tinea pedis and onychomycosis. This infection is likely to go unnoticed [41, 42]. The differential diagnosis includes CDD, inverse psoriasis, atopic dermatitis, congenital syphilis and seborrheic dermatitis [4, 38, 42].

**Laboratory Diagnosis**

The simplest test consists of taking scrapings from the scaly areas and performing direct examinations with KOH (10%), which should reveal long, thin hyphae. Dermatophytes develop slowly in SDA and SDA + antibiotics, and are identified based on macro- and micromorphological characteristics [41, 42].

**Treatment**

If the condition is associated with DD, the same treatment measures should be taken and a topical antimycotic must be added. The most widely used antimycotics are clotrimazole, miconazole and ketoconazole [42, 43]. Ciclopirox [35, 43] and sertaconazole [36] are also effective. It is important to note that
nystatin and mupirocin are not effective against dermatophytosis [19]. Treatment time should be a little longer, 2–3 weeks with one or two applications, depending on the antimycotic selected. It is important to locate the source of the infection and treat it to avoid reinfection.

Malassezia sp. in the Diaper Area

Some species of Malassezia can contribute as exogenous flora to develop various diseases. They have been found in seborrheic dermatitis, atopic dermatitis and psoriasis. They are not believed to be etiological agents [44–49], but do contribute to exacerbation of the condition or as allergens. They can produce specific antibodies and increase the responses of immune cells and IgE, i.e. Malassezia spp.-IgE. This antibody in particular is usually a severity marker in atopic dermatitis. It has been confirmed that an increased number of Malassezia yeasts activates the alternative complement pathway, leading to an inflammatory process and therefore erythema and flaking. It has also been demonstrated that Malassezia yeasts produce enzymes such as phosphatases and lipases, which contribute to activation of the process [44–49].

It should be noted the three conditions mentioned can also occur in the diaper area. Seborrheic dermatitis occurs most often on the scalp, but in children it can spread to the torso and diaper area. Atopic dermatitis can affect nearly all skin and is aggravated in the diaper area. The diaper area is the most frequent location of psoriasis, especially inverted psoriasis. The number of yeasts present is variable, but lower than on the skin of the scalp [45, 47]. The most commonly found species are Malassezia restricta, Malassezia sympodialis, Malassezia dermatis and Malassezia globosa [44, 45, 47, 49].

They are easily recognized with stains such as Gram or Giemsa, which reveal a variable number of yeasts. They are isolated on special media such as SDA + olive oil or in modified Dixon’s agar. They are identified using biochemical methods (assimilation of surfactants) or molecular methods (PCR) [47].

In cases in which yeast numbers increase, another course of treatment must be added. The most responsive topical antimycotics are ketoconazole, ciclopirox and sertaconazole. The first two are available as shampoos, and their use is suggested to help clean the diaper area [49, 50]. Finally, it is important to highlight erythrasma is an infection so similar to diaper candidiasis and dermatophytosis, and this is a pseudomycosis due to Corynebacterium minutissimum (Gram-positive, coryneform actinomycetal). This disease occurs in skin folds as erythematous, scaly, well-defined plaques, covered by a fine; most cases are asymptomatic or cause slight pruritus and clinically indistinguishable from candidiasis and intertriginous tineas [6, 50–52]. Laboratory diagnosis is made with Wood’s light, the plaques fluoresce a coral-red color, and should be confirmed with Gram-positive filaments and cultures in blood agar or brain–heart infusion (BHI) broth and identified through biochemical or molecular testing [6, 51, 52]. The treatment of choice is topical erythromycin, applied once or twice a day for 1 week. Fusidic acid and mupirocin can also be used. Some antimycotics are active against these bacteria; the most important bifonazole, sertaconazole and ciclopirox. Pharmacodynamics could explain many undiagnosed cases resolved with their use [7].

Compliance with Ethical Standards

Conflict of interest All authors declare no conflict of interest.

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