

# Dermatological Manifestations of HIV in Adults and Children, Approach and Management

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## ABSTRACT

**Background:** Currently, HIV infection is considered a pandemic. Acute HIV infection can present with dermatologic manifestations. In some cases, the skin is often the first and only organ affected during most of the course of HIV disease. Antiretrovirals are drugs that are used to treat HIV/AIDS infections.

**Methodology:** A systematic review was carried out through various databases from January 2013 to September 2022; The search and selection of articles was carried out in indexed journals in English and Spanish.

**Results:** Skin disorders during HIV infection are numerous. Depending on the CD4 count we find manifestations such as xerosis, onychomycosis, oral candidiasis, seborrheic dermatitis, Kaposi's sarcoma, among other dermatological manifestations. Although many dermatological manifestations are associated with the CD4 lymphocyte count, it may not be present in the same way in all patients. Therefore, it is very hasty to affirm or classify the dermatological manifestations according to this CD4 count.

**Conclusion:** This review offers up-to-date and detailed information on the main dermatological manifestations in both children and adults in HIV-positive patients, as well as the main manifestations depending on the CD4 count range.

**KEYWORDS:** Dermatology; AIDS; HIV; Adults; Children

## INTRODUCTION

The human immunodeficiency virus (HIV) is transmitted sexually, through blood transfusions, by sharing intravenous needles, and from mother to child during the birth and lactation

process. HIV disease has different phases: viral transmission, acute seroconversion, acute retroviral syndrome, recovery and seroconversion, asymptomatic chronic infection, and symptomatic HIV infection or acquired immunodeficiency syndrome (AIDS) [1].

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HIV is a retrovirus, with two subtypes: HIV-1 and HIV-2. The HIV-1 subtype is the most common and responsible for AIDS in most of the world. HIV-2 is found mainly in West Africa and is much less common. This virus attacks CD4 T lymphocytes and ultimately causes the death of these cells and severe immunodeficiency in the individual who has acquired the infection. Once the CD4 count is too low, the host's immune defenses cannot defend against opportunistic infections and malignancies [1,2].

The presence of a CD4 count of less than 200 or an AIDS-defining illness in a patient with HIV is the criteria for a diagnosis

of AIDS. AIDS treatment focuses on opportunistic disease or condition and on lowering the HIV viral load and controlling the increase in CD4 cells through antiretroviral therapy [3]. Currently, HIV infection is considered a pandemic. Since identification, an estimated 39 million people have died from HIV infection. In Figure 1 we can identify the replication mechanism of this virus [3,4]. HIV is a spherical virus that adheres to host cells with glycoproteins. Later, the virus integrates its chromosomal material into that of the host cell, taking over the cellular machinery to generate more viral proteins and genetic material. Eventually, the host cell will die and other CD4 cells will become infected.

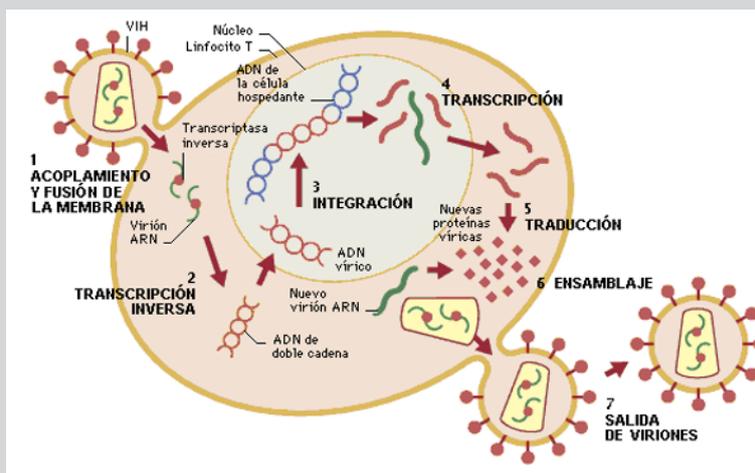


Figure 1: HIV replication mechanism.

This disease can present alterations in different systems, thus contributing to the increase in cardiovascular diseases, presenting symptoms such as chest pain, dyspnea or fatigue, the main cardiovascular pathologies associated with purulent pericarditis or cardiac tamponade caused by Mycobacterium tuberculosis. If these conditions are suspected, observation of Beck's triad of low blood pressure, jugular venous distension, and muffled heart sounds may confirm a compressive pericardial effusion [5]. Among the main pulmonary disorders, we can find upper respiratory tract infections and acute bronchitis. Non-infectious diseases could include Kaposi's sarcoma and non-Hodgkin's lymphoma, sarcoidosis, lung cancer, and emphysema [6].

The gastrointestinal tract is not directly affected by this virus. But at the oropharyngeal level, common complications of HIV or AIDS-defining illnesses are recurrent oral herpes simplex infection, Candida esophagitis, or Cryptosporidium diarrhea. Just like we can find other alterations and manifestations in different systems, such as the central nervous system (Meningitis, focal demyelination or malignant tumors), Hematological system and oncological problems (Pancytopenia, lymphoma); [6,7].

And finally, one of the no less important alterations on which we will focus in this work is the conditions of the dermatological system. Acute HIV infection may present with a maculopapular or morbilliform rash [8]. Oral ulcers or lesions, molluscum contagiosum, and human papillomavirus infection may also occur. The most common AIDS-related skin manifestation is Kaposi's sarcoma, a vascular neoplasm characterized by violaceous spots, nodules, or plaques. If the patient is severely immunosuppressed, disseminated fungal infection is the main manifestation [6,9]. Since this last system is the one that is most exposed for a correct analysis

and timely identification of this infection, this investigation must be carried out.

## MATERIALS AND METHODS

A systematic review was carried out, in which searches were carried out in the PubMed, Scielo and ScienceDirect databases, among others. The collection and selection of articles was carried out in indexed journals in the English language from the years 2013 to 2022. As keywords, the terms were used in the databases according to the DeCS and MeSH methodology: Dermatology; AIDS; HIV; Adults; Kids. In this review, 153 original and review publications related to the subject studied were identified, of which 41 articles met the specified inclusion requirements, such as articles that were in a range of not less than the year 2013, that were articles from full text and inform about the topic studied.

## RESULTS

### Main Dermatological Manifestations in HIV Positive Patient Both in Children and Adults

In 2006, it was estimated that approximately 39.5 million people were HIV-positive in both adults and children. HIV infection is a major health problem worldwide. Dermatological disorders are health problems among HIV-positive patients that present a variety of manifestations.

Skin diseases cause significant morbidity and may be initial signs of immunosuppression. Approximately 80% to 95% of HIV-infected patients are affected by dermatological manifestations or pathologies [10]. The skin is often the first and only organ affected during most of the course of HIV disease. Skin disorders during

HIV infection are numerous. In Figure 2 we can show the main skin manifestations associated with HIV-positive patients and in Table 1 we can identify the main manifestations according to the CD4 count range [11,12]. It has been identified that in general, fungal infections (33.03%) are the most common, followed by bacterial

infections (28.18%) and viral infections (14.55%). Of the non-infectious causes, we found that the main ones are angular cheilitis/stomatitis. Among sexually transmitted diseases, herpes was the most frequent skin manifestation with a prevalence of 10.57%. The CD4+ cell count for fungal infection ranged from 353 to 467.

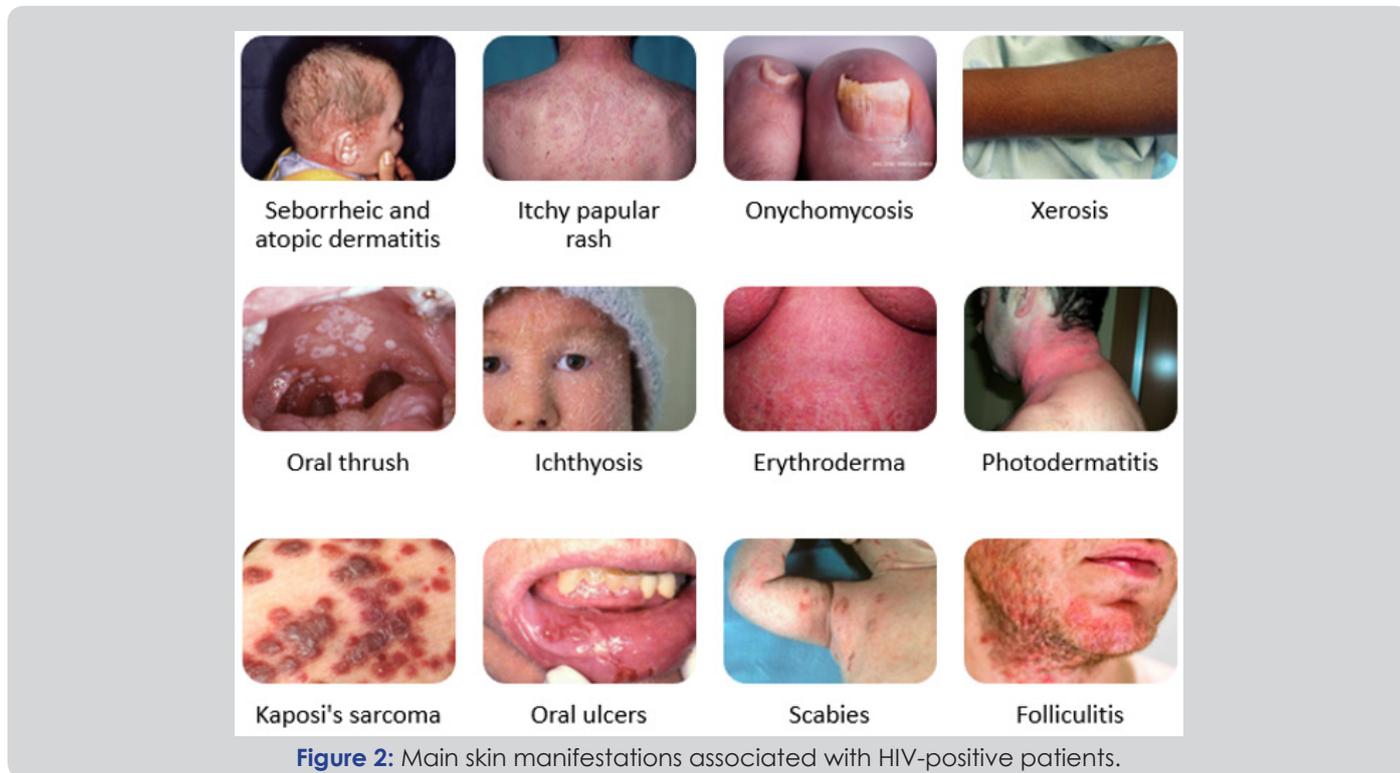


Figure 2: Main skin manifestations associated with HIV-positive patients.

Table 1: Main skin manifestations according to the CD4 count range.

CD4 Count Range	Cutaneous Manifestations
<200/l	Xerosis (65.2%)
	Onychomycosis (39.1%)
	Oral candidiasis (43.4%)
	Seborrheic dermatitis (78.2%)
	Kaposi's sarcoma (0.8%)
>200/l	Xerosis (51.1%)
	Onychomycosis (22.2%)
	Oral candidiasis (0.4%)
	Seborrheic dermatitis (64.4%)

**Current Management to Treat HIV Disease**

Antiretrovirals are drugs used to treat HIV/AIDS infections, and are used in various combinations, commonly known as highly active retroviral therapy (HAART); [13].

Antiretroviral agents include nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), NRTI fixed-dose combinations, integrase inhibitors, non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors, and CCR5 inhibitors. All HIV patients, regardless of CD4 count, should start HAART, which is a lifelong treatment [14].

**Handling a Single Tablet**

Efavirenz/emtricitabine/tenofovir disoproxil is a tablet containing efavirenz 600 mg, emtricitabine 200 mg, and tenofovir disoproxil 245 mg. It should be taken as a single pill once a day [15]. Rilpivirine/emtricitabine/tenofovir disoproxil is a tablet containing rilpivirine 25 mg, emtricitabine 200 mg, and tenofovir disoproxil 245 mg. It is taken once a day Rilpivirine/tenofovir alafenamide/emtricitabine is a tablet containing rilpivirine 25 mg, tenofovir alafenamide 25 mg, and emtricitabine 200 mg. It is taken once a day. Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide is a tablet containing elvitegravir 150 mg, cobicistat 150 mg, emtricitabine 200 mg, and tenofovir alafenamide 10 mg. It is taken once a day. Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil is a drug containing elvitegravir 150mg, cobicistat 150mg, emtricitabine 200mg, tenofovir disoproxil 245mg. It is taken once a day. Dolutegravir/abacavir/lamivudine is an antiretroviral consisting of dolutegravir 50 mg, abacavir 600 mg, and lamivudine 300 mg. It is taken once a day.

**Xerosis**

Xeroderma refers to “dry skin” and is a common condition that results in rough, tight, flaking, and flaking skin. It can cause itching, leading to chafing and increased risk of skin infections [16,17]. Treatment of xeroderma should focus on restoring physiological lipids in the epidermis, improving skin hydration, optimizing skin barrier function, and promoting epidermal differentiation [18,19].

Commonly recommended strategies include:

- a) Infrequent bathing and use of lukewarm water

b) Using Mild Cleansers: Synthetic detergent cleansers are preferred due to their acidic pH, which closely resembles the natural pH of the skin.

c) Routine use of skin moisturizers: Oil-based creams have a thicker consistency than water-based lotions and are more effective at providing moisture.

d) Stay hydrated with adequate fluid intake

### Onychomycosis

Onychomycosis is a fungal infection of the nail unit. When onychomycosis is caused by dermatophytes, it is called tinea unguium. The term onychomycosis encompasses not only dermatophyte infections, but also saprophytic yeast and mold infections [20]. Onychomycosis can infect both fingernails and toenails, but toenail onychomycosis is much more common [21].

The most effective treatments for onychomycosis are systemic antifungals. Due to an increased risk of subungual ulceration, oral antifungal therapy should also be considered in moderate to severe disease, especially in patients with diabetes mellitus and HIV [22]. Combination therapy with topical agents, periodic debridement, or chemical nail avulsion may produce better results than systemic medication alone [23]. Meta-analyses have shown that the mycological cure rate for terbinafine is 76%, itraconazole pulsed dosing is 63%, and fluconazole is 48% effective, while the mycological cure rates for topical therapy are 55% for efinaconazole and 36% for tavaborole or ciclopirox [24]. The evidence concludes that complete cure rates for FDA-approved topical therapies have recently improved from 8.5% for ciclopirox lacquer to 18% for efinaconazole solution. Tavaborole solution has a complete cure rate of 9.1% in mild to moderate distal subungual onychomycosis. [25].

### Oral Thrush

Oral candidiasis is an infection of the oral cavity by *Candida albicans*, first described in 1838 by the pediatrician Francois Veilleux. The condition usually results secondary to immune suppression, which can be local or systemic, including extremes of age (newborns and the elderly), immunocompromised diseases such as HIV/AIDS, and chronic use of steroids and systemic antibiotics [26,27]. Although acute pseudomembranous candidiasis, also known as thrush, is the most common form of oral candidiasis, it is important to recognize that there are other types of oral candidiasis and that *Candida* infection can present as white, erythematous lesions [28]. Treatment in *Candida* species. It should be directed at the extent of involvement and the degree of immunosuppression. Topical antifungal therapy is the first-line therapy for uncomplicated cases of oral candidiasis and should be continued concurrently when systemic treatment is indicated [29]. Systemic antifungal therapy is generally reserved for patient's refractory to topical treatment, those who cannot tolerate topical therapy, and those who are at increased risk of systemic infections. Available topical antifungal medications include nystatin, miconazole, clotrimazole, and ketoconazole [30]. The use of miconazole in the mouth is limited as it induces vomiting and diarrhea. However, it is prescribed to control angular cheilitis and denture stomatitis [31]. Nystatin is a topical antifungal widely used to treat oral candidiasis, available as a lozenge, mouthwash, and oral suspension [32]. For moderate to severe disease, fluconazole 200 mg orally once is recommended, then 100 mg orally once daily for 7 to 14 days. The data on the safety of fluconazole during lactation are reassuring. For refractory

disease, itraconazole oral solution 200 mg once daily without food for 28 days is an option.

### Seborrheic Dermatitis

Seborrheic dermatitis is a common inflammatory skin disease that presents with a papulosquamous morphology in areas rich in sebaceous glands, particularly on the scalp, face, and body folds. The infantile and adult variants reflect the bimodal occurrence of the condition. (33) The approach will vary according to the age of the patient and the distribution and severity of the condition. (34) A typical formulary should include antifungals, keratolytics, and antipruritics. (34, 35).

Evidence supports topical use of ketoconazole 1% or 2%, ciclopirox 1%, and zinc pyrithione 1%. Topical ketoconazole has been shown to be safe in infants with minimal detected systemic absorption. (36).

### Kaposi Sarcoma

Kaposi's sarcoma is an interesting soft tissue tumor that occurs in several different populations with a variety of presentations and courses. In its best-known form, Kaposi's sarcoma occurs in immunosuppressed patients, such as those with acquired immunodeficiency syndrome (AIDS) or those undergoing immunosuppression due to organ transplantation (37). Skin involvement of Kaposi's sarcoma is treated by local excision, liquid nitrogen, and vincristine injection. Chemotherapy is a mainstay of treatment for endemic and systemic forms, particularly in children. (38, 39). Patients with HIV-associated Kaposi's sarcoma respond well to HAART, which can lead to regression or complete treatment of the sarcoma. In patients with severe Kaposi's sarcoma, HAART combined with chemotherapy is the choice. (40, 41).

## DISCUSSION

Even HIV infection remains a great challenge in the field of medical sciences. The mucocutaneous manifestation was first observed in patients with HIV/AIDS in the early 1980s. Although HIV does not directly cause dermatological manifestations, it causes subsequent actions that contribute to its alteration. Within these we find diseases such as Kaposi's sarcoma (KS) and eosinophilic folliculitis, which are highly suggestive of HIV/AIDS. (8, 15, 20).

Dermatological manifestations are common at different stages of HIV/AIDS and manifest as skin infection or inflammation, malignancy, or drug-related diseases. (17) Cutaneous manifestations such as molluscum contagiosum, oral hairy leukoplakia, oral candidiasis, and chronic ulcerative herpes simplex are closely associated with HIV progression to immunodeficiency. Dermatological complaints are more common among HIV-positive patients compared to HIV-negative patients. Its symptoms are more complicated, abnormal and difficult to threaten. (25).

In this work we report the main dermatological manifestations depending on the CD4 count, as reported in Table 1. (11, 12) But the study carried out by M. Ali-Davarpanah et al, in which they report 240 patients with diagnosed by Western Blot and ELISA, with dermatological manifestations, analyzing the manifestations and CD4 count, they conclude that no association was found between CD4 cell counts and dermatological manifestations, even many skin disorders can appear in HIV/AIDS patients with normal CD4 cell counts. Therefore, this study contradicts what was stated in this work. (42).

Although this study contradicts ours in the reported point, these works could have many biases when analyzing all the variants that could give an incorrect result. A strength of the current study is the methodology implemented, regarding the literature search, and steps in the selection of relevant articles, quality assessment, and data extraction. However, this study has several limitations, which should be taken into account before reaching a conclusion, among these are studies of analysis of clinical and laboratory trials that affirm or rule out the correlation that could exist between CD4 levels and dermatological manifestations, so more studies are needed to answer these questions.

## CONCLUSION

In 2006, it was estimated that approximately 39.5 million people were HIV-positive in both adults and children. HIV infection is a major health problem worldwide. The skin is often the first and only organ affected during most of the course of HIV disease. Skin disorders during HIV infection are numerous. Depending on the CD4 count we find manifestations such as xerosis, onychomycosis, oral candidiasis, seborrheic dermatitis, Kaposi's sarcoma, among other dermatological manifestations. Antiretrovirals are drugs used to treat HIV/AIDS infections, and are used in various combinations, commonly known as highly active retroviral therapy. Although many dermatological manifestations are associated with the CD4 lymphocyte count, it may not present in the same way in all patients. Therefore, it is very hasty to affirm or classify the dermatological manifestations according to this CD4 count.

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