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Assessment of Dermatological Manifestations of HIV in Primary Care

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Abstract: HIV infection continues to be a significant problem. Infected patients with HIV/AIDS were the first to show skin infections in the 1980s. It was projected that 35 million individuals would be infected with the Human Immunodeficiency Virus (HIV) in 2013. Before illnesses like diabetes and COPD, skin disorders were considered the 4th most common non-fatal disease burden globally in terms of years lost owing to disability. HIV-related skin disorders have a significant burden on society, have an adverse effect on the quality of life, and are directly linked to death. Pathophysiology of the disease is based mainly on understanding the pathology of the skin's immune system, as CD4 lymphocytes are considered the main key to the immunological response of the dermis and serve to inhibit autoimmune diseases and control infections. Hence, a massive decline is noticed in CD4 lymphocytes in patients diagnosed with HIV/AIDS, as mostly CD4 counts below 200 cells per cubic millimetre, which reveals the absence of immunity in the patients Because HIV-related skin problems are challenging to manage and might even reoccur more frequently than in immunocompetent people in the absence of immunological reconstitution with cART, managing them effectively presents unique challenges. Early detection of skin problems linked to HIV offers the chance for early HIV identification and cART introduction, potentially improving overall survivability. Additionally, in environments with low resources, attention is brought to opportunistic infections that are more likely to be fatal, and skin disorders may go unnoticed. This review aims to summarise current knowledge of pathophysiology, causes, and treatment of HIV-related skin disorders with the objective of more qualitative resources for further research, which contributes to better understanding and reveals the points that need further research.

Keywords: HIV, Dermatology, Immunity, Skin, Autoimmune Disease, HIV/AIDS

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1. INTRODUCTION

A range of illnesses brought on by infection with the human immunodeficiency virus is known as HIV infection and acquired immune deficiency syndrome (HIV/AIDS) (HIV). HIV infection continues to be a significant problem. Infected patients with HIV/AIDS were the first to show skin infections in the 1980s. However, there isn't a single skin condition that HIV solely brings on; conditions like Kaposi's sarcoma (KS) and eosinophilic folliculitis are very indicative of HIV/AIDS. Typically self-limiting skin conditions become persistent, recurring, and treatment-resistant in HIV/AIDS.[1] Globally, it was projected that 35 million individuals were infected with the Human Immunodeficiency Virus (HIV) in 2013 (about 32 million adults and 3 million children under the age of 15) [2]. and 190,000 children died as a result of HIV-related causes, totalling 1.5 million deaths [2]. Acute Immunodeficiency Syndrome (AIDS)-related deaths or opportunistic infections like tuberculosis (TB) and cryptococcal infections are the leading causes of death. The scope of skin diseases includes skin issues linked to early HIV infection as well as a wide variety of skin issues linked to advanced AIDS-related immune deficiencies [3]. Early HIV diagnosis can be aided by recognizing recognizable breakouts. Skin symptoms from a wide range of neoplastic, infectious, and noninfectious disorders might signal the clinician that the patient's immune system is deteriorating [4]. Before illnesses like diabetes and COPD, skin disorders were considered the 4th most common non-fatal disease burden globally in terms of years lost owing to disability [5]. HIVrelated skin disorders significantly burden society, adversely affecting the quality of life, and a direct link to death. Up to 90 per cent of total HIV-infected people are thought to experience related skin, and mucosal problems throughout their illness before effective combination antiretroviral therapy (cART) became available [6.] According to a study conducted in India, inflammatory illnesses caused cutaneous manifestations in about 16% of cases, medication reactions in twenty %, and infectious diseases in 63.34% of cases. [7] The pruritic papular eruption was the most prevalent skin condition in HIV patients with noninfectious skin disorders. In Tehran, a cross-sectional study was carried out to assess the initial skin condition in 25 recently diagnosed patients with HIV. Anogenital and generalized warts, which were present in 36% of cases, were the most frequent dermatological findings, followed by psoriasis and cutaneous abscess. [8] Due to a decrease in antigen-presenting cells and CD4 lymphocytes, HIV infection makes skin more susceptible to neoplastic diseases and secondary infection. [9] The primary HIV infection is acute seroconversion syndrome, with symptoms similar to EpsteinBarr virus infection. In 70% of cases, the patient will have a fever, sore throat, cervical adenopathy, and exanthem. [9] The exanthem is an erythematous maculopapular eruption that can merge. This eruption spreads throughout the trunk and, in some cases, the palms and soles, simulating secondary syphilis. There have also been reports of oral and vaginal erosions. The histology is general. The top dermis has mononuclear cell infiltrates. [10]Because HIV-related skin problems are challenging to manage and might even reoccur more frequently than in immunocompetent people in the absence of immunological reconstitution with cART, managing them effectively presents unique challenges [10,11]. Early detection of skin problems linked to HIV offers the chance for early HIV identification and cART introduction, potentially improving overall survivability [12]. Additionally, in environments with low resources, the attention is brought more to opportunistic infections that are more likely to be fatal, and skin disorders may go unnoticed [13]. In the era of combined antiretroviral therapy, the life expectancy, epidemiological makeup, diagnostic problems, and treatment algorithms affecting persons living with HIV (PLHIV) have all changed dramatically (ART). As a result, the PLHIV population is becoming more diverse and older. In addition, the treatment of PLHIV increasingly encompasses common noninfectious entities such as psoriasis, rare opportunistic infections, and infection-associated cancers.

1.1 Assessment and evaluation

The skin serves as a crucial shield against infections. Effectors of innate or acquired immunological responses are found in the skin. An unusual or excessive immune response causes this immune conflict of the skin. Along with non-specific immune effectors, regulatory T cells, a group of lymphocytes expressing the CD4 receptor, make up most of the specific immunity effectors in the dermis. At the skin's surface, CD4 lymphocytes primarily control how inflammation caused by various infections is resolved and inhibit autoimmune disorders [14]. As the main and preferred targets of the human immunodeficiency virus (HIV), CD4+ cells play a significant role in HIV infection as well. The reduction in absolute and percentage number, which dictates the specific action at the skin level and the continuation of the inflammation with clinical manifestations, is how HIV clinically impacts lymphocytes [15]. Dermatological disease detection can be challenging. While some illnesses consistently develop as stereotyped lesions, other illnesses may have very varied presentations, increasing the likelihood of a missed diagnosis and necessitating a skin biopsy and professional consultation. The method for diagnosing skin lesions comprises evaluating the primary lesions, the site of the lesion, and secondary alterations. The size and intensity of the sores may offer valuable diagnostic hints and shed light on the degree of immunodeficiency. Different skin lesions are identified. On the one hand, Papules and plaques are described as Large, confined cutaneous lesions with a diameter of between 0.1 cm and 1.0 cm that affect both the epidermis and dermis. While on the other hand, Nodules
larger than 2 cm in diameter involve deeper tissues.[16]

1.2 Seborrheic Dermatitis

In Africa, as in the West, seborrhea is a prevalent skin disease associated with HIV infection. Seborrheic dermatitis manifests as a scaly, slightly irritating rash (Figure 1). Erythema and "greasy" scale typically affect the scalp, auditory canals, postauricular skin, and hair-bearing parts of the face and body (eyebrows, alar wrinkles, beard, central chest, and axillae). In Africa, however, seborrhea has a far more variable clinical presentation, according to the authors' experience. [17] It may completely avoid the face, affecting only the scalp, ears, and

skin folds such as the axillae, antecubital fossae, and inner thighs. It can also appear as a rash with a "powdery" scale and very little underlying erythema, primarily on the scalp, ears, neck, shoulders, and buttocks. It could be superimposed with psoriasis, which normally manifests as well-defined plaques with a silver-like scale on the surfaces; pitting and oil patches in the nails can assist in identifying the two conditions. [18, 19] It can sometimes manifest as erythroderma (full-body erythema and scale). There is a possibility of overlap with inverted psoriasis or eczema. The severity determines treatment. A combination of topical antifungal medicines directed targeting Pityrospermum yeast and low- to midpotency topical steroids for inflammation will usually result in improvement. [19] Seborrheic dermatitis affects about 5% of the general population. However, seborrheic dermatitis affects 85-95% of HIV patients and typically begins when their CD4 counts fall below 450-550 cells/mcL. This scaly, inflammatory skin illness can flare up and down over time. Patients have itchy, reddish, or pink skin areas coated by yellowish-greasy flakes or scales that attach to the skin. It most commonly affects the scalp and face, particularly the nasolabial folds, brows, and forehead. Ears, shoulders, upper back, and groin may also be impacted.[20]

1.3 Differential Diagnoses

Contrary to popular belief, those with darker skin types are more likely to experience sun-induced dermatitis, and HIVpositive individuals in Africa experience it frequently. It can occasionally be very challenging to distinguish from seborrhea. Photodermatitis manifests as an itchy, scaly rash on sunexposed skin areas (such as the face, neck, "v" of the breast, dorsal arms, and occasionally lower legs and dorsal feet), sparing areas of skin that are anatomically or physically shielded from the sun (such as under the chin). This distribution is frequently clinically visible when the patient's shirt is taken off. HIV infection causes photosensitization, and many HIV-positive individuals use medications that reduce photosensitization, like sulfonamides. Restoring the immune system, wearing caps and long sleeve shirts, and applying strong topical steroids are all part of the treatment. Since many of these patients work outside, avoiding sun exposure is particularly challenging due to the limited availability of sunscreens. The authors advise against ceasing sulfonamide prophylaxis due to photodermatitis; rather, they advise that these patients should have their immune systems restored to the point where prevention is no longer necessary. Eczema can result from dry skin brought on by advanced HIV illness. Always itchy, eczema can be acute, weeping, or persistently dry and scaly. Xerosis, or dry skin, frequently exists in the background. In adults, the eyelids, neck, flanks, hands, antecubital and popliteal fossae, and lower legs are frequently afflicted locations. The axillary skin and other moister areas are often spared. Topical steroids and emollients are used as part of the treatment, and dessicating chemicals like soap are avoided. After a bath, emollients (like petrolatum) should be used while the skin is still moist.Psoriasis, In the HIV-infected population of Africa, psoriasis is rather widespread. It may manifest as the classic strongly defined, spherical, thick, scaly papules and plaques that favour the extensor extremities. Atypical manifestations are frequent and include erythroderma and inverse psoriasis affecting intertriginous tissues. With the condition affecting the scalp, axillae, and inner thighs, there may be a significant overlap with seborrhea. One potential aspect is destructive arthritis. Antiretroviral medication will help the majority of psoriasis patients. Short-contact anthralin therapy and topical steroids are typically the only additional treatments available. The availability and cost of systemic drugs vary by area and are not typically available or accessible. Antiretroviral therapy-stabilized psoriasis that unexpectedly flares up could be a sign of an underlying dermatologic illness like scabies or staphylococcal infection, or it could be a sign that the antiretroviral treatment is no longer working. Other differential diagnoses to take into account when psoriasis is suspected include reactive arthritis (Reiter disease) and secondary syphilis.[19]

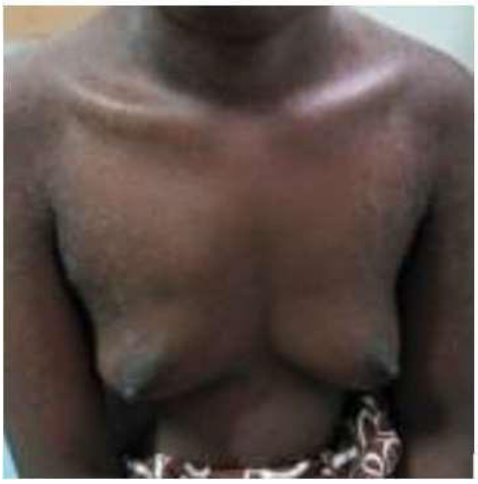

Fig 1. Seborrheic dermatitis. Papules with fine, powdery scale distributed around the neck, shoulders, and axillae. [19]

1.5 Vesicles and bullae

Vesicles and bullae are distinguished by having a lesion filled with clear fluid. In the case of the vessel, the lesion is less than 1 cm, while the bullae have a lesion greater than one cm.[1616]. Finally, flat, confined skin lesions known as macules and patches can appear in localized and extensive patterns [16]. Drug sensitivities are frequently linked to macular eruptions, but viral infections can also cause them. Extreme drug responses like Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) must be ruled out if bullous lesions and desquamation accompany extensive erythema. In addition to serving as signs, dermatological indications are a key sign of the health of the immunity. An accurate medical indicator of a compromised immune system or disease development is the CD4 cell count. One study revealed that 75% of malignancies and infestations (particularly scabies and cutaneous leishmaniasis) were seen in people with CD4 counts below 200 cells per cubic millimetre. [17,18]

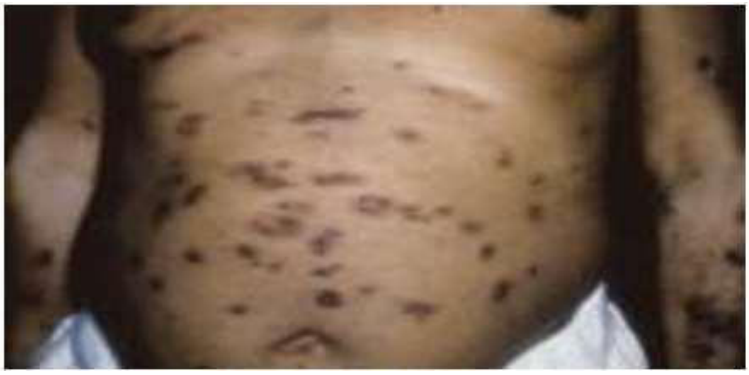

Fig 2. Prurigo nodularis. Large (> 1 cm), symmetric, hyperpigmented nodules [19]

Fig 3. Scabies. Extremely itchy papules clustered in the finger web spaces, with secondary staphylococcal superinfection [19]

1.6 Papular Pruritic Eruption

PPE is a frequent HIV-related skin condition in tropical locales, including Africa. The underlying cause most likely reflects a hypersensitivity to insect bites[2], explaining why tropical areas have a significantly higher frequency than temperate settings. PPE manifests as severely pruritic 0.2- to 1-cm papules that are darker than the patient's normal skin (Figure 4). They may be criticized due to scratching and thicker or glossy as a result of rubbing. The papules are usually numerous and concentrated on the extremities, but the trunk may also be strongly implicated. When a skin biopsy is available, it can be used to confirm the diagnosis. Immune reconstitution with antiretroviral medication is the preferred treatment, but recovery normally takes at least 16 weeks; pruritus may improve with the use of powerful topical steroids or topical steroid creams. [19] Pruritus has emerged as the most prevalent skin-related dermatological symptom experienced by Hiv - infected patients before using antiretroviral drugs [21]. In a study of individuals in the United States of America, Kaushik et al. found a significant incidence of chronic pruritus. 91% of the cases were taking antiretroviral medication. Forty-five per cent of the patients who participated in the poll said their quality of life was negatively impacted by pruritus. Neither CD4 nor eosinophil levels were significantly correlated with the reported

pruritus. Xerosis (23%), fungal infections (12%), seborrheic dermatitis (9%), and eczema (7%) were the most prevalent dermatoses identified.[21] Numerous common etiologies can produce pruritus in HIV-positive patients; some may be more acute or prevalent. Papulosquamous disorders, parasites, pathogens, drug rashes, and occasionally lymphoproliferative conditions like cutaneous T-cell lymphoma are among them (CTCL). Many ailments are specific to people with HIV infection. Pseudo-Sezary, or CTCLsimulant, is another name for the atypical cutaneous lymphoproliferative disorder (ACLD), which manifests as a pruritic, extensive outburst with pigmentary alterations and an unusual lymphocytic infiltration. Rarely does this syndrome proceeds to frank lymphoma; it has been reported in people with late-stage HIV infection. [22] The most prevalent cause of pruritus in HIV patients is a skin condition, but systemic disorders are occasionally blamed for the itching. Sometimes, systemic lymphoma, hypothyreosis, hepatic failure, and renal failure brought on by HIV nephropathy are to cause. [23,24,25] It is most likely uncommon and is diagnosed by ruling out other explanations of the idiopathic HIV pruritus, comparable to Hodgkin's disease pruritus. Most patients will eventually be found to have minor xerosis or another clear source of irritation.[26,27]patient history and physical examination should be included in the workup, along with a full blood count with differential, kidney and liver function tests, hepatitis serologies, and a lung X-ray. [28,29,30] A prospective study examined the CD4:CD8 ratios of the patients with histopathologic analyses. They showed a negative correlation between CD4 levels and skin lesions. All patients with skin lesions showed a CD4: CD8 ratio of 0.5, and most skin lesions were related to CD4 levels of 220/ul. Specific cutaneous manifestations were thought to be a good clinical signal for the patient's immunological status because most patients with skin lesions presented with stage 3 or stage 4 HIV infection [30].

1.7 Differential Diagnoses

A reasonably common condition that resembles PPE is bacterial folliculitis. Lesions are usually less in number, follicular in origin, and tend to be more concentrated on the upper torso, upper arms, upper legs, and buttocks; pustules may be present. Pruritus is variable. Topical antiseptics (such as chlorhexidine) and topical or oral antistaphylococcal medications are available as treatments. Less prevalent in Africa, Eosinophilic folliculitis is a highly itchy HIV-related dermatosis poorly understood. Based on its preferred locations—the face, neck, scalp, and upper trunk—and the rarity of its occurrence below the nipple line, it can be distinguished from PPE. Compared to PPE, the papules are often more urticarial, less glossy, and hyperpigmented. Clinically, it resembles acne, although patients frequently report intense itching, which is not a characteristic of acne. Temporarily, it could start to manifest or get worse during immunological reconstitution. The preferred course of treatment is antiretroviral therapy. However, strong topical steroids or oral itraconazole 200 to 400 mg daily may help to reduce symptoms. Scabies infestations are fairly frequent and can be confused with PPE. Patients arrive with a really itchy rash. The rash can be pustular, eczematous, papulonodular, or even "crusted" in severe HIV illness. The symptoms of crusted, or "Norwegian," scabies include a thick layer of powdery, greyish scale covered in mites. In contrast to PPE, Scabies lesions tend to be grouped, occasionally with obvious burrows in the finger webs, around the waist, and on the wrists and ankles. Doctors should always check the axillae, breasts, umbilicus, and penis in men and boys when diagnosing scabies rather than PPE or folliculitis. The scratching frequently results in bacterial superinfection. Topical benzyl benzoate ester, 6% precipitated sulphur ointment, or oral ivermectin (when available) are common therapeutic options. Prurigo nodularis is a common condition that manifests as swollen, hyperpigmented, excoriated nodules that are extremely itchy. The nodules are bigger (> 1 cm) and more numerous (from 10-100 lesions) than in PPE. Prurigo nodules are bilateral and symmetrical growths that frequently begin on the limbs. They can spread and show up on the trunk with persistent pruritus. Patients are not allowed to scratch certain areas, such as the midback. The severe scratching that causes prurigo nodularis might be secondary to other HIV-related dermatoses (such as photodermatitis, eczema, or PPE), underlying hepatitis C virus infection, renal failure, or cancer. Prurigo nodularis has no one underlying cause. Although the underlying cause should be treated, symptoms can be managed with occlusion to prevent physical itchiness, oral antihistamines, strong topical steroids, and topical capsaicin.[19]

1.8 Drug eruption

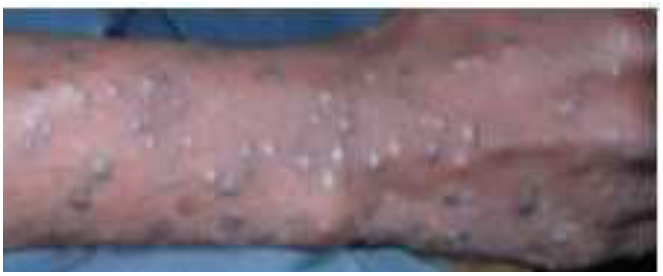

Fig 4. Papular pruritic eruption of HIV. Thickened, hyperpigmented papules of less than 1 cm favoring the extremities.[31]

Drug eruptions that are related to antiretroviral medication are frequent in Africa. Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) and drug eruptions of other sorts require special consideration. Clinical professionals may decide to "treat through" the symptoms using topical steroids and antihistamines in the case of straightforward medication eruptions that are not life-threatening or incapacitating to the patient. Patients in this circumstance need to be cautiously watched for the appearance of blisters, irritation of the mucous membranes, or systemic signs. Sulfonamides or nevirapine are the primary culprits in the vast majority of significant drug eruptions in East Africa. Women who begin nevirapine therapy at CD4+ counts greater than 250 cells/L are especially vulnerable to life-threatening hypersensitivity responses. Since most patients seek therapy late in the disease's progression, SJS/TEN is frequently identifiable by its erosional single or multiple fixed-drug eruptions of mucous membranes (especially the lower lip) and skin. The authors advise against using oral steroids for treatment unless administered during the first 24 hours of symptom onset because systemic steroid use is debatable. Treatment includes stopping the offending medication, additional unnecessary oral medications, and supportive care. Fixed-drug eruptions often appear as impressively rounded, clearly defined areas that are very hyper-pigmented. The lips and genitalia are frequently affected areas, yet they can be found everywhere on the body, solitary or many. With each exposure, the eruption can occur in the same spot or impact a different area of skin. In the authors' experience, an antibiotic, most frequently a sulfonamide, is the most frequent offender, though various other medications may also be responsible for this eruption. Fixed-drug eruptions are common in areas where antibiotics are sold over the counter.[19]

1.9 Skin Cancer

The risk of skin cancer has been observed to be twice higher overall in HIV individuals [32]. The rate of basal cell carcinoma was estimated to be 2.1, while for Squamous cell carcinoma, SCC was 2.6 for HIV-positive compared to HIV-negative patients. Patients with decreased CD4 levels showed an elevated incidence of SCCs. For BCCs, such relationships could not be demonstrated. The symptoms of BCCs in HIVpositive people were shown to be less severe and to occur more frequently on the limbs, according to Silverberg et [32]. ART usage has improved the overall outcome of multiple cancer types [33,34,35]. Cervical cancer, non-Hodgkin lymphoma, and Kaposi sarcoma are all assumed to be related to the suppression of the immune system, according to Hleyhel et al., based on the data about the long-term patterns for these incidences. All the malignancies showed a general decline, but the occurrences remained elevated compared to the normal patients. Incidence rates in individuals with recovered immunity were similar to those in the general population for Kaposi Sarcoma KS). HIV-positive patients were discovered to have earlier diagnoses, which facilitates its management. Epidemic KS is referred to as AIDS-related KS. [36] The most prevalent cancer is linked to HIV. [37]HIV is regarded as the pathogenesis's starting point for KS. The virus has reportedly been found in the lesions, according to reports. [38] Homosexuals are more likely to contract it through sexual contact than heterosexuals. A substantial potential risk is an oral or anal sex. Very few cases of epidemic KS have been found in heterosexual males, who made up most of the early reports of the disease. In discussing the clinical differences between classical KS and that one related to HIV, it is known that the latter is associated with a fast clinical course [39.] The skin, mucous membranes, digestive system, lymph nodes, and lungs are typically affected. In 10–20% of all HIV-associated KS, the oral mucosa is the primary site of localization, typically including the palate. [40]It typically happens when the CD4 level is below 200 cells/mm3 and worsens the course of the disease of HIV infection. [41] Symptomless KS lesions typically begin as macules before developing into papules, plaques, and nodules. Sometimes lesions can be uncomfortable. Bacillary angiomatosis, lichen planus, drug eruptions, coccidioidomycosis, pyogenic granuloma, angiodermatitis or pseudo-KS, and oral hemangioma are among the clinical differential diagnoses. The diagnosis is typically confirmed by histopathology, characterized by excessive vascular growth, slit-like gaps, solid cords and fascicles of spindle cells grouped between vascular channels. The accurate diagnosis of KS depends on the immune-histological identification of CD31, CD34 antigens, FVIII-Rag, and sialic acid expression [42].

1.10 2.3 Viral and bacterial infections

Even though disease control has improved, infections are still a significant complication in HIV-infected people. They can indicate the level of immunodeficiency and include fungal, bacterial, and viral infections. Decolonization initiatives have had mixed results, and colonization significantly contributes to infection [43,44]. Infections with community-associated methicillin-resistant Staphylococcus aureus CA-MRSA are more common in HIV-positive people than in HIV-negative people, which may be related to a higher colonization incidence [45]. According to Popovich et, only 11% of HIVnegative and 20% of patients with HIV had CA-MRSA colonization [45]. The most frequent mucocutaneous presentation was fungal candida, which comprised 33.03 per cent of the total. Studies by Singh et al. [46] and Spira et al. [47], and others produced similar results. Viral Infectious diseases (14.55%) and bacterial infections (28.18%) were the most prevalent infectious symptoms. These results were comparable to those of studies by Oninla [48] that looked at the incidence of bacterial, viral, and fungal skin-related disorders, respectively (50%, 12%, and 3.2%). In the current investigation, 2nd stage of the illness was where fungal infections were most frequently observed, but they were not restricted to these phases. For oral candidiasis, Sharma et al. [49] and Goh et al. [50] reported a CD4+ cell count of 200 cells/mm3. As significant immunodeficiency is linked to oral candidiasis,

particularly when it involves the oesophagus, these conditions are reliable clinical indications of advanced infection with HIV [51]. All stages of the disease were shown to have viral infections, with herpes being the most common in the second stage. It is a secondstage disease, according to WHO. In the current investigation, people with stage 3 HIV had genital warts. However, the WHO has categorized it as stage 2. Genital warts are more common in patients with a CD4+ cell count of more than 300 cells/mm3, according to Mawenzi et al. study [52]. Herpes infection made up the majority of all sexually transmitted diseases (6%), which was consistent with prior investigations [51]. Syphilis (1.76%), vaginal warts (1.32%), and chancroid (0.44%) were among the additional STDs identified in this investigation. In the early and middle stages of HIV clinical staging, bacterial infections were shown to be common, with CD4+ cell counts ranging from 200-660 cells/mm3. Bacterial infections were discovered by Nnoruka et al. with CD4+ cell counts between 200 and 500 cells/mm3. It was suggested that HIV-associated immunosuppression played a significant but diminished influence compared to transplant patients. Squamous cell carcinomas (SCCs) have been linked to infectious causes, particularly viral illness, which may explain why these conditions are more common in people with low CD4 counts. In patients with weakened immune systems, acquired epidermodysplasia verruciformis (EV) manifests as extensive verruciform cutaneous lesions. Rare incidences of the lesions, which are HPV-associated, have been reported [53]. Two hundred forty juvenile patients with HIV were found to have 5 cases of acquired EV, according to Vicente et al. [54]. It was discovered that three of the five carried high-risk HPV strains [54].

1.11 Medication Toxicity

It has been suggested that increased drug exposure or lowered immunity may cause dermatological HIV disorders.

Antiretroviral medications have been implicated in developing Stevens-Johnson syndrome SJS frequently, and they seem to increase the risk of disease-related damage. In a short series by Dziuban et al. [55]nevirapine, a non-nucleoside reverse transcriptase inhibitor, was linked to 84% of the cases of SJS in a juvenile population. In a study of individuals by Saka et al. [56], sulfonamides were the most commonly implicated drug (38.4%), closely followed by nevirapine (19.8%). Over fifty per cent (54.8%) of the patients had HIV. Additionally, there was a tendency for more severe reactions among the HIV-positive population. Anticonvulsants, allopurinol, and antibiotics have been linked to the biggest rise in the risk of SJS in studies conducted in Europe and the West, which can be attributed to the lower frequency of HIV infection in those regions.

1.12 kaposi sarcoma

AIDS-related Kaposi sarcoma (KS) is an angiogenic tumour associated with the human herpes virus. Many epidemiological subgroups of KS were identified: classic KS (in the Mediterranean and Eastern European regions), more aggressive endemic KS (in Africa), and transplantationassociated KS. Before the AIDS crisis, KS was uncommon in the United States. However, the AIDS outbreak changed that. Before the invention of antiretroviral therapy (ART), this new form, known as AIDS-associated or epidemic KS, developed in up to 30% of AIDS patients. The ART era substantially altered the incidence and outcome of AIDS-related KS. Since the advent of ART, the incidence of KS in the United States has decreased by 80%. KS is a multicentric hyperproliferative disease characterized by violaceous skin lesions. Lesions are composed of spindle-shaped tumour cells, which are presented mainly with fibrosis, inflammatory infiltrates, and hemosiderin. CD31 immunohistochemical staining is positive, and KSHV LANA staining of spindle cells is sensitive and specific[57]. Only if a pathogenic diagnosis is present may specific KS therapy be initiated. Surgery's only duty, aside from getting a biopsy for diagnosis, is to eliminate an anatomically troublesome lesion. Furthermore, while long-term remissions are possible, KS is not considered a "curable" tumour, and the therapy's objective is to provide tolerable palliation. This may necessitate long-term, intermittent therapy. A smart method is to continue with a particular therapy till a recovery or response plateau is reached, then taper or discontinue it. There is no indication that KS acquires resistance to any therapeutic drug, and previously effective medications can frequently be utilized if regrowth occurs. Patients are sometimes given anti-herpes medicines because KSHV is a herpes virus. While cidofovir and ganciclovir are efficacious against KSHV in the lab, no clinical action has been demonstrated in individuals with established KS in prospective studies. Fcorticosteroids can significantly worsen KS and should be avoided wherever possible.

1.13 Differential Diagnoses

Bacillary angiomatosis_Because histopathology and skin biopsy services are not generally accessible, BA is probably more frequent than the literature indicates, even though it has only been sporadically recorded in Africa. Like KS, it typically manifests as a single or group of asymptomatic red-purple pimples. If left untreated, BA can be lethal and harm the bone and viscera. A silver stain of a skin biopsy sample that shows the presence of Bartonella henselae or B Quintana, the causal bacterium, confirms the diagnosis. Oral erythromycin or doxycycline must be taken for at least six weeks as part of the treatment. Three months of antibiotic treatment should be taken into consideration for visceral involvement. Lymphoma. Although non-Hodgkin lymphoma skin metastases are relatively uncommon, they might emerge as red to purple papules or plaques on the skin, frequently seeming more transparent or "jellylike" than KS. Again, a skin biopsy can be used to determine the diagnosis. Others. In individuals with dark skin, pyogenic granuloma, warts, scars, post-inflammatory hyperpigmentation, lichen planus, and inflammatory tinea corporis or tinea face are among the other conditions that might mimic KS.[19]

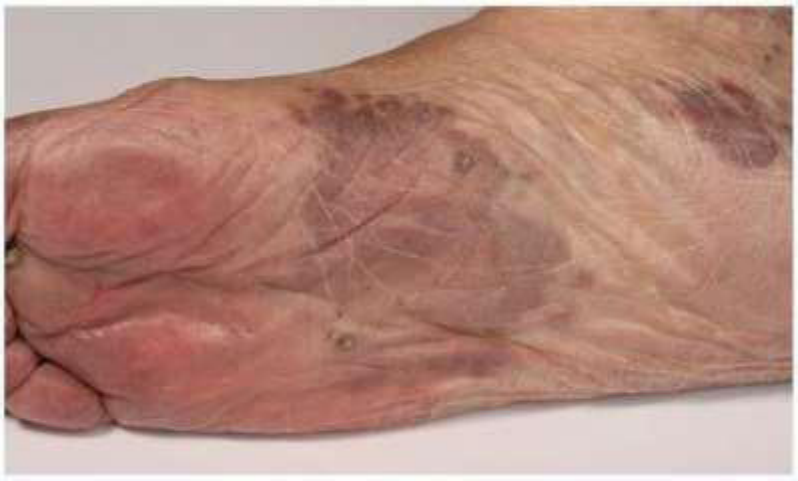

Fig (2) Patch stage Kaposi's sarcoma. Red to brownish irregularly shaped macules and plaques [58]

1.13 Molluscum Contagiosum

Molluscum contagiosum (MC) is a well-known benign selflimiting mucocutaneous viral illness caused by the Pox virus family's molluscum contagiosum virus (MCV). Preschool children have the highest incidence. The disease is typically transmitted through sexual contact. When coupled with Human Immunodeficiency Virus (HIV) infection, the disease is self-limiting in immunocompetent persons but severe and persistent. The clinical presentation is unusual in the context of HIV infection. The upper trunk and the face are the most commonly implicated locations. It affects 10-20% of persons with symptomatic HIV illness or AIDS. MC lesions in HIVinfected patients are typically numerous. Most AIDS patients have extragenital MC lesions. The lesions can be found all over the face, along with the eyelids. Other locations affected include the neck and thighs. In a study undertaken by Ratnam I et al., four of 199 HIV + patients reported having molluscum contagiosum as part of the immunological reconstitution inflammatory syndrome (IRIS).[59] Molluscum lesions in HIV patients might be verrucous, pruritic, or eczematous.

Molluscum lesions can show as comedones, abscesses, furuncles, condylomas, syringomas, keratoacanthomas, basal cell carcinomas, ecthyma, Jadassohn's sebaceous nevus, and cutaneous horn. Differential Diagnosis: Cryptococcosis, penicillinoses, histoplasmosis, pneumocystosis, pyogenic granuloma, basal cell carcinoma, keratoacanthoma, and unusual mycobacterial infections are all differential diagnoses for molluscum contagiosum viral disease. In immunocompromised people, the disease has a prolonged course and is frequently

refractory to numerous treatments. Individual MC lesions with a diameter of ten mm or more are called "giant molluscum contagiosum". Several factors have been proposed to have a role in the development of large molluscum contagiosum in HIV patients, including a reduction in T cell count, decreased cytotoxic t cell function, reduced blastogenic responses to mitogens and antigens, and a drop in
Langerhans cells.[60]

1.14 Herpes Simplex Virus and Varicella-Zoster Virus

Human herpes simplex virus type 1 (HSV-1) and type 2 (HSV2) infections are prevalent. HSV-1 seroprevalence is 47.8% among people aged 14 -49 in the US, and HSV-2 seroprevalence is 11.9%. 1 Approximately 70% of HIV patients are HSV-2 seropositive, and 95% are HSV-1 or HSV-2 seropositive. HSV-2 infection raises the probability of HIV acquisition by two to threefold, and HSV-2 reactivation boosts HIV RNA amounts in blood and vaginal secretions. The most common manifestation of HSV-1 infection is orolabial herpes. Oral HSV-1 symptoms typically begin with a sensory prodrome in the affected area, followed by lesions on the lips and oral mucosa that progress in phases from papule to vesicle, ulcer, and crust. In untreated patients, the disease lasts 5 to 10 days. Genital herpes is the most prevalent manifestation of HSV-2 infection and is primarily caused by HSV-2. HSV-1 is increasingly causing first-episode genital herpes, which is indistinguishable from HSV-2 infection. However, recurrences and viral shedding are less common with genital HSV-1 infection. Typical genital mucosal or skin lesions evolve through stages of papule, vesicle, ulcer, and crust [61] These lesions have been documented most frequently in people with CD4 counts of 100 cells/mm3 and may be linked to acyclovir-resistant HSV. Atypical presentations, such as hypertrophy genital HSV, which mimics neoplasia and requires biopsy for diagnosis, may also be found in HIV-infected individuals. HSV DNA polymerase chain reaction (PCR) and viral culture are the primary procedures for diagnosing HSVrelated mucocutaneous lesions. The most accurate method of diagnosis is PCR. HSV seen in genital lesions should be identified as HSV-1 or HSV-2.[62] Herpes zoster affects roughly 3.6 incidences per 1,000 person-years in the general population, with a substantially higher prevalence reported in the elderly and immunocompromised persons. Before the availability of antiretroviral therapy (ART), the incidence of herpes zoster in individuals with HIV was more than 15-fold greater than in age-matched controls without HIV. Herpes zoster can develop in adults with HIV at any CD4 T lymphocyte (CD4) cell level. However, the risk of illness is increased at CD4 values of 200 cells/mm3. 5-8 Furthermore, HIV viremia is linked to increased herpes zoster outbreaks. [63] Varicella rash has a central distribution, with lesions emerging first on the head. The trunk, and lastly, on the extremities, progressing through phases of macules, papules, vesicles, pustules, and crusts. The rapid evolution of lesions distinguishes the rash within the first 8 to 12 hours after commencement, consecutive harvests of new lesions, and the presence of lesions in various stages of development. The production of new vesicles lasts 2 to 4 days and is followed by pruritus, fever, headache, malaise, and anorexia.[64]

Varicella may be difficult to distinguish from disseminated herpes zoster
(as opposed to dermatomal herpes zoster) in immunocompromised individuals; a history of VZV exposure, a rash that started with a dermatomal pattern, and VZV serologic testing may help distinguish varicella from disseminated herpes zoster. When lesions are atypical or difficult to identify from those caused by other probable etiologies, swabs or tissue samples might be presented for viral culture, direct fluorescent antigen detection, or histopathology.

1.15 Tinea

The name "tinea" refers solely to dermatophyte infections. It is classified according to the infected site into tinea capitis (scalp), tinea barbae (beard area), tinea pedis (feet), tinea manuum (hands), and tinea unguium(nails). Tinea infections are common worldwide, with tinea corporis being more common in hotter and more moist climates. According to estimates, fungal skin infections impact 10%- 20% of the world's population. Tinea pedis, the most prevalent dermatophytosis in HIV patients, is characterized by characteristic interdigital maceration with scaling and generalized hyperkeratosis of the sole. In HIV-infected people, nail infection is prevalent. The nails are frequently discoloured, swollen, and brittle. Nail infection has been linked to advanced HIV disease and is thought to be a clinical indication of HIV infection [65] All kinds of routinely used topical antifungals achieve significant mycological and clinical cure rates. However, there is currently insufficient information to identify whether one class or individual topical antifungal is preferable for mycological and clinical cures. Topical miconazole and terbinafine are specifically mentioned in the recommendations since they are on the WHO Model list of essential medications. 1 Furthermore, topical terbinafine may be more appealing because it requires fewer administrations and a shorter length of treatment, and the intervention is widely available globally. Local antifungal treatments also have a few negative effects. Topical miconazole 2% or terbinafine 1% is thus a solid indication for non-extensive tinea corporis.

1.16 4- Management

Although skin conditions rarely pose a life-threatening risk, they could be fatal. While highly active antiretroviral therapy HAART helps HIV-infected people live longer, drug-induced facial lipoatrophy is a problem for many. The severe pruritus brought on by eosinophilic folliculitis may significantly reduce the patient's quality of life in addition to causing cosmetic deformity. Therefore, it is important not to ignore the management of these supposedly minor illnesses. Most of the time, HIV-positive patients receive the same treatment for skin conditions as HIV-negative people. However, sustained highdose systemic steroids should be cautiously administered due to the immunosuppressive effects. The use of

phototherapy is limited by the elevation of HIV transcription, even though it can reduce pruritus or improve psoriasis in HIV-infected individuals. [66,56]

2. CONCLUSION

HIV/AIDS-related dermatological problems result from a wide range of illnesses with numerous underlying causes. Therefore, quick diagnosis and treatment of dermatological problems in HIV patients should be carefully considered. In addition to the therapeutic challenges of preventing and treating skin conditions, patients' general appearance and quality of life are also impacted by their skin. Further research into the immune system's participation in dermatologic manifestations among HIV patients is necessary given the high frequency of skin conditions, the severity of the sequelae, and the overall impact on patients' quality of life.

3. AUTHOR CONTRIBUTION STATEMENT

Dr. Najlaa Mohammad Alsudairy conceptualized and designed the study. Dr. Alnahari, Nouran Ahmed A and Dr. Aletayani Hatun Nuwaymi M and Dr. Qahtani, Saad Hussain A, searched databases for literature review. Dr. Alahmadi, Arwa Faisal and Dr. Abdullah Ali N Aljalfan and Dr. Altaymani , Abdulaziz Talal A, helped in study screening and filteration. Dr. Allihaibi, Malak Mohammad E and Dr. Asiri,Bahni Mohammed A and Dr. Maghrbi , Ali Mohammed A and Dr. Mohammed Sulaiman Naif Alkathery wrote up the manuscript. Dr. Bader Abdulwahab N Alamer and Dr. Alaklabi,Mohammed,Shari J and Rimah Omar A Alfawzan revised and finalized the paper.

4. CONFLICT OF INTEREST

Conflict of interest declared none

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