

Original Research Article

Viral skin infections in adult patients with HIV/AIDS in a tropical rural practice in Nigeria.

Abstract

Background: Cutaneous diseases are common in patients with HIV/AIDS. This is particularly so with viral skin disorders where impaired cellular immunity seems to be a common pathway of susceptibility. There are however few documented studies of these lesions from some parts of world such as Nigeria and West Africa.

Objective: The aim of our study was to identify viral cutaneous pathologies in patients attending an adult outpatient (HIV/AIDS) clinic department in a rural/suburban centre in the south south geopolitical zone of Nigeria and determine if there are differences/similarities in pattern of presentation to that of other similar studies.

Methods/ Design: This is a prospective observational study conducted in the adult antiretroviral (ART) clinic of Irrua Specialist Teaching Hospital Irrua Edo State Nigeria over a 12 month period involving HIV positive patients. All patients with skin complaints are included in the study while other patients without skin complaints are generally excluded.

Results: A total of 9460 patients were seen during this period in the clinic including old, new and repeat visits. Four hundred and ninety patients had various dermatologic complaints at various times. This gives a prevalence of 5.17% for cutaneous complaints. The mean age of the patients was 38 ± 10 years with a male: female ratio of 1:1.4.

One hundred and eighty two of these patients had clinical features of cutaneous viral infections giving a prevalence of 37.1% of cutaneous complaints. Herpes Zoster (27%), Genital warts (19.2%), Plain viral warts (15.4%) and Herpes Simplex (15.4%) are the commonest cutaneous viral pathologies encountered. Others include Pityriasis Rosea (11.5%), Molluscum Contagiosum (7.7%), and Varicella Zoster (chicken pox - 3.8%).

Conclusion: Viral skin infections are very common in the HIV/AIDS population and they constitute a significant cause of morbidity in these patients.

Key words. Cutaneous; Viral; HIV/AIDS; Pathologies.

Introduction.

The HIV infection is associated with several dermatological conditions which may be the first pointer towards the existence of this infection. These may present with unusual and atypical manifestations in the course of the HIV infection. Viral infections, in particular, are a major cause of opportunistic infections in HIV-infected adults, and can lead to significant morbidity and sometimes mortality¹.

Infection with HIV or AIDS has a great impact on skin diseases, not only by affecting the immune system and thereby host defense against bacterial, viral, or mycotic infections, but also by changing tumor immune response and autoimmune reactivity. Skin lesions particularly viral infections are common in patients with HIV infection more than in the general population and may be more severe. Some lesions are markers of HIV or AIDS and are important signs heralding an improving or declining immune system and the success or failure of antiretroviral therapy. An improved understanding of the incidence of and risk factors for viral infections in HIV-positive patients has important implications for clinical practice.

Cutaneous viral sexually transmitted infection (STI) such genital warts from human papilloma viral infection significantly increases HIV transmission. This type of infection may be asymptomatic and therefore remain undiagnosed in HIV-positive persons until neoplastic complication arises².

The changing pattern of cutaneous viral lesions in association with HIV/AIDS becomes significant as there is a high prevalence of skin and mucocutaneous disorders in patients with HIV infection and recognition of this ultimately improves the care of these patients.

This study therefore aims to determine the pattern of viral skin disorders among adult HIV patients accessing care in a rural/suburban medical centre in south-south Nigeria and contribute to the available literature on this subject from this part of the world.

Methodology

This is a prospective observational study conducted in the adult antiretroviral (ART) clinic of Irrua Specialist Teaching Hospital Irrua Edo State Nigeria.

All adult non-pregnant HIV infected patients are offered specialist care in this clinic ranging from counselling to treatment for those requiring it (Pregnant women are generally referred to the PMTCT (Prevention of Mother To Child) Clinic for care till delivery before being transferred back to the adult clinic).

Patients with skin complaints are provided dermatologic consultation in the clinic apart from the other regular HIV care. Averages of 200 patients are seen per week.

The study was conducted over a 12 month period from the beginning of January 2011 to the last working day in December 2011.

All patients with skin complaints are included in the study while patients without skin complaints are generally excluded. Patients with viral skin conditions are subsequently re segregated out afterwards. All diagnoses are clinical. A consent form is signed by patients after adequate explanation by the clinic nurses that they may be included in a study and patients that decline are not denied appropriate care.

Approval was obtained from the hospital research and ethics committee.

Simple statistical analysis by means and averages are applied to interpret the data obtained.

73 Results

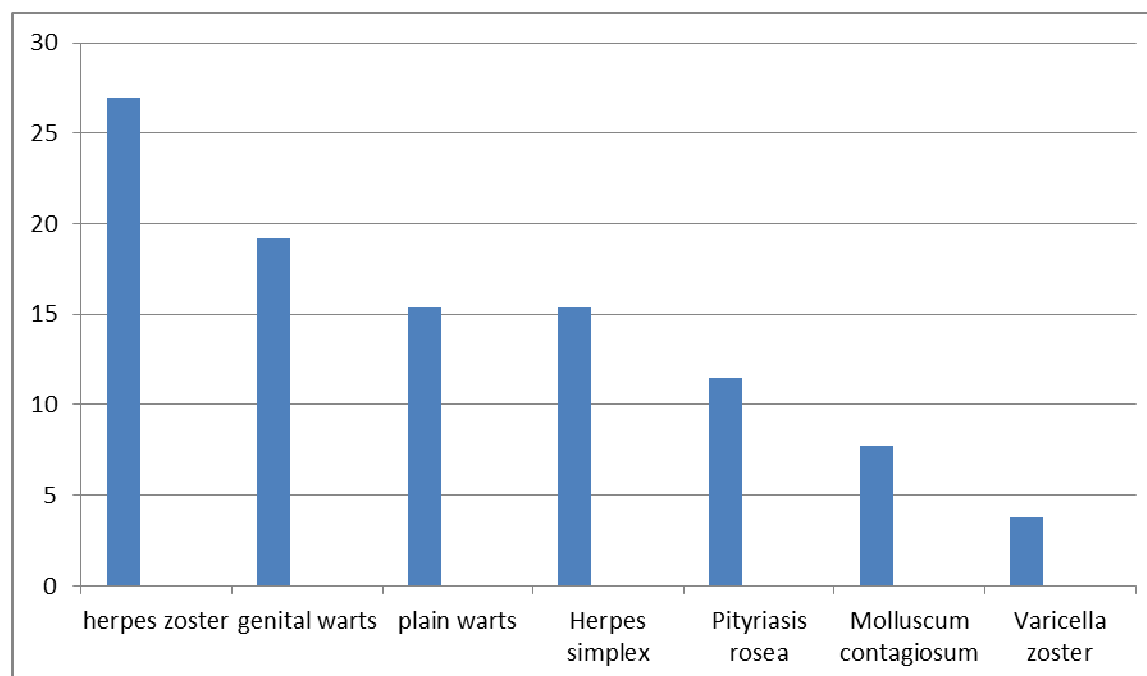
74 A total of 9460 patients were seen during this period in the clinic including old, new and repeat
 75 visits. Four hundred and ninety patients had various dermatologic complaints at various times.
 76 This gives a prevalence of 5.17% of all complaints. The mean age of the patients was 38 ± 10
 77 years with a male: female ratio of 1:1.4. (140:350)

78 One hundred and eighty two of these patients had clinical features of cutaneous viral infections
 79 giving a prevalence of 37.1% of cutaneous complaints. A breakdown of the various viral skin
 80 conditions encountered with the mean CD4 counts is shown in the table below.

81 Table1. Prevalence viral skin infections.

Pathology	Frequency	Percentage %	Average CD4 count (cells/ul)
Herpes Zoster	49	27.0	281 ± 67
Genital warts	35	19.2	176 ± 52
Plain viral warts	28	15.4	187 ± 66
Herpes simplex	28	15.4	135 ± 23
Pityriasis Rosea	21	11.5	250 ± 55
Molluscum contagiosum	14	7.7	30 ± 13
Varicella Zoster	7	3.8	277 ± 56
Total	182	100	

82



Discussion.

The prevalence of cutaneous complaints found in this study was 5.17%. This is similar to the 5.4% prevalence found by Nnoruka in Enugu south east Nigeria³. This may be due to the similar socio-demographic characteristics of the study locations. It however differs slightly from the 4.3% prevalence recorded by Yahya⁴ in Kaduna North central Nigeria. This is a reflection of the dynamic nature of HIV infection in different parts of Nigeria.

The prevalence of viral skin conditions found in this study is however 37.1%. This differs from the 29.7% of viral infections found by Lanjewar et al and 27.8% by Chopa et al among their cohort of Indian patients' studied⁵⁻⁶. It however still represents the largest percentage of the cutaneous pathology seen in both studies. This may be a reflection of different patterns of opportunistic infections prevalent in their subjects compared to that found in this study.

Regardless of this it still confirms the general observation that viral infections, are a major cause of opportunistic infections in HIV-infected adults, and can lead to significant morbidity and mortality. These may be because cell mediated immunity is required to clear viral infections from the human body. Also delayed recognition of viral lesions for what they are and lack of prompt treatment where available contribute to this high prevalence. According to Tsigrelis et al the primary reason for these may be the lack of access to HAART for most people living with

HIV/AIDS¹ and for those patients that have access to HAART some may not have an effective response to therapy, due to reasons such as medication toxicity, poor adherence, or drug-resistant strains of HIV.

Herpes Zoster accounted for the highest cutaneous viral lesions seen at 27% of the viral skin manifestations. This is similar to what was observed by Josephine et al⁷ in which herpes zoster accounted for 28.1% of cutaneous features among their cohort of patients. Herpes zoster is also the commonest viral skin pathology reported from patients in Togo⁸ and Dares- Salam⁹. Onunu et al in Benin city Nigeria had noted earlier that herpes zoster occurs with higher frequency among persons who are seropositive for human immunodeficiency virus (HIV) than among those who are sero-negative¹⁰. In other parts of the world, the prevalence of Herpes zoster is lower but still represents the largest viral infection in HIV infected patient as observed by Sivayathorn et al who found it in 16.1% of their patients in Thailand¹¹. Declining virus-specific cell-mediated immune responses, which occur naturally as a result of aging or are induced by immunosuppressive illness such as HIV infection, increase the risk of developing herpes zoster¹². HIV-infected patients have been noted to be at higher risk of developing zoster than age-matched, HIV-uninfected individuals¹⁰. Herpes Zoster may occur at any time in the course of HIV-induced immunosuppression, and may be the first clinical clue to suggest undiagnosed HIV infection¹². An episode of zoster in a young individual therefore warrants consideration of underlying HIV infection. Recurrent episodes of herpes zoster also may occur in HIV-infected patients, and appear to be more common than in the HIV-uninfected population¹²⁻¹⁵.

However the prevalence of varicella zoster infection (chicken pox) due to the same virus in this study was 3.8%. This may be a reflection of the baseline prevalence of the virus in the community because varicella zoster represents an acute presentation while herpes zoster is a reactivation of a previously dormant virus, therefore varicella zoster infection may not be a reflection of a waning immune system as is herpes zoster infection. Varicella usually is a benign and self-limiting illness, but can be more severe in adults and in individuals with cellular immunodeficiency such as that occasioned by infection with the HIV virus¹⁶. These individuals are at much higher risk of pneumonia¹⁷ and disseminated disease¹⁸ with visceral involvement though none was observed in this study.

Genital warts are responsible for the second largest group of viral skin condition noted in this study occurring in 19.2% of patients. This is higher than the 7% rate found by Katusiime et al in an urban clinic cohort of HIV positive patients². Similarly Low et al also found 7% prevalence among HIV positive women in Burkina Faso¹⁹. This may be a reflection of a reduced transmission rate of human papilloma virus infection in the studied population compared to that of this study. Genital infection with human papillomavirus (HPV) is the most common sexually transmitted infection in most parts of the world including the developed countries like the United States of America²⁰. The association between HIV and HPV infections may be related to the similar risk factors responsible for the acquisition and transmission of the two viruses. Human papilloma virus infections are one of the most common sexually transmitted infections globally, and genital warts, caused by HPV-6 and 11, causes considerable morbidity and sometimes mortality due to the risk of associated complicating neoplasia²¹. HIV infection and associated immunodeficiency are known to alter the course of human papillomavirus (HPV) infections and of associated diseases²². Genital warts occur much more frequently among HIV-1 infected patients particularly women in Africa, particularly among those with low CD4 cell counts²¹. HIV infection and immunodeficiency has been known to synergistically modify the relation between HPV 6 or 11 infection and genital wart prevalence²². Coinfection with HIV and HPV increases the risk for genital intraepithelial neoplasia in both women and men, and the increase in this risk reflects the severity of immunosuppression²¹. Detectable cervical and anal HPV infection is more prevalent among women and men with HIV infection than in the HIV-seronegative population, and the magnitude of the increase in prevalence is proportionate to the severity of immunosuppression. According to De Vuyst et al, despite the scarcity of high quality cancer registries and lack of reliable mortality data, it is clear that human papillomavirus (HPV)-associated diseases, particularly cervical cancer, are major causes of morbidity and mortality in Sub-Saharan Africa (SSA) especially with HIV infection increasing the incidence and prevalence of all HPV-associated diseases²³. Cervical cancer incidence rates in SSA are the highest in the world and the disease is the most common cause of cancer death among women in the region.

Plain viral warts occur in 15.4% of our patients in this study. It appears common in HIV infected patients from this part of Africa particularly in paediatric patients as has been previously reported by Umoru et al²⁴ and Salami et al²⁵ in Nigeria. Doni et al however found a lower prevalence of

160 8% among a cohort of HIV positive children living in an orphanage in Ethiopia²⁶. Plain viral
 161 warts found are flat wart like lesions that present as scaly hyper- or hypopigmented confluent
 162 linear patches and mildly raised plaques are widely distributed on the hands, arms, and face.
 163 There is increasing evidence that the major predisposing factor to the development of this viral
 164 infection is a dysfunction in cell-mediated immunity as a result of the HIV infection that is a
 165 potent suppressor of all forms of immunity²⁷. These usually develop as the immune status of the
 166 patient continues to decline.

167 Herpes simplex viral infections also occur in 15.4% of the patients in this study. This is similar
 168 to the 17.7% found by Goh et al²⁸. It is however in contrast to the 10.9% found by Sivayathorn
 169 et al¹¹. In both studies however, it still represents one of the commonest cutaneous manifestations
 170 among their cohorts of HIV infected patients. Herpetic infections are a common group of
 171 infections in this environment however it assumes a special significance in the HIV population as
 172 it can present with florid and systemic manifestation.

173 Molluscum contagiosum accounted for 7.7% of the viral infection seen in this study. This is
 174 lower than the 21% found by Doni et al among HIV infected children in Ethiopia²⁶. This may be
 175 due to the paediatrics predisposition of the infection and this has been confirmed by other
 176 researchers in paediatrics patients with HIV infection²⁹⁻³¹. Molluscum contagiosum is generally
 177 less common in adults unless the immune system is compromised with conditions such as HIV
 178 infection or malignancy. In adult patients with HIV, there is a general tendency to occur in
 179 unusual sites such as the eyes as noted by Emina et al³². This is reflected in the low CD4 counts
 180 of patients molluscum contagiosum found in this study.

181 Pityriasis Rosea like lesions was found in 11.5% of our patients. Its etiology has been linked to
 182 the human herpes virus 7(HHV-7), reported in 1990 as a lymphotropic member of the beta
 183 herpes virus subfamily of herpes viruses³³⁻³⁴. The virus is a highly sero-prevalent, primary
 184 infection that usually occurs in children and young adults. The effect and prevalence of this virus
 185 on the skin has been poorly studied particularly as regards its occurrence in patients with HIV
 186 infection. Several reviews on cutaneous manifestations of HIV infection have mentioned the
 187 occurrence of pityriasis rosea occurring in patients with HIV infection. Staughton even
 188 speculated that the features might be an acute seroconversion illness of HIV infection³⁵. HHV-7

infection has a variety of effects on host cells including up regulation of interleukin 15 and down-modulation of the cell surface molecule of CD4 T-Lymphocytes which serves as the cellular membrane receptor for HHV-7. Since HIV also infects T-cells via the CD4 molecule, the interactions of these viruses within T-cells during the course of AIDS are important areas of further investigation³⁶.

In conclusion, cutaneous viral infections are a common presentation in the HIV/AIDS population and their presence may be the first pointer of HIV infection or maybe a pointer of a deteriorating immune system that will require prompt attention without which it may herald significant morbidity or may eventually be a precursor of a malignant transformation. Its prompt recognition and appropriate and adequate attention reduces these endpoints. Knowledge of the changing pattern of cutaneous viral lesions in association with HIV/AIDS may help the clinical dermatologist and venerologist to identify these dermatoses and act in the most appropriate manner to support the patient particularly as there is a high prevalence of skin and mucocutaneous disorders in patients with HIV infection. An early detection of these lesions optimizes the care of many of these opportunistic cutaneous disorders and improves the patients' quality of life.

References.

1. Tsigrelis C, Berbari E, Temesgen Z. Viral opportunistic infections in HIV-infected adults. *J Med Liban*. 2006 Apr-Jun;54(2):91-96.
- Katusiime C, Schlech WF 3rd, Parkes-Ratanshi R, Sempa J, Kambugu A. Characteristics of Sexually Transmitted Infections among High-Risk HIV-Positive Patients Attending an Urban Clinic in Uganda. *J Int Assoc Provid AIDS Care*. 2013 Oct 21. 72(854):25-30
2. Nnoruka EN. Skin diseases in south-east Nigeria: a current perspective. *Int J Dermatol*. 2005 Jan;44(1):29-33.
3. Yahya H. Change in pattern of skin disease in Kaduna, north-central Nigeria. *Int J Dermatol*. 2007 Sep;46(9):936-943.
4. Lanjewar DN, Bhosale A, Iyer A. Spectrum of dermatopathologic lesions associated with HIV/AIDS in India. *Indian J Pathol Microbiol*. 2002 Jul;45(3):293-298

- 217 5. Chopra S, Arora U. Skin and Mucocutaneous Manifestations: Useful Clinical Predictors
218 of HIV/AIDS. *J Clin Diagn Res.* 2012 Dec;6(10):1695-1698.
- 219 6. Josephine M, Issac E, George A, Ngole M, Albert SE. Patterns of skin manifestations and
220 their relationships with CD4 counts among HIV/AIDS patients in Cameroon. *Int J*
221 *Dermatol.* 2006 Mar;45(3):280-284.
- 222 7. Pitche P, Tchangai-Walla K. Prevalence of Skin Manifestations in AIDS Patients in the
223 Lome-Tkom University Hospital (Togo). *Sante* 1995: 349–352.
- 224 8. Muhammad B, Eligius L, Mugusi F, Aris E, Chale S, Magao P, Josiah R, Moshi A, Swai
225 A, Pallangyo N, Sandstrom E, Mhalu F, Biberfeld G, Pallangyo K. The prevalence and
226 patterns of skin diseases in relation to CD4 counts among HIV-infected police officers in
227 Dar es Salaam. *Trop Doct* 2003; 33: 44–48
- 228 9. Onunu A.N, Uhumwangho A. Clinical spectrum of Herpes Zoster in HIV infected versus
229 Non- HIV infected patients in Benin city, Nigeria. *West Afr J Med* 2004 Oct-Dec
230 23(4):300-304.
- 231 10. Sivayathorn A, Srihra B, Leesanguankul W. Prevalence of skin disease in patients
232 infected with human immunodeficiency virus in Bangkok, Thailand. *Ann Acad Med*
233 *Singapore.* 1995 Jul;24(4):528-533.
- 234 11. Buchbinder SP, Katz MH, Hessel NA. Herpes zoster and human immunodeficiency virus
235 infection. *J Infect Dis* 1992;166:1153-1156.
- 236 12. Cone LA, Schiffman MA. Herpes zoster and the acquired immunodeficiency syndrome.
237 *Ann Intern Med* 1984;100:462.
- 238 13. Colebunders R, Mann JM, Francis H. Herpes zoster in African patients: A clinical
239 predictor of human immunodeficiency virus infection. *J Infect Dis* 1988;157:314-318.
- 240 14. Glesby MJ, Moore RD, Chaisson RE. Herpes zoster in patients with advanced human
241 immunodeficiency virus infection treated with zidovudine. *J Infect Dis* 1993;168:1264-
242 1268.
- 243 15. Weller TH. Varicella and herpes zoster: Changing concepts of the natural history,
244 control, and importance of a not-so-benign virus. *N Engl J Med* 1983;309:1362-8, 1434-
245 1440.
- 246 16. Popara M, Pendle S, Sacks L, Smego RA Jr, Mer M. Varicella pneumonia in patients with
247 HIV/AIDS. *Int J Infect Dis.* 2002 Mar;6(1):6-8.

17. Jayakrishnan A, Vrees R, Anderson B. Varicella zoster meningitis in a pregnant woman with acquired immunodeficiency syndrome. *Am J Perinatol*. 2008 Oct;25(9):573-575.
18. Low AJ, Clayton T, Konate I, Nagot N, Ouedraogo A, Huet C, Didelot-Rousseau MN, Segondy M, Van de Perre P, Mayaud P; Yérélon Cohort Study Group. Genital warts and infection with human immunodeficiency virus in high-risk women in Burkina Faso: a longitudinal study. *BMC Infect Dis*. 2011 Jan 20;11:20.
19. Vernon SD, Holmes KK, Reeves WC. Human papillomavirus infection and associated disease in persons infected with human immunodeficiency virus. *Clin Infect Dis*. 1995 Aug;21 Suppl 1:S121-124.
20. Conley LJ, Ellerbrock TV, Bush TJ, Chiasson MA, Sawo D, Wright TC. HIV-1 infection and risk of vulvovaginal and perianal condylomata acuminata and intraepithelial neoplasia: a prospective cohort study. *Lancet*. 2002 Jan 12;359(9301):108-113.
21. Silverberg MJ, Ahdieh L, Munoz A, Anastos K, Burk RD, Cu-Uvin S, Duerr A, Greenblatt RM, Klein RS, Massad S, Minkoff H, Muderspach L, Palefsky J, Piessens E, Schuman P, Watts H, Shah KV. The impact of HIV infection and immunodeficiency on human papillomavirus type 6 or 11 infection and on genital warts. *Sex Transm Dis*. 2002 Aug;29(8):427-435.
22. De Vuyst H, Alemany L, Lacey C, Chibwesha CJ, Sahasrabudhe V, Banura C, Denny L, Parham GP. The burden of human papillomavirus infections and related diseases in sub-saharan Africa. *Vaccine*. 2013 Dec 29;31 Suppl 5:F32-46
23. Umoru D, Oviawe O, Ibadin M, Onunu A, Esene H. Mucocutaneous manifestation of paediatric human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) in relation to degree of immunosuppression: a study of a West African population. *Int J Dermatol* 2012; 51: 305-312.
24. Salami T.A.T, Samuel S.O. Epidermodysplasia Verruciformis in paediatric patients with HIV infection- Report of two cases. *The Nigerian Clinical Review Journal*. 2008; Vol 72: 7-9

25. Doni SN, Mitchell AL, Bogale Y, Walker SL. Skin disorders affecting human immunodeficiency virus-infected children living in an orphanage in Ethiopia. *Clin Exp Dermatol.* 2012 Jan;37(1):15-19.
26. Prose NS, Von Knobel-Doeberitz C, Miller S, Milburn PB et al. Widespread flat warts associated with human papillomavirus type 5: a cutaneous manifestation of human immunodeficiency virus infection. *J Am Acad Dermatol.* 1990;23(5 Pt2):978-981.
27. Goh BK, Chan RK, Sen P, Theng CT, Tan HH, Wu YJ, Paton NI. Spectrum of skin disorders in human immunodeficiency virus-infected patients in Singapore and the relationship to CD4 lymphocyte counts. *Int J Dermatol.* 2007 Jul;46(7):695-699.
28. Zichichi L, Maniscalco M. The challenges of a neglected STI: Molluscum contagiosum. *Ital Dermatol Venereol.* 2012 Oct;147(5):447-453.
29. Mankahla A, Mosam A. Common skin conditions in children with HIV/AIDS. *Am J Clin Dermatol.* 2012 Jun 1;13(3):153-166.
30. Skerlev M, Husar K, Sirotković-Skerlev M. [Mollusca contagiosa. From paediatric dermatology to sexually transmitted infection]. *Hautarzt.* 2009 Jun;60(6):472-476.
31. Emina MO, Odjimogho SE. Ocular problems in HIV and AIDS patients in Nigeria. *Optom Vis Sci.* 2010 Dec;87(12):979-984.
32. Poljacki M, Rajić N, Matić M. [Etiopathogenic importance of human herpes viruses type 6, 7 and 8 in manifestations of certain skin diseases]. *Med Pregl.* 2001 Sep-Oct;54(9-10):459-463
33. Black JB, Pellett PE. Human herpesvirus 7. *Rev Med Virol.* 1999 Oct-Dec;9(4):245-262.
34. Staughton R. Skin manifestations in AIDS patients. *Br J Clin Pract Suppl.* 1990 Sep;71:109-13.
35. Sadick NS, McNutt NS, Kaplan MH. Papulosquamous dermatoses of AIDS. *J Am Acad Dermatol.* 1990 Jun;22(6 Pt 2):1270-1277