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ORIGINAL ARTICLE

Muco-Cutaneous Infections in HIV Infected Children at a Nigerian Tertiary Hospital

Infections Muco-Cutanées Chez les Enfants Infectés Par le VIH à Un Hôpital Tertiaire Nigérian

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ABSTRACT

BACKGROUND: Studies on mucous infections in HIV infected children are sparse. Cutaneous infections though common, vary in pattern and prevalence over time and location.

OBJECTIVES: To provide updates on the prevalence and pattern of muco-cutaneous infections among HIV infected children attending a Nigerian tertiary hospital and identify neglected muco-cutaneous infections.

METHODS: Consecutive HIV infected children seen over a 5-year period were studied. Relevant information on the subjects, HIV and presence or absence of skin infections was obtained. Data was analysed with SPSS version 16 software.

RESULTS: One hundred and thirty-two children were studied with ages ranging between 3 months and 17 years of which 68(51.5%) were boys and 64(48.5%) girls. Of the 132 children 64(48.5%) had muco-cutaneous infections, comprising 50(78.1%) cutaneous and 14(21.9%) mucous infections. Superficial fungal, viral, bacterial and parasitic infections were recorded in 45(34.1%), 18(26.6%), 12(9.1%) children and 1 (0.8%) child respectively. Thirty-six (56.2%) of the 64 children with muco-cutaneous infection were unaware of their skin infection prior to consultation. The rates of skin infection were significantly higher amongst children with advanced HIV disease, children whose caregivers had skin disease and children whose parents had no formal education and educational attainments limited to the primary school.($p< 0.05$). Presence of phlyctenular conjunctivitis in a child with hitherto undiagnosed tuberculosis was recorded.

CONCLUSION: Muco-cutaneous infections are common disease conditions of HIV infected children. Awareness of muco-cutaneous infections amongst those infected is poor. Interventions mitigating associated factors are expected to reduce the burden of this disease. **WAJM 2022; 39(4): 362–368.**

Keywords: Paediatrics, infective, dermatoses, human immuno-deficiency virus.

RÉSUMÉ

CONTEXTE: Études sur les infections muqueuses chez les personnes infectées par le VIH les enfants sont clairsemés. Les infections cutanées, bien que courantes, varient en le modèle et la prévalence au fil du temps et de l'emplacement.

OBJECTIFS: Fournir des mises à jour sur la prévalence et la tendance des infections muco-cutanées chez les enfants infectés par le VIH fréquentant un hôpital tertiaire nigérian et identifier les muco-cutanés négligés Infections.

MÉTHODES: Enfants infectés par le VIH consécutifs vus pendant 5 ans période ont été étudiés. Informations pertinentes sur les sujets, le VIH et la présence ou l'absence d'infections cutanées a été obtenue. Les données ont été analyses avec le logiciel SPSS version 16.

RÉSULTATS: Cent trente-deux enfants ont été étudiés avec âges compris entre 3 mois et 17 ans, dont 68 (51.5 %) étaient des garçons et 64 (48.5 %) des filles. Sur les 132 enfants, 64 (48.5 %) avaient infections muco-cutanées, comprenant 50 (78.1 %) cutanés et 14 (21.9 %) infections muqueuses. Fongique superficiel, viral, bactérien et des infections parasitaires ont été enregistrées chez 45 (34.1 %), 18 (26.6 %), 12 (9.1 %)enfants et 1 (0.8%) enfant respectivement. Trente-six (56.2 %) des 64 enfants atteints d'une infection muco-cutanée n'étaient pas au courant de leur infection cutanée avant la consultation. Les taux d'infection cutanée étaient significativement plus élevé chez les enfants atteints d'une maladie à VIH avancée,les enfants dont les soignants avaient une maladie de la peau et les enfants dont les parentsn'avaient pas d'éducation formelle et de niveau de scolarité limité à l'école primaire. ($p< 0.05$). Présence de conjonctivite phlycténulaire chez un enfant atteint de tuberculose jusqu'alors non diagnostiquée a été enregistré.

CONCLUSION: Les infections muco-cutanées sont des maladies courantes les conditions des enfants infectés par le VIH. Sensibilisation à la muqueuse-cutanéeles infections parmi les personnes infectées sont faibles. Interventions atténuantes on s'attend à ce que les facteurs associés réduisent le fardeau de cette maladie. **WAJM 2022; 39(4): 362–368.**

Mots-clés: Pédiatrie, Infectieux, Dermatoses, Humain virus de l'Immuno déficience.

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Abbreviations: HAART, Highly Active Antertroviral Therapy; **HIV,** Human Immunodeficiency virus.

INTRODUCTION

Muco-cutaneous infections are common in HIV infected children. Previous studies on this subject show that prevalence of skin infections range between 30–83 percent.[1–5] The study of muco-cutaneous infections in HIV infected individuals is important because the infections can serve as markers for underlying HIV disease or co-infections such as tuberculosis. Cutaneous infections can also indicate the clinical staging or severity of HIV disease.[4,6] Cutaneous infections also interfere with the anatomic and physiologic function of skin which is both the largest organ as well as the interface between the individual and his environment.

Previous studies on the pattern of muco-cutaneous infections in the HIV infected children document disparities in the absolute and relative rates of superficial fungal, viral, bacterial and parasitic infections.[2,4,7,] The prevalence and pattern of muco-cutaneous infections in HIV infected children attending the Paediatric Anti-Retroviral clinic at University of Osun (UNIOSUN) Teaching Hospital, Osogbo, South-Western Nigeria is unknown. The aim of the present study is to determine the pattern and prevalence of muco-cutaneous infections in HIV infected children as well as possibly identify neglected muco-cutaneous infections. Furthermore, the study also aims to determine the association between immunologic and socio-demographic factors that influence the prevalence of skin infections.

University of Osun Teaching Hospital, is a tertiary facility located in the capital city of Osun State, Nigeria. It provides specialist and general health care to the people of Osun state and the neighbouring states of Nigeria. The anti-retroviral clinic of UNIOSUN Teaching Hospital caters for all HIV diagnosed and exposed children aged from birth to 16years and is manned by 2 consultants and 4 registrars and 2 specially trained nurses.

SUBJECTS MATERIALS AND METHODS

Consecutive consenting HIV infected children and their accompanying care givers attending the paediatric ARV clinic between January 2015 and August 2020 were studied. Ethical approval was obtained from the Ethics and Research committee of the UNIOSUN Teaching Hospital, Osogbo, prior to undertaking the research and a protocol number LTH/EC/2009/04/107 was assigned to this study. Consent was obtained from accompanying caregiver and older children, while assent was obtained from the younger children where applicable.

Some of the information obtained from the children and their accompanying care givers include socio-demographic details of the children and their parents; such as the age, sex and domiciles. The HIV clinical stage of the patients were determined and classified based on the WHO clinical staging.[8]Stages III and IV were classified as advanced disease, while stages I and II were classified as non- advanced. Additional details obtained from the caregivers include the ages, educational attainments and HIV statuses of the parents. Vertical transmission of HIV was presumed in children whose mothers were HIV positive with no history or risk factors indicative of horizontal HIV transmission. The educational attainments were classified into 4 groups namely no formal education, primary school and equivalent training, secondary school and equivalent training and all forms of tertiary education.

All the studied children were carefully examined after undressing for the presence or absence of skin infection. The caregivers were also examined. Diagnosis of muco-cutaneous infections was based on the morphologic appearance of the skin lesions.[5] Diagnosis of tinea infection was taken to be itchy oval or concentric ring like structures with raised inflamed edges and central clearing. Thrush lesions were whitish materials adhering to the tongue or oral cavity that could not be scrapped away with a spatula. Impetigo lesions were raised lesions with erythematous edges either containing clear or golden or pussy fluid or broken down papules or vesicles with crusting. Furuncles or carbuncles were inflammation of the hair follicle or conglomeration of furuncles respectively. Pyogenic skin infection was confirmed by culture and sensitivity of the swab of the surface or secretion from the lesion where applicable. Viral warts were skin coloured papules or warty swellings presenting as solitary or multiple lesions, with some of the lesions showing evidence of koebner phenomenon. Herpes labialis lesions presented as grouped vesicles around the lips while, Mulloscum contagiosum lesions were skin coloured papules with central umbilication.

All the information obtained was recorded in a proforma specially designed for the study. Digital photographs of lesions were taken in cases where lesions were difficult to recognize and assessed by a consultant dermatologist, who was provided with clinical information about the cases. Diagnosis was adjusted thereafter based on photograph and dermatologist impression.

The CD4 count of the children was obtained from the haematological investigation of HIV infected children on the day of clinic attendance, based on standard clinical care for patients attending the clinic. The CD4 counts of the patient were grouped as CD4 <200 cell/ul, CD4 between 200–350 and CD4 > 350cell/ul for the purpose of this study. The information obtained was recorded in a personal computer. Data obtained was analysed using the SPSS version 16 software.[9] Numerical variables were expressed in proportions, ratios and percentages. Categorical variables were compared using the Chi-square (χ^2) test and statistical significance was set at 'p' value less than 0.05.

RESULTS

General Characteristics of the Children Studied

A total of 132 HIV infected children and their caregivers were studied. The ages of the children ranged between 3 months and 17 years, while the ages of the parents ranged between 18 and 56 years. In ninety five(75.0%) children the accompanying care givers were their mothers, while 14(10.6%) children were accompanied by their fathers and 9(6.8%) by their grandmothers. Six(4.5%) of the adolescents were unaccompanied by any

care giver, while in 2(1.5%) cases each the care giver was an elder sister, aunt and grandfather. In the remaining 1(0.8%) case each the caregiver was the uncle and a guardian respectively.

Prevalence and Pattern of Muco-cutaneous Infection in Children Studied

Of the 132 children studied 64(48.5%) had muco-cutaneous infections while 68(51.5%) had no skin infection. Superficial fungal infections were found in 45(34.1%) of the children, while 18(26.6%) had viral infections, 12(9.1%) bacterial infections and 1(0.8%) had parasitic infection. Table 1 shows the breakdown of infections amongst the 132 children. Ten children had more than one infection. Two of the children with tinea corporis presented with atypical or incognito patterns. The single case of phlyctenular conjunctivitis was a pointer to hitherto undiagnosed tuberculosis which was later confirmed with a chest radiograph and good response to anti-tuberculous treatment. Chest radiograph was used to confirm the diagnosis because the child could not produce sputum for AFB and non-availability of stool Gene Xpert.

Mucous infections were recorded in 14(10.6%) out of the 132 total studied children. The mucous infections were seen in 8 children with thrush, 3 with perineal candidiasis, 2 with herpes labialis and a child with phlyctenular conjunctivitis

Prior Knowledge of the Muco-cutaneous Infection by Patient/Caregiver

Of the 64 children with skin infections, 28(43.8%) were hitherto aware of having skin disease prior to consultation, while the remaining 36(56.2%) were unaware of their skin infection prior to consultation.

Age and Sex Distribution of the Children Studied

The range of the ages of the children studied was between 3 months and 17 years with a mean of 5.9 ± 4.0 years. Of the 132 children 69(52.3%) were aged between 1–5 years, 45(34.1%) between 6–10 years, 13(9.8%) between 11–15 years and 5(3.8%) between 16 and 17 years. Of the 132 children studied 68(51.5%) were boys and 64(48.5%) were girls, giving a male to female ratio of 1.1:1.0. Of the 68 boys 33(48.5%) had skin infection, while 31(48.4%) of the 64 girls had skin infection. The differences in the rates of skin infection across the sexes and age brackets were not statistically significant. Other details pertaining to this association are shown in Table 2.

Table 1: Pattern of Muco-Cutaneous Infections in the 132 Studied Children

Infection	Number of Patients Infected	Percentage (%)
Dermatophytoses		
Tinea capitis	15	11.4
Thrush	8	6.1
Tinea corporis	9	6.8
Tinea facei	3	2.3
Tinea auricles	3	2.3
Tinea unguim	3	2.3
Perineal candidiasis	3	2.3
Tinea Cruris	1	0.8
Viral Infection		
Viral warts	10	7.6
Molluscum contagiosum	3	2.3
Measles	2	1.5
Herpes labialis	2	1.5
Chicken pox	1	0.8
Bacterial Infection		
Impetigo	7	5.3
Carbuncle	2	1.5
Ecthyma	1	0.8
Blistering dactylitis	1	0.8
Phylctenular conjunctivitis	1	0.8
Parasitic Infection		
Scabies	1	0.8

Mode of Transmission of HIV to the Children Studied

Of the 132 children studied 112(65.1%) were presumed to have acquired HIV infection vertically and the remaining 20(11.6%) presumed to have acquired the infection horizontally through receipt of unscreened blood transfusion prior to diagnosis of HIV.

Clinical Staging of HIV in the Studied Children

The majority 87(65.9%) children studied did not have advanced HIV disease. Fourteen (8.1%) had stage I disease, while 70(40.7%), 42(24.4%) and 6(3.5%) had stages II, III and IV HIV disease respectively. Of the 14 children with stage I disease, 2(14.3%) had skin infection, while 31(44.3%) of the 70 with stage II disease, 27(64.3%) of the 42 with stage III and 4(66.7%) of the 6 with stage IV HIV disease had skin infection. The association between skin infection and clinical stage of the children is shown in Table 2. Of the 10 children that had more than 1 skin infection, 4 had stage II and 6 had stage III HIV diseases. None of the patients with 2 or more infections had stage I or IV disease. Of the 87 children with stage I and II HIV disease, four had more than 1 skin infection while 6(13.3%) of the 45 HIV infected children with stage III and IV disease had more than one infection. ($\chi^2 = 2.61$, P = 0.20 with Yates correction).

CD4 Count of Children with and without Muco-cutaneous Infection

The CD4 count of the 132 children studied ranged between 7 and 2682 cells/ul, with a mean of 686.40 ± 481.73. The mean CD4 count in the children with skin infections was 580.63 ± 457.08 compared with 785.96 ±486.36 cells/ul in those without skin infection. ($\chi^2 = 6.23$, P = 0.01).

Table 2: Association between Muco-Cutaneous Infection, Clinical and Immunologic States and some Socio-demographic Characteristics

	Infections Present N = 64	Infection Absent N = 68	χ^2 (with yates correction)	P value
Gender				
Boys	33	35	0.00	1.00
Girls	31	33		
Age groups (years)				
3months – 5 years	36	34	2.93	0.40
6 – 10	22	22		
11 – 15	5	7		
16 –17	1	5		
Immunologic Status				
CD4 < 200	5	6	0.00	1.00
CD4 > 200	59	62		
CD4 < 350	22	10	5.915	0.02
CD4 > 350	42	58		
Clinical Staging				
Non-advanced Stages 1 & II	35	52	6.03	0.01
Advanced Stages III & IV	29	16		
HAART Administration				
Yes	29	38	1.08	0.30
No	35	30		
Care Giver with Skin Disease				
Yes	9	1	5.78	0.02
No	55	67		
Mothers Educational Status				
Post primary school education	21	35	3.97	0.04
Primary school education only & No formal education group	43	33		
Fathers Educational Status				
Post primary school education	24	35	2.1	0.15
Primary school education only & No formal education group	40	33		

Association between CD4 and Muco-cutaneous Infection

Five (45.5%) out of the 11 children with CD4 < 200 cells/ul had skin infections and 17(81.0%) of the children with CD4 between 200 and 350 cells/ul had skin infections. The remaining 42(42.0%) of the 100 children with CD4> 350 had skin infection. The association between the CD4 counts and skin infection is shown in Table 2.

Parents Age and Condition

The mothers' ages ranged between 19 and 60 years with a mean of 33.9± 6.1, while the ages of the fathers ranged from 23–71 years with a mean of 41±8.5 years. Of the 132 children studied 126(95.5%) fathers and 123(93.2%) mothers are alive while 6(4.5%) and 9(5.9%) fathers and mothers respectively were dead as at the time of the study.

HIV Status of the Parents Studied

Of the 132 mothers studied 126(95.5%) had a positive HIV status while 5(3.8%) had retro-negative status and the remaining 1 mother did not know her HIV status. On the other hand amongst the fathers 46(34.8%) had a retro-positive status, 52(39.4%) were retro-negative and the remaining 34(25.8%) did not know their status as they had not tested.

Educational Attainments of the Parents Studied

Of the 132 fathers studied, 23(17.4%) had no formal education, while 50(37.9%) and 22(16.7%) either completed or uncompleted their primary and secondary school education respectively. The remaining 27(20.5%) fathers had tertiary institutional training. On the other hand amongst the 132 mothers, 35(26.5%) had no formal education, while 41(31.1%) and 31(23.5%) mothers respectively either completed or not completed their primary school and secondary school education respectively. The remaining 25(18.9%) mothers had tertiary training.

Care-givers' Skin Infection

Of the 132 caregivers studied, ten (7.6%) had skin infections, while 122(92.4%) did not. The diseases recorded in the ten care givers are viral warts in 3 and Tinea unguim in 2 care givers respectively. One case each of pityriasis versicolor, Molluscum contagiosum , Tinea facei, oral thrush and secondarily infected papular urticaria respectively were recorded.

Association between Parental Educational Status and Muco-cutaneous Infection in their Children

Of the 35 mothers with no formal education 16(45.7%) had infections, while 27(65.9%) of the 41 mothers with primary school training had skin infection also,12(38.7%) of the 31 with secondary school training. Nine(36.0%) of the remaining children of the 25 mothers with tertiary education had skin infection. Eleven(47.8%) of the 23 children of the fathers with no formal education had skin infections, while 29(58.0%) children of the 50 fathers with primary school training had skin infection and 9(40.9%) children of the 22 fathers with secondary school training had skin infections. The remaining 15(42.9%) children of the 35 fathers with tertiary education had skin infection. The association between parental education status and skin infection in their wards is shown in Table 2.

Initiation of HAART

Of the 132 children studied 67(50.8%) had been initiated on highly active anti-retroviral therapy (HAART), while 65(49.2%) had not. Twenty nine (43.3%) of the 67 children on HAART had skin infection, while 35(53.8%) of the 65 children not on HAART had skin infection. The association between skin infection and administration of HAART is shown in Table 2.

DISCUSSION

The present study shows that muco-cutaneous infections are common

in HIV infected children, with cutaneous infections dominating the presentation and mucous-cutaneous infections accounting for at least 10%. The prevalence in the present study is lower compared to an Ethiopian and another Nigerian study that both recorded a prevalence estimate of approximately 82%.[1,2] Bandi et al and Obiagwu et al in two separate studies reported a lower prevalence estimate of 32.5 and 1% respectively, which is a lower estimate compared to the 48.5% prevalence rate obtained in the present study.[3,10] Disparities in the pattern of infections were also observed across the various studies in terms of the relative rates of the superficial fungal, viral, bacterial and parasitic infections documented. The observed differences in the prevalence and pattern of infections may be adduced to differences in the hygiene status and methodologies adopted in the different geographic settings from which the various reports emanated.[1–3,7,10]

Superficial fungal or Tinea infections were the most common infections recorded in the present study, with a considerable proportion such as thrush and perineal candidiasis presenting on mucous membranes. Viral infections like warts and bacterial skin infections were the second and third most common muco-cutaneous infections recorded respectively. A high prevalence of infectious dermatoses is to be expected because of the depletion of the Langerhan's cells which are responsible for immunity.[6,11] It is also possible that the anti-retroviral drugs and routine Cotrimoxazole prophylaxis therapy in HIV infected children have selected antibiotic activity over opportunistic viral and bacterial infections respectively, thus leading to the greater preponderance of superficial fungal infections as recorded in the present study. Some other researchers have also documented similar trends.[1,2,10] On the other hand, studies conducted in Zimbabwe and Ethiopia record viral infections as the leading causes of infective dermatoses.[4,7]

Uncommon forms of Tinea corporis were recorded in the present study and this has seldom been reported in children, also it poses a diagnostic challenge.[12] Previous studies affirm that different forms of cutaneous infection can indicate underlying HIV disease or severity of HIV disease.

Diagnosing childhood tuberculosis is very challenging.[13] However, a new case of HIV-tuberculosis co-infection was made from the identification of the muco-cutaneous lesion (phlyctenular conjunctivitis). The identification of this mycobacterial skin marker is a significant diagnostic tool and aid for the diagnosis of childhood tuberculosis.[13]

The present study shows that the rates of muco-cutaneous infection were slightly higher among the boys and the children aged below 5 years. These differences were however not statistically significant. This finding is not unexpected because there is probably no significant difference in exposure to risk factors for skin infection across the sexes and the age group. Our findings in the present study are largely confirmatory of previous reports.[1,2,14]

The high rate of vertical transmission of HIV in the present study is alarming. Previous studied indicate that most of the HIV infections in Nigerian children are acquired vertically.[14–16] A lot needs to be done to reduce mother to child transmission of HIV in Nigeria. The high rates of the number of fathers not knowing their HIV status is both worrisome and a call to action for increased promotion of screening amongst both sexes in Nigeria. The mean age of the parents is also important as it shows that most of the parents are in their sexually reproductive ages. Thus, there is a need to take the prevention of HIV virus seriously and adhere to the national guidelines strategies to prevent transmission of HIV.[8,17]

More than a third of the HIV infected children did not know that they were infected prior to the study. Previous studies on skin infections shows that majority of the affected children and their care givers are unaware of their infections.[18,19] Expectedly, health seeking habit of the patients and their parents will be poor because they are unaware of their skin infection. Previous studies show that African patients and their caregivers have poor health seeking habits.[19,20]

Children without muco-cutaneous infections had a higher mean CD4 count and accounted for the majority of patients with stage I and II HIV disease in contrast to those with lower mean CD4 with advanced HIV disease. This difference was statistically significant. Our findings in the present study are similar to those of other researchers. A significantly greater proportion of children with CD4 <350cells/ul had skin infections compared to their counterparts with CD4> 350 cells/ul. These findings support the evidence for initiating HAART as a priority at a CD4 counts cut-off point of 350cells/ul in resource constrained settings if anti-retrovirals cannot be made available for all HIV-infected individuals.[8] The national guideline recommendation of initiating HAART in all HIV children regardless of HIV clinical staging is however the best practice.[9]

The differences across the greater proportion of HIV infected children with muco-cutaneous infections, yet to initiate HAART compared with the smaller proportion who had initiated HAART was not significant. This finding is consistent with a similar study conducted among Indian children.[21] Lower skin infection rates are expected among HIV-infected children on HAART, probably due to the positive immune modulating effect of HAART.[22] Unfortunately issues surrounding the period for which HAART was administered and adhered to were not addressed in the present study, thus making comparison inappropriate with other studies in which these issues were addressed. Furthermore, the criteria for initiating Cotrimoxazole prophylaxis and HAART are similar.[8] Thus, most children on HAART are invariably on Cotrimoxazole prophylaxis which has some anti-bacterial and anti-protozoal activities. A previous study has shown that prolonged Cotrimoxazole prophylaxis had a significant protective effect against bacterial skin infection.[23] The present study however did not examine the effect of Cotrimoxazole prophylaxis on skin infections.

A significant association was recorded between the presence of muco-cutaneous infection in both patients and the caregivers. This is as expected because infectious diseases can be easily transmitted among individuals with close contact. The present study could not

however establish that the skin infections in the patient were acquired from the caregiver. This subject will require more detailed studies as it may have a part to play in the holistic management of the patient and control of further transmission of skin infection.

Parental education was another factor which showed some form of association with the rates of muco-cutaneous infection encountered in the children studied. The association between the higher rates of skin infections recorded among the mothers who lacked formal education or received only primary school education or its equivalent which was statistically significant compared to the lower rates of infection amongst mothers with secondary school and tertiary training level of education. A similar association though not significant was recorded among the fathers. This finding further highlights the value of female education, thus emphasizing the importance of an educated mother. Educated mothers are more likely to take better care of their children and have better health seeking behaviour.[17,24]

It is concluded that the most common muco-cutaneous infections amongst HIV-infected children are tinea, viral warts and pyoderma bacterial infections. Furthermore, a non-advanced WHO clinical stage and good immunologic status with CD4 > 350 cells/ul are associated with lower rates of skin infections. The presence of skin infection in the caregivers and poor maternal education are also associated with a significant risk of cutaneous infections in HIV infected children. Tinea incognito and phlyctenular conjunctivitis, though uncommon, should be carefully sought by a thorough examination of the skin by attending healthcare worker in order to detect and manage these conditions, considering the fact that most of the infected children were hitherto unaware of their muco-cutaneous infections.

We recommend the adoption of strategies that will reduce the preponderance of skin infections amongst caregivers and improve maternal education coupled with utilization of interventions that will enhance the immunologic status and prevent progression of HIV disease progression in order to reduce the prevalence of skin infections. Most importantly, the reduction or prevention of HIV infections altogether should remain a primary goal in the management of HIV disease.

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Duality of Interest

There is no conflict of interest.

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