A Comparative Study of Mucocutaneous Disorders among Human Immunodeficiency Virus (HIV) Infected Children and Non-HIV Infected Children in a Teaching Hospital in Kano, Northern Nigeria

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ABSTRACT

Background: Mucocutaneous disorders are common among children, most especially infections and infestation as immunity is not fully developed during childhood. They are especially important in HIV-infected children and contribute to the risk of other life-threatening illnesses.

Objectives: To assess the prevalence of mucocutaneous disorders among HIV-infected children and that among non- HIV-infected children. To compare the pattern of mucocutaneous disorders among HIV-infected children and non- HIV-infected children. This study is expedient because comparative data on the prevalence and pattern of mucocutaneous disorders among HIV-infected and non-HIV-infected children in this environment are few

Materials and methods: An analytical cross-sectional study was conducted among 223 HIV-infected children aged 6 weeks to 14 years and an equal number of non- HIV-infected children from the study area. The chi-square test and Fisher's exact test were used where necessary to determine the difference between the proportions of categorical variables and the level of significance was set at 0.05.

Results: The prevalence of mucocutaneous disorders among HIV-infected children was 78.0% compared to 24.7% among non-HIV-infected children ($p < 0.001$). The leading categories were infections and infestations accounting for 55.1% among HIV-infected subjects and 18.3% among non-HIV-infected children ($p < 0.001$), then inflammatory skin disorders (20.6% among cases and 5.8% controls).

Conclusion: This study found that the prevalence of mucocutaneous disorders among HIV-infected children is higher (78.0 %) compared to that in non-HIV-infected children (24.7%).

Keywords: Paediatric dermatoses, HIV, Nigeria

Étude Comparative des Troubles Cutanéo-muqueux chez les Enfants Infectés par le Virus de l'immunodéficience Humaine (VIH) et les Enfants non Infectés par le VIH dans un Hôpital Universitaire de Kano, dans le Nord du Nigeria

Contexte : Les troubles cutanéo-muqueux sont fréquents chez les enfants, en particulier les infections et les infestations, car l'immunité n'est pas complètement développée pendant l'enfance. Ils sont particulièrement importants chez les enfants infectés par le VIH et augmentent le risque de développer d'autres maladies potentiellement mortelles.

Objectifs : Évaluer la prévalence des troubles cutanéo-muqueux chez les enfants infectés par le VIH et chez les enfants non infectés par le VIH. Comparer l'évolution des troubles cutanéo-muqueux chez les enfants infectés par le VIH à celle des enfants non infectés par le VIH. L'intérêt de cette étude est la rareté des données comparatives sur la prévalence et le profil des troubles cutanéo-muqueux entre les enfants infectés par le VIH et ceux non infectés dans cet environnement

Matériels et méthodes : Une étude transversale analytique a été menée auprès de 223 enfants infectés par le VIH âgés de 6 semaines à 14 ans et d'un nombre égal d'enfants non infectés de la zone d'étude. Le test du khi-deux et le test exact de Fisher ont été utilisés lorsque cela était nécessaire pour déterminer la différence entre les proportions de variables catégorielles et le niveau de signification a été fixé à 0,05.

Résultats : La prévalence des troubles cutanéo-muqueux chez les enfants infectés par le VIH était de 78,0 % contre 24,7 % chez les enfants non infectés ($p < 0,001$). Les principales catégories étaient les infections et les infestations,

représentant 55,1 % chez les sujets infectés par le VIH et 18,3 % chez les enfants non infectés (p < 0,001), puis les dermatoses inflammatoires (20,6 % chez les cas et 5,8 % chez les témoins).

Conclusion : Cette étude a révélé que la prévalence des dermatoses cutanéo-muqueuses chez les enfants infectés par le VIH est plus élevée (78,0 %) que chez les enfants non infectés par le VIH (24,7 %).

Mots-clés : Dermatoses pédiatriques, VIH, Nigeria

Introduction

Infection with the human immunodeficiency virus (HIV) is a global health issue. By the end of 2019, it was anticipated that HIV/AIDS had infected more than 38 million individuals around the world. Around 1.8 million of those infected were children under the age of 15, the majority of them were from Sub-Saharan Africa. Nigeria has a countrywide HIV prevalence of 1.4 percent, with more than 1.9 million Nigerians living with HIV/AIDS by the year 2021, making Nigeria the world's fourth-highest HIV burden country.[1-3]

Among children, mucocutaneous diseases are prevalent, especially infections and infestations, because their immune system is not fully developed during childhood.[4] Skin problems, together with malaria and diarrhea, are among the most common causes of morbidity in Sub-Saharan African countries.[5] Among children, mucocutaneous problems are a big source of concern. HIV/AIDS can affect practically all organs and systems in the body, and the skin is one of the first systems to be impacted.[6]

The pathophysiology of several mucocutaneous abnormalities linked with HIV/AIDS in children is currently unknown. The decline in CD4+T cell count, the shift to a Th2 cytokine profile, molecular mimicry, and superantigen overexpression are all important aspects in the development of mucocutaneous disorders in HIV infection.[7-10]

Mucocutaneous disorders among HIV/AIDS-infected children are prevalent. Some in Sub-Saharan Africa reported a prevalence rate of about 90%.[11] El Hachem et al[12] investigated 166 children in Rome, Italy, 85 of whom were HIV-positive and 81 of whom were not. Of the HIV-positive children, 89.5 percent had one or more skin disorders, compared to 42.0 percent of the non-HIV-positive children.

Objectives: To assess the prevalence of mucocutaneous disorders among HIV-infected children and to compare the pattern of mucocutaneous disorders among HIV-infected children and non- HIV-infected children.

Materials and methods

It was a cross-sectional study among children aged 6 weeks to 14 years from the study area. The age of 14 years was used because the hospital policy regards 14 years as the age limit for paediatric patients.

Sample size determination

The minimum sample size for the study was calculated using the standard formula for comparative studies.[13]

$$N = \frac{(Z\alpha + Z_{1-}\beta)^2 (P_1q_1) + (P_2q_2)}{(p_1 - p_2)^2}$$ [13]

Where; N - minimum sample size.

Z = the standard normal deviate corresponding to the level of significance of 5%=1.96 (obtained from the normal distribution table).

Z_{1-} = Standard deviate corresponding to a power of 80% = 0.84 (obtained from normal distribution table).

p_1 = estimated prevalence of skin disorders in HIV-infected children in a previous study in Kano Nigeria which was 27.3%.[14]

p_2= Prevalence of skin disorder in the control group in the previous study in Ibadan, Nigeria taken as 18.1%.[15]

$q_1 = 1-p_1$ $q_2 = 1-p_2$

Therefore,

$$N = \frac{(1.96+0.84)^2 (0.273X1-0.273) + (0.181X1-0.181)}{(0.273-0.181)^2}$$

= 200.89 approximately 201.

A response rate of 90% (0.9) was anticipated therefore the sample size was calculated as follows:

$$n = N/0.9 \qquad = 201/0.9$$
$$= 223.3$$

N is the originally calculated sample size and n is the sample size after adjusting for an anticipated response

rate of 0.9. Consequently, a sample size of 223 HIV-infected children and 223 non-HIV-infected children was studied.

Sampling technique

Selection of HIV- infected children

A systematic sampling method was used for recruiting participants into the study. Both new and follow-up clients were included. An average of 50 HIV-positive paediatric patients are seen weekly with an average of 10 patients seen daily in the Paediatric infectious disease Clinic as obtained from the Records Department of Aminu Kano Teaching Hospital.[16] Maximum duration before routine follow-up consultation in the clinic is three months. Therefore, the researcher carried out the study over 3 months (12 weeks). The clinics run daily, five days a week. The sampling frame was [50 (average number of HIV-positive paediatric patients seen weekly) x4 (number of weeks in one month)] x3 (duration for the study)] = 600. The sampling fraction = sample size /sampling frame = 223/600 = 0.37. The sampling interval was obtained by calculating the reciprocal of the sampling fraction that is, 1/0.37 = 2.7 which is approximately 3. Therefore, every 3rd patient was recruited for the study until the required number was achieved.

Ethical clearance was obtained from the Ethical committee of the hospital (Appendix I) and also informed consent from the parents of the children as well as verbal assent from those aged 7 or more years. An equal number of non-HIV-infected children were recruited from the Paediatric Out-patient Department of the same hospital as the comparison group. Confidentiality was maintained. Exclusion criteria were children who refused examination, children with malignancies, children on steroids for more than one month, and children on cytotoxic drugs.

The research was conducted between 10th July and 20th October 2017. A pre-tested questionnaire was used to collect data. A sociodemographic history was gathered, as well as the history of any skin lesions that might have been present. The participants' socioeconomic status was determined using the approach proposed by Oyedeji.[17]

A thorough physical examination was conducted by the researcher including dermatological examination of the hair, scalp, trunk, nails, oral mucosa, genital, and extremities. All observed lesions were photographed. The examination was conducted in a well-lit room with the aid of a chaperone after good exposure. Most of the diagnoses were made on a clinical basis but those that required further care were referred to the dermatology clinic and those with easily treatable conditions had appropriate medications prescribed. Rapid HIV antibody testing by determine® method, PCR, CD4+ count, and Full blood count are part of the routine workup for all patients attending the PIDC which is sponsored by the Institute of Human Virology (IHVN-N CDC/UMD-PEPFAR) program and were retrieved from the subject's record. The current CD4+ count done about 3 months before recruitment was used. Controls were confirmed HIV-negative at the Voluntary Counselling and Testing Unit of Paediatric Outpatient Unit.

The following categories of children were excluded from the study: All HIV-infected children whose HIV status has not been disclosed to them. All HIV-infected children who have been on steroids for long periods (more than one month) or are on cytotoxic drugs.

The data was entered into SPSS version 24, a computational kit for social sciences. Frequency tables and charts were created using the data. The Chi-square test or the Fisher exact test was used to assess differences in proportions of categorical variables (where necessary) and the level of significance was set at 0.05.

Results

There were 110 males (49.3%) and 113 females (50.7%) HIV-positive children and HIV-negative children respectively. The male-to-female ratio is 1:1.1. This is shown in Table I which also displays the socio-economic class and ethnicity of the children. Most of the subjects (43.9%) were in the 5-9-year age group while 110 (49.3%) were from lower socio-economic class.

Prevalence of mucocutaneous disorders among the study population

Skin disorders were found among 174 (78.0 %) HIV-

infected children in this study, and 55 (24.7%) non-HIV-infected children ($p < 0.001$). Some children had more than one mucocutaneous disorder. There was a significant statistical association between HIV-seropositivity and the occurrence of skin lesions ($\chi^2 = 127.1, p < 0.001$).

According to Table II, the mucocutaneous disorders identified among the HIV-infected children and non-HIV-infected children belong to three broad groups of skin disorders (infections and infestations, inflammatory and miscellaneous skin disorders). Infections and infestations were the most common category observed among both HIV-infected and non-HIV-infected children followed by inflammatory skin disorders. Among the HIV-infected children, dermatophytoses (16.1%), Pruritic papular eruption (10%), and Oral candidiasis (8.1%) were the most frequent lesions. On the other hand, seborrheic dermatitis (3.1%) was the most frequent lesion followed by dermatophytoses (2.7%) among the non -HIV infected children and this is shown in Table III.

Discussion

The prevalence of mucocutaneous disorders among HIV-infected children in this study was high 78.0 % compared with 24.7% among non -HIV-infected children. This is similar to what Umoru *et al*[18] and Katibi *et al*[19] found in Benin and Ibadan respectively, where the prevalence of mucocutaneous disorders was 64.0% and 12.0 %, 53.5% and 18.1% among HIV-infected children and non -HIV-infected children respectively. Another study in Lagos state, Nigeria by Osinaike *et al*[11] also reported a higher prevalence of mucocutaneous disorders among HIV-infected children (83.0%) compared with non-HIV-infected children (67.0%).

This similar trend in prevalence is perhaps because this study also employed a methodology that was similar to that of the aforementioned studies in terms of study sites (hospitals) and study design (cross-sectional). A similar higher prevalence of mucocutaneous disorders among HIV-infected children compared with non-HIV-infected children was reported by Lowe *et al*[20] in Zimbabwe (88.0% and 14.0%) and Elhachem *et al*[12] in Rome, Italy (89.5% and 42.0 %) among HIV infected children and non -HIV infected children respectively. This higher prevalence of mucocutaneous disorders among HIV- infected children shows that mucocutaneous disorders are more common among HIV-infected children than non- HIV-infected children. The higher prevalence of skin disorders among HIV-infected children may be due to impaired immunity as a result of the reduced ability of the Langerhans cells in the skin of the HIV-infected children to cause T lymphocyte proliferation.[21]

Among HIV-infected children in this study, infections and infestations (55.2%) were the most common category of skin disorders. This is similar to findings by other works [12,22-24]Conversely, studies in Lagos[11] and Abuja[22] Nigeria, and that in Zimbabwe,[20] reported inflammatory skin disorders as the commonest seen among HIV-infected children.

Different types of skin disorders observed in dermato-epidemiologic studies underscore the fact that the occurrence of skin diseases is often subject to a variety of factors such as environmental conditions as well as the age of the study population recruited among others, which differ among various studies mentioned above. Some skin disorders have a higher prevalence among some age groups and in certain localities which points to the effect of socio-demography in the occurrence of skin disorders.[25]

This study also found infections and infestations to be the most common lesion among non -HIV infected children which is comparable to findings by Umoru *et* al[18] in Benin. Umoru *et* al[18] however, reported dermatophytoses (66.7%) and acne (16.7%) as the most common lesions among non-HIV infected children different from what was obtained in this study where seborrheic dermatitis and dermatophytoses were the most common among 9.4% of the non- HIV- infected children. The differences in age groups recruited by this study (6 weeks to 14 years) and their study[18] (18 months to 16 years) perhaps contributed to the observed differences in findings from the two studies. Acne has long been considered a disease of the adolescent age group. Studies have shown that it affects between 70 to 87% of adolescents.[28] In Nigeria, the prevalence of acne among adolescents is said to be up to 90.7%. [29] Benin study included adolescents up to 16 years which may be the reason why acne was among the two common

lesions observed among non- HIV infected children in their study, while this study included more of younger children which may be the reason why acne was not among the common skin lesions in this study as observed in Benin study.

Conversely, miliaria was the most common skin disorder observed among non-HIV-infected children in the Ibadan study.[18] The differences observed among non-HIV infected children in this study and that in Ibadan,[19]Nigeria may be due to differences in weather conditions between the study areas at the time both studies were conducted. Ibadan study was conducted between April and June when the temperature was usually very hot.[15] This study was conducted between July and October. The skin is the most exposed part of the body; therefore, components of the skin are highly sensitive to climatic change. Humidity and changes in temperature can also increase the incidence of skin colonization and infection by some bacterial and fungal agents. Hence certain skin diseases like miliaria appear to be more prevalent in some climates and almost non-existent in others.[30]

This study will serve as a baseline for further studies and for healthcare planning of HIV-infected children in this environment.

Limitations of the study

This study was not able to assess the effect of ART use on the prevalence and pattern of skin disorders among HIV-infected children as 98.0 % of the subjects were on ART according to the current National guideline for the treatment of HIV-infected people.

Line of future study.

A study on the impairment in dermatology-specific Quality of Life among HIV-infected children. Conclusion

This study found that the prevalence of mucocutaneous disorders among HIV-infected children is higher (78.0 %) compared to that in non-HIV-infected children (24.7%).

Infections and infestations were the most common category found among both HIV-infected children and non-HIV-infected children followed by inflammatory skin disorders.

Conflict of interest: None

Orcid iD: https://orcid.org/0000-0003-2004-349X

Funding: Nil

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Table I: Socio-demographic characteristics of the study population

Characteristic	HIV infected cases n= 223 (%)	HIV-negative controls n=223 (%)
Gender		
Male	110 (49.3)	110 (49.3)
Female	113 (50.7)	113 (50.7)
Age		
0-4 years	77 (34.6)	77 (34.6)
5-9 years	98 (43.9)	98 (43.9)
10-14years	48 (21.5)	48 (21.5)
Socioeconomic class*		
Lower	110 (49.3)	110 (45.3)
Middle	80 (35.9)	97 (43.5)
Upper	33 (14.8)	25 (11.2)
Child's ethnicity		
Hausa	185 (82.9)	192(86.0)
Yoruba	14 (6.3)	9 (4.1)
Igbo	12 (5.4)	8 (3.6)
Others	12 (5.4)	14 (6.3)

* Social class I&II: upper, social class III: middle and social class IV&V: lower

Table II: Types of mucocutaneous disorders among HIV-infected and non-HIV-infected children

Category of skin disorder	**HIV infected n= 223 (%)**		**Non-HIV-infected n=223(%)**		**χ^2**	**P value**
	Present	**Absent**	**Present**	**Absent**		
Infections and infestations	123 (55.2)	100 (44.8)	41 (18.3)	182 (81.7)	64.84	< 0.001**
Viral	40 (17.9)	183 (82.1)	15 (6.7)	208 (93.3)	12.96	0.001**
Fungal	54 (24.2)	169 (75.8)	12 (5.4)	211 (94.6)	31.37	<0.001**
Parasitic	8 (3.6)	215 (96.4)	1 (0.4)	222 (99.6)	#	0.04**
Bacterial	21 (9.4)	202 (90.6)	13 (5.8)	210 (94.2)	2.04	0.21
Inflammatory	46 (20.6)	177 (79.4)	13 (5.8)	210 (94.2)	21.27	<0.001**
Miscellaneous	13 (5.8)	210 (94.2)	4 (1.8)	219 (98.2)	4.95	0.05

Some subjects had more than one diagnosis.
Fishers exact test, **significant, χ^2 –Chi-square, % percentage

Table III: Various types of infections and infestations among the study population

Type of infection / infestation	HIV infected children n=223 (%)	Non-HIV infected children n=223 (%)	χ^2	P value
Viral	**40(17.9)**	**15 (6.7)**	#	**0.001****
Molluscum contagiosum	6 (15.0)	4 (26.6)	#	**0.75**
Herpes stomatitis	3 (7.5)	1 (6.6)	#	**0.25**
Oral warts	6 (15.0)	1 (6.6)	#	**0.12**
Facial warts	5 (12.5)	0 (0.0)	#	**0.01****
Chicken pox	3 (7.5)	6 (40.0)	#	**1.00**
Planter warts	2 (5.0)	0 (0.0)	#	**0.06**
Measles	2 (5.0)	3 (20.0)	#	**1.00**
Herpes zoster	7 (17.5)	0 (0.0)	#	**0.02****
Epidermodysplasia verruciformis	6 (15.0)	0 (0.0)	#	**0.02****
Fungal infections	**54 (24.2)**	**12 (5.4)**	**31.37**	**<0.01****
Oral candidiasis	18 (33.3)	1 (33.3)	**15.89**	**<0.01****
Tinea unguim	4 (7.4)	0 (0.0)	#	**0,12**
Tinea capitis	23 (42.6)	6 (50.0)	**14.43**	**<0.01****
Ptyriasis vesicolor	2(3.7)	3 (25.0)	#	**1.00**
Tinea facie	2(3.7)	1 (8.3)	#	**0.25**
Tinea coporis	5(9.3)	1 (8.3)	#	**0.06**
Parasitic	**8 (3.6)**	**1 (0.4)**	#	**0.34**
Scabies	8 (100.0)	1(8.3)	#	**0.04****
Bacterial	**21 (9.4)**	**13 (5.8)**	**2.04**	**0.15**
Folliculitis	5 (23.8)	3 (23.0)	#	**0.45**
Ecthyma	4 (19.0)	1 (7.7)	#	**0.12**
Furunculosis	8 (38.2)	4 (30.8)	#	**0.38**
Impetigo	4 (19.0)	4 (30.8)	#	**1.00**
paronychia	0 (0.0)	1 (7.7)	#	**1.00**

Fishers exact test, **significant, χ^2 –Chi-square, % percentage