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ORIGINAL ARTICLE

Prevalence of mucosal and cutaneous disorders among HIV/AIDS adult Filipino patients 18-60 years old seen in a tertiary hospital in Makati City

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ABSTRACT

BACKGROUND With the recent rise in number of HIV/AIDS patients in the Philippines, knowledge of the most common mucosal and cutaneous findings among HIV/AIDS patients can be a valuable tool of assessment.

OBJECTIVES To determine the different mucosal and cutaneous disease findings of HIV/AIDS patients; evaluate their frequency and association with the latest CD4 cell counts, and to determine patients' demographic and medical profiles.

METHODS This is a cross-sectional study done at a tertiary hospital in Makati city from January 2017 to September 2018. Walk-in patients or those referred by Infectious Disease specialists were evaluated using a standardized history and physical examination form. Latest CD4 counts were also obtained.

RESULTS A total of 93 patients were enrolled. Majority were males (98%), with a mean age of 32 +/- 7.08, employed (64%), and on HAART (87%). A large part of the group (45%) has severe immunosuppression (CD4 counts <200/mm3). The most common manifestations were the following: non-infective, fungal, and drug-related dermatoses, with the most common dermatoses being seborrheic dermatitis, xerosis, pruritic papular eruptions (PPE), superficial fungal infections, drug hypersensitivity reactions, and syphilis. PPE was noted to be significantly associated with low CD4 counts.

CONCLUSION Due to small population size, significant associations between the other dermatoses with their CD4 counts were not seen except for PPE, which was significantly associated with CD4 counts <200/mm3. Nevertheless, a strong suspicion for any underlying HIV//AIDS infection is still warranted in the presence of these dermatoses.

KEYWORDS HIV, AIDS, CD4 cell count

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INTRODUCTION

Mucosal and cutaneous lesions are frequent occurrences among Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS) patients. Skin is the usual initial site of involvement, and it has been documented that these changes occur at around 90% among people living with HIV.[1-4] They are also valuable tools of assessment that can serve as clinical indicators of HIV/AIDS when correlated with their CD4 counts.[3-5]

For the month of January 2021, the Department of Health (DOH) HIV/AIDS and Antiretroviral Treatment (ART) Registry of the Philippines reported 890 newly diagnosed HIV cases. This comprises 1% of the total 83,755 total cases since January 1984, with National Capital Region (NCR) (41%), Calabarzon (20%), and Central Luzon (13%) being the regions with the highest number of reported cases.[6]

With increasing number of HIV/AIDS cases in the Philippines, it is just appropriate that a study be made exploring the relationship between the clinical spectrum of the disease particularly the mucosal and cutaneous manifestations with their CD4 counts as they can help assess disease severity and prognosis.

Hence, this study was done to determine the different mucosal, and cutaneous diseases findings of HIV/AIDS patients and evaluate their frequency and association with the latest CD4 cell counts. In addition, the study also aimed to determine the demographic and medical profile of these patients.

METHODS

SETTING AND PARTICIPANTS

This is a cross sectional study conducted at a tertiary hospital in Makati city from January 2017 to September 2018. The following were the exclu-

sion and inclusion criteria:

INCLUSION CRITERIA

1. Patients aged 18 to 60 years, of either sex, diagnosed with Human Immunodeficiency Virus through initial screening via rapid test and confirmed by Western blot.
2. Patients who were seen at the tertiary hospital as walk-in patients or those who were referred by Infectious Disease specialists.
3. Patients who were or were not treated with highly active anti-retroviral therapy (HAART).

EXCLUSION CRITERIA

1. Patients with no available or incomplete clinical and investigative information such as CD4 counts.

SAMPLE SIZE

A minimum of 93 subjects was required for this study. The sample size was calculated based on the estimated proportion of 41.1% seen among HIV patients with oral/esophageal/vaginal candidiasis, as noted from the study of Oninla et al.[1] The width of the 95% confidence interval was to be 20% of the proportion estimate (or an accuracy of ± 10%).

DESCRIPTION OF STUDY PROCEDURE

Purposive and referral sampling methods were used for the study. Flyers and posters were sent out and posted in the HIV treatment hub and Out-patient Department (OPD) of the hospital. Letters to ID specialists were also sent out to inform them regarding the ongoing study. Patients who opted to join the study were first assessed for eligibility, and interviews were conducted in the HIV treatment hub, OPD, or in a private clinic which was scheduled by appointment to ensure privacy. Eligible patients were requested to provide consent to participate in the study.

Each session comprised of a history taking followed by a complete physical and dermatologic examination of recruited patients. Assessment of the skin lesions was done by the Principal Investigator using a standardized history and physical examination form. The latest CD4 counts (within the last 6 months) were obtained from the history or medical records, and documentation of lesions were done when consent was provided. Diagnostic procedures were also done if deemed necessary. Diagnosis was based on clinical criteria in most of the cases, and treatment was provided for positive skin findings.

ASSESSMENT OF OUTCOMES

Primary outcomes include the demographic and medical profile of the patients as well as the frequency of the different mucosal and cutaneous manifestations and CD4 count levels. The secondary outcome includes the presence of 1, 2 or 3 or more dermatoses.

STATISTICAL ANALYSIS

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, and mean and SD for normally distributed continuous variables. One-way ANOVA and Fisher's Exact test were used to determine the difference of mean and frequency, respectively, within three CD4 count groups. Missing variables were neither replaced nor estimated. Null hypotheses were rejected at 0.05α-level of significance, and STATA 13.1 was used for data analysis.

ETHICAL CONSIDERATIONS

The study protocol adhered to the ethical considerations and principles set out by the Declaration of Helsinki, WHO guidelines, International Conference on Harmonization-Good Clinical Practice, and National Ethics Guidelines for Health Research. The study also commenced upon the approval of the Institutional Review Board. Participants signed an informed consent and all data including photos were recorded and handled by the principal investigator which were kept in a secure office. All measures to ensure confidentiality and privacy were taken.

RESULTS

DEMOGRAPHIC PROFILE OF PATIENTS

A total of 95 subjects were screened and 93 subjects were found to be eligible and recruited for the study. Majority were males (98%), single (98%) and with a mean age of 32 ± 7.08. Most were also employed (65%) and obtained a bachelor's degree (72%). Students make up 9% of the study patients.

MEDICAL PROFILE OF PATIENTS

For the review of systems, weight loss (11%) was the most common symptom, seen especially in patients with CD4 counts <200/mm3 followed by fever (8%), cough (5%) and headache (4%). Previous history of herpes zoster infection (15%), presence of concomitant pneumonia (10%) and tuberculosis (9%) were among the top 3 medical conditions.

A large number of the patients were already receiving highly active anti-retroviral therapy (HAART) (87%). For sexual history, 28% had previous history of treated sexually transmitted infections and that majority (48%) had 5-10 sexual partners with sexual contact among male to male as the most common mode of transmission in 85%.

OUTCOMES

A total of 126 dermatoses were seen among the 93 study patients where 73% presented with only one dermatosis, followed by 23% who presented with two dermatoses and 4% who had three or more dermatoses. A large part of the group also has severe immunosuppression as 45% had CD4 counts of <200/mm3 (Table 1).

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Non-infective dermatoses (52%) were the most commonly observed manifestations followed by fungal infections (22%) and drug related dermatoses (13%). Top non-infective dermatoses include the following: seborrheic dermatitis (22%), xerosis (10%) and pruritic papular eruptions (PPE) (9%) where PPE was noted to be significantly associated with low CD4 counts (P=0.045). Oral candidiasis (6%) and superficial fungal infections (10%) were the most common types of fungal dermatoses while drug hypersensitivity reactions secondary to HAART and non HAART (8%) were the most common drug related dermatoses. Syphilis also accounted for 9% of the cases.

DISCUSSION

Demographic profile of the study patients revealed that majority were males, belonged to 25-39 age group with a history of sexual contact among males having sex with males. This finding is consistent with the latest registry from DOH HIV/AIDS and ART and a cross-sectional study done by Pan et al. in China where the majority of study patients were also between 20 and 40 years of age with sexual contact among male to male as the most common mode of transmission.[6,7] It was also seen that 65% were employed and belonged to the productive age group hence may have more access to treatment (HAART) and health care facilities.

Weight loss (11%) was the most common clinical complaint similar with other studies done by Joshi et al. in Nepal and Kaur et al. in India.[8,9] Likewise, AIDS-defining illnesses such as tuberculosis was also noted to be among the top 3 medical conditions among the patients, similar to other epidemiologic studies done in South Africa by Kaprowicz et al. where TB/HIV coinfection epidemic is severe.[10]

Several studies worldwide have been conducted to explore the relationship between mucocutaneous manifestations and the CD4 lymphocyte counts. In our study, though a large part of the group was severely immunocompromised (45%), there is only a small percentage of patients (4%) who presented with 3 or more dermatoses. These less severe presentations may be due to the fact that majority were already on HAART (87%) and may have access to health care. In contrast, Lowe et al.[4] found in their study that there is a higher percentage of patients who presented with 3 or more or dermatoses among those who were severely immunocompromised. This may have been due to the fact that only 32% of their study patients were on antiretroviral treatments who were mostly hospitalized as well.

The most common dermatoses in our study were the following: seborrheic dermatitis, xerosis, pruritic papular eruptions, superficial fungal infections, drug hypersensitivity reactions and syphilis.

It is said that 85% of HIV patients will have seborrheic dermatitis at some point of their illness. They can occur at any stage of infection and may flare and subside over time.[11] In our study, seborrheic dermatitis accounted for the highest number of dermatoses seen at 22%, similar with the studies done by Lowe et al. and Blanes et al. where seborrheic dermatitis was also one of the most common dermatoses seen among the severely immunocompromised.[4,12] As mentioned earlier, the chronicity of this lesion as well as its appearance in any stages of HIV infection, may have contributed to its high number of cases.

Pruritus secondary to xerosis is also a common symptom among HIV/AIDS patients. In our study, there is also a high percentage of patients who presented with xerosis (10%), similar to a study done by Kaushik et al.[13] and Mirnezami et al.[14] where xerosis is the most prevalent dermatosis among HIV patients. Studies by Lee et al. also noted that low levels of CD4 counts were seen to be associated with xerosis.[15] As most of our study patients had CD4 counts <200/mm^3, there was also an increased frequency of xerosis. This higher incidence of xerosis among HIV patients can be attributed to their decreased epidermal lipids and excessive levels of epidermal carotenoids such as lycopene, causing premature skin aging.[16]

Pruritic papular eruption (PPE) is a chronic condition characterized by the presence of pruritic papules and pustules commonly seen on the extensor surfaces of the extremities, trunk, and face sparing the palms and soles. The etiology of PPE remains unclear, however some suggested its association with arthropod bite reactions since the disease commonly occurs in the tropics, mostly involving extremities.[17]

In our study, PPE is also among the top dermatoses (9%) seen to be significantly associated with low CD4 counts <200/mm3 (P=0.045) similar with the studies done by Lowe et al.[4] and Nnoruka et al.[5] where PPE was among the frequently seen dermatoses. This higher prevalence of the disease could be attributed to its chronic nature as well as the limited success of the available therapeutic options.

For the past few years, fungal infections accounted for majority of the dermatoses seen among HIV/AIDS patients who were not on HAART. This was evidenced by a study done by Oninla in Nigeria, where fungal infections accounted for most of the cases (50%).[1] In our study, a high number of fungal dermatoses (22%) such as superficial fungal infections were also seen but came only second to the non-infective dermatoses. It is possible that because majority of our study patients (87%) were already on HAART, the number of opportunistic fungal infections may have been greatly reduced.

Though the incidence of opportunistic skin lesions among patients with HIV has been greatly reduced due to HAART, there was also an increase in number of drug eruptions both from HAART and non-HAART. In our study, common HAART drugs such as lamivudine, tenofovir, efavirenz, nevirapine, and non HAART drug such as co-trimoxazole were the common causes of drug reactions accounting for 13% of the cases. This higher incidence of drug reactions has been associated with polyclonal B-cell or T-cell activation secondary to a decline in CD4 counts.[17] Other reasons for increased adverse drug reactions as cited by

Table 1.

Characteristics	Total	CD4 count			p-value
		<200/mm3 (n=42)	200-500/mm3 (n=29)	>500/mm3 (n=22)	
Number of dermatoses					0.128
1	68 (73.12)	26 (61.90)	25 (86.21)	17 (77.27)	
2	21 (22.58)	12 (28.57)	4 (13.79)	5 (22.73)	
3 or more	4 (4.30)	4 (9.52)	0	0	
Non-infective dermatoses	48 (51.61)	21 (50)	14 (49.28)	13 (59.09)	0.745
Pruritic papular eruptions	8 (8.60)	7 (16.67)	1 (3.45)	0	0.045
Dyshidrotic eczema	2 (2.15)	0	0	2 (9.09)	0.054
Contact dermatitis	1 (1.08)	0	0	1 (4.55)	0.237
Seborrheic dermatitis	20 (21.51)	10 (23.81)	7 (24.14)	3 (13.64)	0.616
Xerosis	9 (9.68)	4 (9.52)	1 (3.45)	4 (18.18)	0.257
Acute urticaria	2 (2.15)	0	1 (3.45)	1 (4.55)	0.298
Eosinophilic folliculitis	6 (6.45)	5 (11.90)	1 (3.45)	0	0.194
Post-inflammatory hyperpigmentation	5 (5.38)	1 (2.38)	0	4 (18.18)	0.013
Acne vulgaris	4 (4.3)	1 (2.38)	2 (6.90)	1 (4.55)	0.812
Xerotic eczema	2 (2.15)	1 (2.38)	1 (3.45)	0	1.000
Atopic dermatitis	1 (1.08)	1 (2.38)	3 (10.34)	0	0.199
Lichen simplex chronicus	1 (1.08)	0	1 (3.45)	0	0.548
Cherry angioma	1 (1.08)	0	0	1 (4.55)	0.237
Acrochordon	1 (1.08)	0	1 (3.45)	0	0.548
Keratosis pilaris	1 (1.08)	1 (2.38)	0	0	1.000
Vasculitis	1 (1.08)	0	0	1 (4.55)	0.237
Fungal	20 (21.51)	10 (23.81)	7 (24.14)	3 (13.64)	0.616
Oral candidiasis	6 (6.45)	5 (11.90)	1 (3.45)	0	0.194
Superficial fungal infections	9 (9.68)	3 (7.14)	5 (17.24)	1 (4.55)	0.289
Onychomycosis	1 (1.08)	0	0	1 (4.55)	0.237
Pityriasis versicolor	2 (2.15)	0	1 (3.45)	1 (4.55)	0.298
Pityrosporum folliculitis	3 (3.23)	2 (4.76)	1 (3.45)	0	0.794
Cutaneous cryptococcosis	1 (1.08)	1 (2.38)	0	0	1.000
Drug-related	12 (12.90)	7 (16.67)	3 (10.34)	2 (9.09)	0.499
Toxic epidemal necrolysis	2 (2.15)	2 (4.76)	0	0	--
Drug hypersensitivity reaction	7 (7.53)	4 (9.52)	2 (6.90)	1 (4.55)	0.886
Fixed drug eruption	1 (1.08)	0	1 (3.45)	0	0.548
Acneiform eruption	2 (2.15)	1 (2.38)	0	1 (4.55)	0.715
Hair and nail changes	9 (9.68)	6 (14.29)	1 (3.45)	2 (9.09)	0.393
Alopecia areata	1 (1.08)	0	1 (3.45)	0	0.548
Melanonychia	2 (2.15)	1 (2.38)	0	1 (4.55)	0.715
Androgenetic alopecia	1 (1.08)	0	0	1 (4.55)	0.237
Paronychia	1 (1.08)	1 (2.38)	0	0	1.000
Telogen effluvium	4 (4.30)	4 (9.52)	0	0	0.146
Bacterial	8 (8.60)	2 (4.76)	4 (13.79)	2 (9.09)	0.357
Syphilis (Secondary)	8 (8.60)	2 (4.76)	4 (13.79)	2 (9.09)	0.357

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Viral	6 (6.45)	3 (7.14)	2 (6.90)	1 (4.55)	1.000
Herpes zoster	1 (1.08)	1 (2.38)	0	0	1.000
Condyloma acuminate	2 (2.15)	1 (2.38)	1 (3.45)	0	1.000
Herpes simplex	2 (2.15)	1 (2.38)	1 (3.45)	0	1.000
Herpes stomatitis	1 (1.08)	0	0	1 (4.55)	0.237
Cytomegalovirus retinitis	1 (1.08)	1 (2.38)	0	0	1.000
Malignancies					
Kaposi sarcoma	1 (1.08)	1 (2.38)	0	0	1.000
Parasitic/arthropod borne dermatoses					
Arthropod bite	1 (1.08)	1 (2.38)	0	0	1.000
Mucosal membrane lesions					
Aphthous ulcers	1 (1.08)	1 (2.38)	0	0	1.000

Prabhakaran et al. include the following: Epstein-Barr virus and cytomegalovirus reactivation, glutathione depletion, immune dysregulation and polypharmacy.[18]

In the past, the worldwide incidences of curable STDs such as syphilis has significantly declined after the discovery of penicillin, however recently has been on the rise again. As mentioned earlier, syphilis was also among the top dermatoses in our study, similar to the study done by Mutagoma et al. where HIV/Syphilis co-infection was seen to be high among female sex workers[19] as well as with the study done by Dai et al. in China who noted a high prevalence of HIV/Syphilis co-infection among men who have sex with men.[20] All of the patients seen in our study were on the secondary stage of syphilis who presented with maculopapular lesions on the trunk and extremities inclusive of palms and soles. Once confirmed using nontreponemal and treponemal serologic tests, patients were referred to infectious disease specialists for further management.

The presence of other benign epithelial tumors such as acrochordon and cherry angioma was also noted. As they are not usually a common feature among HIV patients and may also be seen among normal healthy individuals, they may be regarded as incidental findings.

One of the limitations of this study is that due to the evolving nature of some dermatologic lesions, diagnosis was only limited during the time of consult. Since CD4 count levels are also affected by different factors such as disease duration, time since initiation of ART, and viral load levels, clinical presentations may vary depending on these factors when the patients were examined. In addition, due to financial constraints, additional work ups were also limited. The study reflected an epidemiologic data obtained in a private institution with a small sample size, hence the investigators recommend multicentric studies for a larger, and more accurate statistical data.

CONCLUSION

In our study, the most common manifestations were the following: non infective dermatoses, fungal and drug-related dermatoses with the most common dermatoses being seborrheic dermatitis, xerosis, pruritic papular eruptions, superficial fungal infections, drug hypersensitivity reactions, and syphilis. Majority of our study patients were males, employed, severely immunocompromised, and on HAART. Due to a small population size, significant associations between the other dermatoses with their CD4 counts were not seen except for PPE which was significantly associated with low CD4 counts <200/mm^3. Hence, larger studies are recommended. Nevertheless, due to increasing incidences in the Philippines, the presence of these distinct dermatoses should still warrant a strong suspicion for any underlying HIV/AIDS infection, playing a vital role in the screening and overall disease management of the patients.

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