Original article

ORAL MELANOTIC HYPERPIGMENTATION (OMH) AMONG HIV SERO-POSITIVE PATIENTS: A CLINICAL STUDY AT THE UNIVERSITY COLLEGE HOSPITAL, IBADAN

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ABSTRACT

BACKGROUND: Oral melanin hyperpigmentation (OMH) has been classified as a HIV associated condition which may present as a brown-black macule or patch of the oral mucosa in HIV seropositive patients. HIV-OMH may be idiopathic, drug- induced or due to adrenal insufficiency. This cross-sectional study was conducted to determine the prevalence of HIV- OMH among HIV seropositive patients attending the Infectious Disease Institute centre, UCH Ibadan.

METHODOLOGY: Consecutive, consenting HIV seropositive patients attending PEPFAR clinic, UCH, Ibadan were enrolled. Data collected included age, gender, duration since diagnosis of HIV and commencement of HAART, history of smoking, any systemic disease, WHO staging of HIV, CD4 count, presence of OMH and site affected. Data analysis was done using SPSS version 15.

RESULTS: The study group of 150 HIV sero-positive patients comprised 24 males (16%) and 126 females (84%). Out of all the patients seen, OMH was seen in 97 of them, majority reported not being aware of the condition, some noted it before being diagnosed of HIV, while only 14(14.4%) reported the presence of OMH after being diagnosed with HIV and commencement of HAART (p= 0.032). Concerning the OMH sites, gingiva was most noted followed by tongue, palate, buccal and labial mucosa.

CONCLUSION: The prevalence of HIV-OMH in this study was 14.4%. Gingiva was the most common site affected.

Key words: Oral melanin hyperpigmentation, HIV, α-melanocyte stimulating hormone.

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INTRODUCTION

HIV-associated Oral Melanotic Hyperpigmentation (HIV-OMH) has been categorized as being less commonly associated with HIV infection[1]. It affects any part of the oral mucosa and usually appears as asymptomatic, single or multiple, well or ill-defined, light to dark brown macules of variables size and shapes[2]. Oral Melanotic Hyperpigmentation in HIV patients has been attributed to the use of antifungal agents or antiretroviral drugs; while some have reported HIV- induced cytokine dysregulation causing activation of melanin stimulation pathway[2,3]. Oral hyperpigmentation

might be a marker of immune suppression, since it may be associated with a low CD4 T cell count in HIV seropositive individuals[4]. The prevalence of HIV-OMH varies in different parts of the world and between different ethnic/racial groups, most probably owing to genetic, environmental, biochemical, pathological or immunological factors[2,4]. Also, the drug regimen used to treat the HIV disease and its complications have been noted to be contributory[3].

The pathologic significance of HIV- associated OMH is currently unknown especially on long term basis. Also, the prevalence and distribution of HIV- OMH is unknown in our environment. Therefore, this study was conducted to assess the prevalence of HIV- OMH presentation among HIV sero-positive patients and to analyse the associations between their demographic features and immunological characteristics of patients.

MATERIALS AND METHODS

The study was a descriptive cross- sectional type conducted among HIV-seropositive patients attending the outpatient HIV clinic of the Infectious Diseases Institute of College of Medicine, University of Ibadan/ University College Hospital (UI/ UCH), Ibadan. The study was conducted over a period of three months from May to July 2017. All consenting patients who came for either collection of drugs or consultation were included in the study.

Data collection was done using interviewer-administered questionnaire method; information collected included age, gender, time of HIV diagnosis, time of HAART use, previous history of smoking, any systemic disease, drug history, WHO staging and CD4 count. Oral examination was done by one of the authors to check for the presence of OMH and site(s) affected. Data analysis was done using SPSS version 15. Quantitative variables such as age and CD4 count were summarized using means and standard deviation, while qualitative variables such as gender and presence of OMH were expressed as proportions and percentages; 5% significance level was used.

RESULTS

The study group comprised of 150 HIV sero-positive patients consisting of 24 males (16%) and 126 females (84%) Table 1. The mean age of the participants was 45.2 ±10.6, while according to gender was 50.4 (SD ±9.9) for males and 44.2 (SD ±10.5) for females which was statistically significant (p= 0.009). Also, the mean CD4 count among the study group was 522.5 (SD ±293.7), while according to gender was 468.1(SD ±330.7) and 553.04 (SD ±286.3) for males and females respectively (p= 0.323).

The time span of HIV diagnosis and HAART therapy time of the patients ranged from 1- 16 years with a mean of 7.5 years (SD ±4.0) and 7.3 years (SD ±3.8) respectively. More than half of the patients presented at the early stage of HIV infection according to WHO staging. Table 1

Table 1: Socio- demographic data of the study participants

Characteristics	N (%)
Gender	
Male:	24 (16%)
Female:	126 (84%)
Age group	
<30 years:	10 (6.7%)
31- 40 years:	40 (26.7%)
41-50 years:	60 (40%)
>50 years:	40 (26.7%)
CD4 count group	
<200 cells/ mm^3:	21 (14%)
200-500 cells/mm^3:	59 (39.3%)
>500 cells/mm^3:	67 (44.7%)
Unrecorded count:	3 (2%)
WHO staging	
Early stage (1&2):	72 (60%)
Late stage (3&4):	49 (40%)
Systemic disease	
Yes:	23 (15%)
No:	127 (85%)

Out of all the patients seen, OMH was seen in 97 (64.7%) but only 14(14%) among these reported the presence of OMH after being diagnosed with HIV and commencement of HAART; and only 2 out of the 14 patients are newly diagnosed and yet to commence HAART (p= 0.032) The OMH group (97) comprised of 10 males and 87 females; only 6 out of the 97 patients reported previous history of smoking. WHO staging of the patients as at the time of their HIV diagnosis, in the OMH group revealed stage 2 as the most

frequent, followed by 1, 3 and 4 respectively. Table 2

Table 2: Clinical and Immunological features of the OMH group

	OMH		
	Yes	No	P value
HAART: Yes	89	49	1.000
No	8	4	
Gender: Male	10	14	0.018*
Female	87	39	
WHO staging: 1	21	15	0.056
2	29	7	
3	18	17	
4	10	4	
CD4 count: <200	12	9	0.853
200-500	40	19	
>500	43	24	
Not recorded	2	1	
Smoking: Yes	6	6	0.347
No	91	47	

(* significant)

Majority of the OMH group reported either not being aware of the condition (53.6%) or noted it before being diagnosed of HIV (32%), while only 14(14%) reported the presence of OMH after being diagnosed of HIV and commencement of HAART. A proportion of those on HAART (12/89) and those not yet on HAART/newly diagnosed (2/8) within the OMH group (14/97) was found. Table 3

Also, most of the patients seen with hyperpigmentation (OMH group) as well as those associated with HIV (OMH- HIV group) had CD4 count >200cells/mm3, with no statistical significance. Table 4

Concerning the OMH sites, gingiva was most noted followed by tongue, palate, buccal and labial mucosa. (Figures 1, 2, 3)

Only 15% of the patients had associated medical conditions they were being co- managed for, alongside their retroviral status. Hypertension was the most reported, others were liver disease, diabetes, tuberculosis, hypercholesterolemia and asthma (Figure 4).

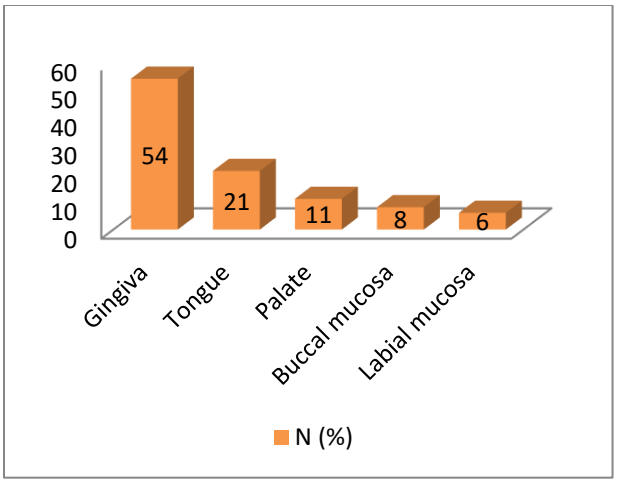

Figure 1: Oral Melanin Hyperpigmentation sites

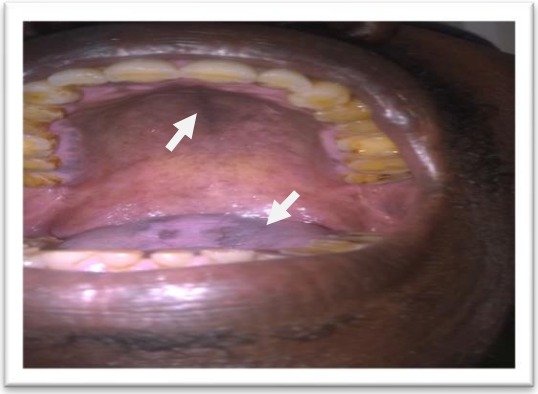

Fig: 2a

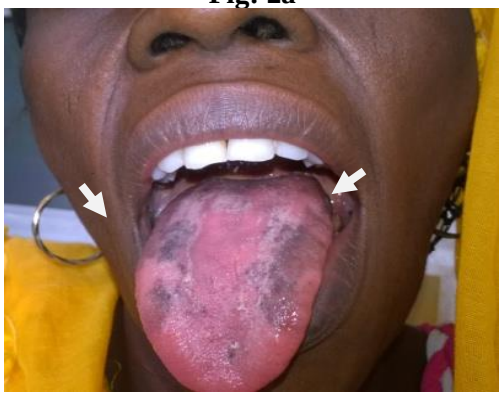

Fig: 2b

Figures 2a, b, c, d: HIV-oral melanotic hyperpigmentation sites

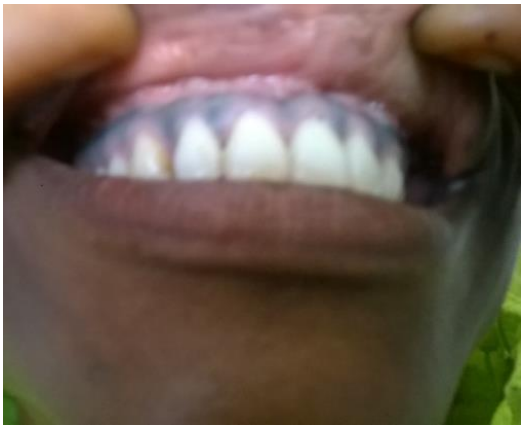

Figure 3: Gingival tattooing

DISCUSSION

Oral lesions in HIV infection have been well-documented in developed and developing countries with candidiasis being the most commonly reported[3,7-9]. However, there are few reports on OMH being noted as one of the common oral findings in HIV infected people[5,6]. The prevalence of HIV-OMH in our study population sample was 14.4%, this figure may not represent an exact prevalence as a greater percentage seen with OMH were unaware of its presence, some of which could have been captured in the HIV-OMH group. However, the prevalence noted from our study is significantly higher than those from other countries in sub-Saharan Africa (Tanzania 4.7%[12], Kenya 6%[13]) and in Europe (Italy 6.4%)[7] but lower than that of South Africa (18.5%)[2], Uganda (17.3%)[8] and India (26% to 35%)[9] reports. Some authors have also reported OMH as the second and third most common oral lesion seen in Nigeria and Ghana respectively, among the HIV population in their studies[5,6]

The cause of HIV oral melanosis is not fully understood but may be associated with HIV-induced cytokine dysregulation, medications including zidovudine, clofazimine, and ketoconazole, or adrenocortical dysfunction which is not uncommon in HIV-seropositive subjects with AIDS[10]. Although it is clear that HIV does not infect melanocytes, because the receptors for HIV are lacking, it is not known whether HIV proteins have the capacity to activate melanocytes directly[11].

Hyperpigmentation of the oral mucosa is well documented and is considered to involve multifaceted etiologies. Acquired hyperpigmentation of the skin or oral mucosa may occur as a result of hormonal disturbances during pregnancy, systemic disorders like Addison's disease, acromegaly, acanthosis nigricans, Albright's disease, neurofibromatosis, or as a result of prolonged administration of various drugs including clofazimine, minocycline, chloroquine, bleomycine and ketoconazole[14]. None of the patients in our study was found to have any possible systemic condition or other medications that could likely have been implicated with OMH in them except for the HAART regimen.

Moreover, hyperpigmentation may occur as a fixed drug eruption in intravenous drug abusers of morphine, opium, and codeine or as smoker's melanosis associated with nicotine abuse[15]. Also, deposition of exogenous substances may cause mucosal pigmentation or stimulate melanogenesis, these include heavy metal exposure, amalgam tattoo and betel nut chewing[15]. Notably, one of the females among our study participants had gingival pigmentation which she noted as a form of tattooing done in Mali over twenty years ago for cosmetic reasons (Figure 4)

Majority of the OMH group in our study reported either not being aware of the condition or noted it before being diagnosed of HIV, while only 14(14%) among these reported the presence of OMH after being diagnosed with HIV and commencement of HAART. Comparing the ratio of OMH-HIV (14) among those on HAART (12/89) and those not yet on HAART/newly diagnosed (2/8), approximately one to two was found conferring a higher prevalence among those not yet on HAART. HIV-induced cytokine dysregulation roughly parallels a decreasing CD4 + T cell count, and oral melanin hyperpigmentation is observed more frequently in HIV-seropositive subjects with a CD4+ T cell count of 200 cells/mm^3 or less[4]. Though our study revealed that most of the patients having HIV-OMH had CD4+ T cell count greater than 200 cells/mm^3, the fact that majority of the patients in our HIV-OMH group had already commenced

HAART except two who were newly diagnosed; may be responsible for the improved levels of CD4 counts in the patients. Concerning OMH site, our study revealed gingiva as the most common site seen which is in agreement with the study from South Africa[2] but differ from India[7] who reported buccal mucosa as the most commonly found.

CONCLUSION

In summary, the prevalence of OMH-HIV in this study was 14.4% which comprised of those on HAART and those not on HAART. We noted more females with OMH though they were largely represented in the study, and OMH was not found to be associated with immunosuppression.

Thus, as it is the best practice now to start administration of HAART almost immediately after the diagnosis of HIV infection, it is difficult to delineate between HAART induced HIV-OMH and idiopathic HIV-OMH. Nonetheless, our study confirmed that OMH can result from either HIV- induced or HAART induced pathways. We therefore recommend further studies of possible pathogenesis of HIV- OMH among the newly diagnosed HIV patients.

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Table 3: Patients' responses to the presence of OMH

OMH Groups	**HAART**		
	Yes	No	Total (%)
Not aware (1)	51	1	52 (53.6)
Before HIV diagnosis (2)	26	5	31 (32)
After HIV diagnosis (3)	6	2	8 (8.2)
After HAART commenced (4)	6	0	6 (6.2)

Table 4: CD4 variation among the OMH- HIV group

OMH HIV group	**CD4 count (cells/mm^3)**			
	<200	200-500	>500	Not recorded
After HIV diagnosis (3)	0	5	2	1
After HAART commenced (4)	1	1	4	0

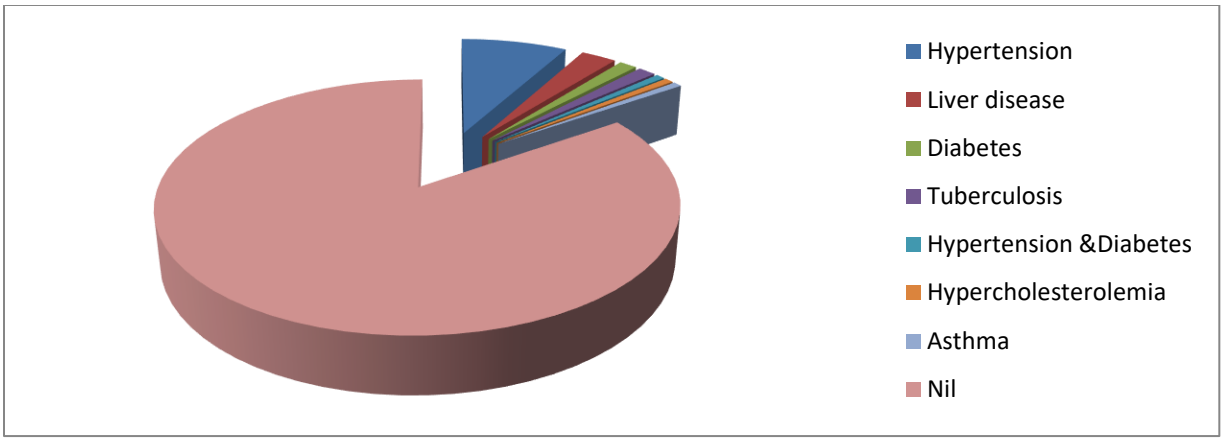

Figure 3: Co-morbidity status of the study participants

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