Original Article

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Dermatological Manifestations of HIV/AIDS Patients in the Era of HAART: Report from an ART Center of Chattogram.

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Abstract:

Introduction: Skin diseases are common striking features of HIV/AIDS patients and may vary considerably due to ethnic and geographic regions and currently by the influence of HAART also. However, there is a dearth of information in Bangladeshregarding the dermatological manifestations in HIV/AIDS patients. The purpose of this study is to find out the spectrum of cutaneous disorders in HIV/AIDS patients in the era of HAART.

Materials and Methods: A descriptive cross-sectional study has been carried out to find the targeted results in the Chittagong Medical College Hospital, Bangladesh between the periods 2017 and 2020.

Results: Of the 40 patients with HIV/AIDS, 22 (55%) were males and 18 (45%) were females. The age of the patients ranged from 8 to 60 years with mean age 38 (±0.966 SD) years. The age-specific cumulative HIV/AIDS cases at 31-40 years were high 19 (47.5%) among all age groups. The majority of the patients were migrant worker 22 (55%) with low socio-economic 32 (80%) background and common transmission mode was heterosexual 36 (90%). Most of the patients 32 (80%) had mucocutaneous disorders and Infective dermatoses accounted 30 (75%) and the non-infective inflammatory dermatoses were 21 (52.5%). Eight (20%) patients presented with 3 or more skin disorders. Common infective dermatoses were fungal infections 15 (37.5%) followed by viral infections 8 (20%), bacterial infections 4 (10%) and scabies 3 (7.5%). Common non-infective dermatoses were generalized pruritus 6 (15%) followed by prurigo simplex 4 (10%), psoriasis 4 (10%), eczema 3 (7.5%), pruritic papular eruption 1 (2.5%), seborrhoeic dermatitis 1 (2.5%), urticaria 1 (2.5%) and xerosis 1 (2.5%).Patients treated with HAART had decreased rates of oral candidiasis, herpes simplex, but increased rates of drug reactions 19 (47.5%). The most common drug eruption following HAART is morbiliform rash 11 (27.5%) and the commonest offending agent is nevirapine. The prevalence of mucocutaneous disorders were higher in patients with CD4 <200 cells/mm^3.

Conclusions: A wide range of skin disorders (80%) is observed in Bangladeshi HIV/AIDS patients and HAART had an impact on the spectrum of HIV/AIDS associated mucocutaneous disorders. They are seen at every stage of HIV/AIDS and are often the initial presentation in most instances within our environment. There is a need for increased attention to the diagnosis and treatment of skin diseases affecting the quality of life of HIV/AIDS patients.

Key words: HIV/AIDS, Cutaneous, HAART, Chattogram, Bangladesh.

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Introduction:

The twenty thousand twenty one (2021) marks the 40th anniversary of the discovery of HIV/AIDS.

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Since American researchers found the first case of acquired immunodeficiency syndrome (AIDS) in 1981, AIDS has spread rapidly all over the world and has become a global public health problem [1]. Skin manifestations are very common in human immunodeficiency virus (HIV) infected individuals and are associated with significant morbidity. Greater than 90% of patients develop at least one skin or mucous membrane manifestation during the course of their infection [2]. Several studies have reported a correlation between skin disease and underlying immune status [3-9], thus making diagnosis of certain skin conditions a valuable clinical tool in staging and predicting progression of disease. The introduction of highly active antiretroviral therapy (HAART) significantly decreased the prevalence of opportunistic infections and Kaposi's sarcoma and the prevalence of most inflammatory conditions [10]. Since the introduction of HAART, there has been a dramatic decrease in the incidence and severity of HIV associated dermatoses that were commonly seen in the pre-HAART era[11]. However, HAART itself has bought about a series of additional skin problems, such as drug-related adverse reactions and immune reconstitution syndrome (IRS) related skin disease [12, 13]. Variations however exist in the incidence, clinical heterogeneity and severity of disease between different ethnic and racial groups. Environmental, cultural or genetic backgrounds may explain these variations. Dermatological manifestations, however, may differ both qualitatively and quantitatively between tropical and temperate countries depending on the availability of HAART, and due to genetic background or prevailing microorganisms in different geographic regions, but there have been limited studies made to classify these disease taking ethnic and geographic variations into consideration [14]. There is a scarcity of published data in Bangladesh regarding cutaneous manifestations in HIV/AIDS patients. The main purpose of this study is to analyze the prevalence and clinical importance of cutaneous lesions in HIV/AIDS patients for early diagnosis and prompt intervention to prevent complications.

Materials and methods:

Study design and setting

This is a descriptive cross-sectional type of study carried out in the ART clinic at the department of Dermatology and Venereology, Chittagong Medical College Hospital (CMCH) during the period between 2017 and 2020. CMCH is the oldest tertiary care teaching hospital in Bangladesh.

Patient selection

Inclusion criteria

1) Person who tested positive to two separate HIV test by Enzyme Linked Immunosorbent Assay (ELISA). Reactive tests are supplemented by rapid test in two different methods as per WHO guidelines. 2) Diagnosed case of HIV/AIDS for HAART therapy. 3) All cases of HIV/AIDS who are already on HAART therapy.

Exclusion criteria

1) Patients with mucocutaneous lesions other than HIV/AIDS patients. 2) Those who are known to have concomitant diabetes mellitus, asthma or other immunosuppressive conditions and on prolonged steroids/cytotoxic therapy. 3) Those who decline to consent for enrollment in the study.

Data collection procedure

Clinical work-up

A structured questionnaire was administered to participants to ascertain demographic characteristics and history of HIV testing. A standardized clinical history was recorded and all participants underwent a full dermatologic examination, as part of a comprehensive clinical evaluation including WHO staging. Dermatological examination was done in daylight. Chronic mucocutaneous disorders were diagnosed by the clinical manifestations. Oral cavity was inspected carefully. Intra-oral examination was performed under supervision of an oral medicine specialist on a dental unit. Diagnoses of most dermatoses were done according to WHO case definitions. True years are considered for age determination. Data including sexual orientation, intravenous drug abuse, blood transfusion, addiction, other

diseases and opportunistic infections were extracted from the patient files.

Drug rashes were diagnosed when eruptions occurred within a month of commencement of a new drug, after exclusion of inter-current sepsis. The diagnostic criteria of drug eruptions were as follows: (i) the suspected drug was used in temporal relation to symptoms; (ii) the mucocutaneous manifestations were typical for the suspected drug; and (iii) the eruptions were improved after withdrawal of the suspected drug.

First-line antiretroviral treatment consisted of one non-nucleoside reverse transcriptase inhibitor plus two nucleoside reverse transcriptase inhibitors. All HIV positive patients were given free access to HAART in Bangladesh. As a result of economic reasons, viral load determinations were not done.

Laboratory methods

Where necessary, appropriate laboratory tests like skin scrapings for fungus, pus for culture sensitivity and skin biopsy for histopathology were performed to confirm the diagnoses. The clinical diagnosis was supplemented with laboratory procedures like microscopy (the KOH preparation), Venereal Disease Research Laboratory test (VDRL) and Treponemapallidumhemagglutination assay (TPHA) wherever they were applicable. Skin scrapings for mycology were performed to confirm diagnoses of tinea and pityrosporm folliculitis. Diagnosis of folliculitis furuncle was only indicated to bacterial folliculitis, which was confirmed by bacterial culture. Complete blood count (CBC), Urinalysis, Chest X-ray (CXR) and peripheral blood lymphocyte count were also estimated for all the subjects. Hepatitis serology and viral markers were done accordingly. Diagnosis of diffuse Non-Hodgkin lymphoma (NHL) was made by histopathological examinations of lymph nodes.

HIV antibodies status was determined with the use of ELISA kits and reactive samples were confirmed using Western Blot. CD4 cell counts were determined within 4 h of collecting the blood with the use of a flow cytometer. All assays were performed using the methods recommended by the manufacturers. The level of immunosuppression in each patient was classified according to CDC classification by CD4 count and based on WHO immunologic staging as absent (>800/ ml), moderate (>500/ml) and severe (<200/ml).

Data Processing:

Data is processed and analyzed using computer software SPSS (Statistical Packages for Social Sciences). Version 21. Data is presented by chart and table accordingly.

Ethical Adherence:

The study was approved by our ethical committee of the institute.

Results:

Of the 40 patients with HIV/AIDS, 22 (55%) were males and 18 (45%) were females. The age of the patients ranged from 8 to 60 years with mean age 38 (±0.966 SD) years. The age-specific cumulative HIV/AIDS cases at 31-40 years were high 19 (47.5%) among all age groups (Figure- 1). The majority of the patients were migrant worker 22 (55%) with low socio-economic 32 (80%) background and common transmission mode was heterosexual 36 (90%). Eight (20%) had sexually acquired co-infection and 12 (30%) HIV/AIDS patients had significant weight loss, 11 (27.5%) had fever and 10 (25%) had persistent diarrhea (Table- 1). Most of the patients 32 (80%) had mucocutaneous disorders and Infective dermatoses accounted 30 (75%) and the non-infective inflammatory dermatoses were 21 (52.5%). Eight (20%) patients presented with 3 or more skin disorders. Common infective dermatoses were fungal infections 15 (37.5%) followed by viral infections 8 (20%), bacterial infections 4 (10%) and scabies 3 (7.5%). Common non-infective dermatoses were generalized pruritus 6 (15%) followed by prurigo simplex 4 (10%), psoriasis 4 (10%), eczema 3 (7.5%), pruritic papular eruption 1 (2.5%), seborrhoeic dermatitis 1 (2.5%), urticaria 1 (2.5%) and xerosis 1 (2.5%). Common mucosal lesions were vulval lesion 5 (12.5%) followed by oral thrush 4 (10%), periodontal disease 2 (5%), penile lesion 2 (5%) and angular cheilitis 1 (2.5%) (Table- 2).Patients treated with HAART had decreased rates of oral candidiasis, herpes simplex, but increased rates of drug reactions 19

(47.5%). The most common drug eruption following HAART is morbiliform rash 11 (27.5%) and the commonest offending agent is nevirapine (Figure-2).

Table- 1: Patient characteristics (n=40):

Variables	Frequency	Percentage
Sex		
Male	18	45.0
Female	22	55.0
Marital status		
Married	34	85.0
Unmarried	5	12.5
Others	1	2.5
Socio-economic status		
Low	32	80.0
Average	7	17.5
High	1	2.5
Occupation		
Migrant Worker	22	55.0
House Wife	15	37.5
Service	1	2.5
Student	1	2.5
Others	1	2.5
Co-infections		
Syphilis	2	5.0
Genital herpes	2	5.0
Chancroid	1	2.5
Donovanosis	1	2.5
Genital wart	1	2.5
Hepatitis B Virus	1	2.5
Illness history		
Weight loss	12	30.0
Fever	11	27.5
Diarrhea	10	25.0
Non-Hodgkin lymphoma	1	2.5
Transmission		
Heterosexual	36	90.0
Intravenous drug users	2	5.0
Vertical	2	5.0

Table 2: Distribution of Mucocutaneous disorders in HIV/AIDS patients

Subject	Frequency	Percentage
Total mucocutaneous disorders	32	80.0
Infectious mucocutaneous disorders	30	75.0
Bacterial mucocutaneous disorders		
• Impetigo	4	10.0
• Folliculitis	2	5.0
Viral mucocutaneous disorders	2	5.0
• Orolabial herpes	8	20.0
• Herpes zoster	3	7.5
• Verruca vulgaris	2	5.0
• MC	2	5.0
Fungal mucocutaneous disorders	1	2.5
• Tineacorporis	15	37.5
• Candidiasis (Oral)	5	12.5
• Tineacruris	4	10.0
• Pityriasisversicolor	3	7.5
• Mycetoma	1	2.5
• Chromoblastomycosis	1	2.5
Parasitic mucocutaneous disorders (Scabies)	1	2.5
	3	7.5
Non-Infectious mucocutaneous disorders	21	52.5
Generalized pruritus	6	15.0
Prurigo simplex	4	10.0
Psoriasis	4	10.0
Eczema	3	7.5
PPE	1	2.5
SD	1	2.5
Urticaria	1	2.5
Xerosis	1	2.5
Mucosal lesions	14	35.0
Oral thrush	4	10.0
Penile lesion	2	5.0
Vulval lesion	5	7.5
Angular cheilitis	1	2.5
Periodontal disease	2	5.0

MC, Molluscumcontagiosum; PPE, Papular pruritic eruption; SD, Seborrhoeic dermatitis # n does not correspond to 100%, because of multiple mucocutaneous manifestations.
*Figures in the parenthesis indicate corresponding %.

Table 3: Distribution of CD4 counts among HIV/AIDS patients

CD4 count	Frequency	Percentage
<50	5	12.5
50- 200	12	30.0
200- 500	20	50.0
>500	3	7.5
Total	**40**	**100.0**

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Figure I: Age distribution of the HIV/AIDS patients (n=40).

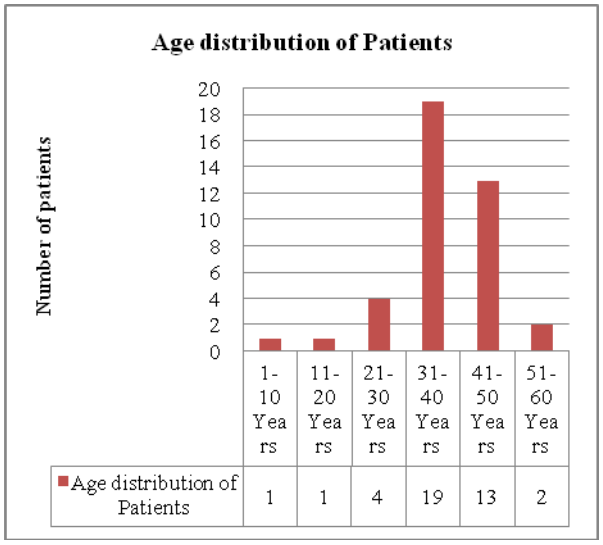
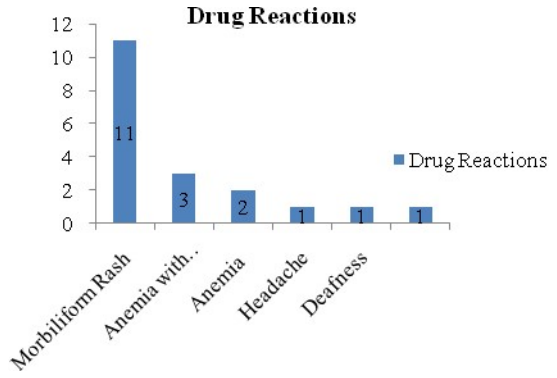


Figure 2: Distribution of drug reactions HAART among HIV/AIDS patients



Discussion:

This descriptive type of cross-sectional study has been carried out to see the pattern and prevalence of cutaneous manifestations in HIV/AIDS patients at the regime of HAART, as there is no sufficient published data in this field in Bangladesh.

The age of the patients enrolled in the study group ranged from 8 to 60 years with mean age 38 (±0.966 SD) years. The age-specific cumulative HIV/AIDS cases at 31-40 years are high 19 (47.5%) among all age groups. This result is consistent with the work of Han J et al.[1] from China who has shown that the mean age is 39.64 (±11.79) years. But Brodtet al.[15] of Germany has found that median age varied between 37 and 38 years.

Of the 40 patients with HIV/AIDS, 22 (55%) were males and 18 (45%) were females. The preponderance of HIV/AIDS in male also reported by Han J et al.[1] from China who has shown the male 225 (64.66%) and female 123 (35.34%) and Nnoruka et al.[7] from Nigeria has also reported that 320 (67.1%) are males and 157 (32.9%) are females in HIV/AIDS patients. But Chopra [16] from India has declared male: female ratio is 1: 1.05 and a study from Cameroon by Josephine et al.[9] has found that 236 (61.5%) are males and 148 (38.5%) are females among HIV/AIDS patients.This fewer figure of female could be due to the stigma or shame and reluctance to mention their problems regarding STIs. They have symptoms for longer period and less often they seek treatment than men. Also, when women are economically dependent on men, they have problems even informing the disease to their partner's and less often they visit a health center without a male relative.

The majority of the patients were migrant worker 22 (55%) with low socio-economic 32 (80%) background and common transmission mode is heterosexual 36 (90%). Two (5%) patients are intravenous drug users (IVDUs) and 1 (2.5%) patient is a commercial sex worker (CSW). The pattern of transmission of HIV in Bangladesh is mostly heterosexual – involving sex with female and male sex workers and between married couples. Homosexuality is rather rare in Bangladesh. Migration for work abroad is very common in Bangladesh. Men who stay away from their homes for prolonged periods may be practicing riskier behaviors which make them more vulnerable to HIV/STIs. In this study, most of the females get infected by their husband. Return from working in a high prevalence country is one of the ways HIV is introduced into low-prevalence countries. Available data show that the HIV epidemic is still at relatively low level and concentrated mainly among intravenous drug users (IVDUs) in Dhaka city. [17]

Eight (20%) HIV/AIDS patients are co-infected by other STIs. Among co-infections 2 (5%) are with syphilis, 2 (5%) with genital herpes, 1 (2.5%) with chancroid, 1 (2.5%) with donovanosis, 1 (2.5%) with genital wart, 1 (2.5%) with HBV. Sexually transmitted co-infections are prevalent among people living with HIV/AIDS (PLWHA) [18]. Sexually transmitted co-infections pose considerable health threats to people living with HIV (PLHIV). Multiple sexually transmitted co-infections are common because the pathogens share same transmission routes and with HIV infection can have a multiplicative impact on health. Co-infection of STIs in HIV-positive individuals can compromise their health in various ways.

In the current study, 34 (85%) patients get 3TC + ZDP + NVP regimen, 4 (10%) gets 3TC + ZDV + EFV and 1 (2.5%) gets EFV + FTC + TDF. Only 1 (2.5%) patient is not getting HAART currently. The advent of HAART has enhanced long-term viral suppression, decrease of opportunistic infections and increased quality of life (QoL) of infected individuals [19]. However, the long-term treatment with HAART is associated with substantial toxicity and adherence difficulties which can lead to drug resistance [20]. There was a relatively high incidence of drug eruptions in this study, especially in the patients with HAART. We observed 19 (47.5%) patients have manifested drug reactions and the commonest drug reactions are morbiliform rash 11 (27.5%) followed by anemia with morbiliform rash 3 (7.5%), only anemia 2 (5%), headache 1 (2.5%), deafness 1 (2.5%) and myelosuppression 1 (2.5%). The offending drugs are nevirapine, efavirenz and cotrimoxazole used to combat bacterial opportunistic infections (OIs). It is similar to the findings of Han et al.1, where they observed 31 cases of drug eruptions in patients receiving HAART, of which 25 cases were caused by nevirapine, four were caused by efavirenz and two were caused by sulfonamides. HIV-infected patients are predisposing to developing drug eruptions because of their defective metabolism of drugs and altered immune function [21]. Drug eruptions in AIDS patients were much more frequent than in non-AIDS patients [22].

Most of the patients (80%) have mucocutaneous disorders. Infective dermatoses 30 (75%) outnumbered the non-infective inflammatory dermatoses 21 (52.5%). There are 25 different types of mucocutaneous disorders associated with HIV/AIDS from the present study. Fifteen (37.5%) patients manifested one skin disorder, 9 (22.5%) patients with two skin disorders and 8 (20%) patients presented with 3 or more skin disorders. Eight (20%) patients did not present with any skin disorder. Subjects with multiple and widespread cutaneous and mucocoutaneous lesions had increased immunosuppression as noted by CD4 counts. Subjects with less immunosuppression had more localized lesions and fewer diagnoses.[16]

Common infective dermatoses were fungal infections 15 (37.5%) followed by viral infections 8 (20%), bacterial infections 4 (10%) and scabies 3 (7.5%). Tineacorporis is the most common 5 (12.5%) fungal infection followed by candidiasis 4 (10%), Tineacruris 3 (7.5%), pityriasisversicolor 1 (2.5%), eumycetoma 1 (2.5%) and chromoblastomycosis 1 (2.5%). For viral infections orolabial herpes is 3 (7.5%), herpes zoster was 2 (5%), verruca vulgaris 2 (5%) and molluscumcontagiosum 1 (2.5%). Among bacterial infections impetigo is accounted 2 (5%) and folliculitis also 2 (5%). The parasitic infections include only scabies 3 (7.5%). In a study from Nigeria by Nnorukaet al.[7] has reported dermatophytosis in 24.3% patients while Chopra [16] from India mentioned only 3.33% of dermatophytosis in their series. However, Chopra [16] annunciated about high prevalence of oral candidiasis (32.22%), but in this study the figure of oral candidiasis is only 4 (10%). Probably, this might be due to variation in the study design, recruitment of patients, environment, life style of patients and the effect of HAART. Thrush is recognized as an early clinical marker of immunosuppression, an initial manifestation of symptomatic HIV infection [23]. In the present study, other oral lesions include periodontal disease 2 (5%) and angular cheilitis 1 (2.5%). Gingival and periodontal disease has recently been recognized as a possible early presentation of HIV infection [24]. Oral manifestations are the early indicators of HIV infection.

In the present study, among the fungal infections, 1 (2.5%) patient is identified as eumycetoma and another (2.5%) is chromoblastomycosis. These are cases of subcutaneous fungal infections. These are already challenging clinical entity becomes even more complex against a background of HIV infection. Therefore, it is not surprising that subcutaneous fungal infections and HIV co-infection manifest in different clinical presentations. It could be due to profound immunosuppression of HIV/AIDS patients.

In the current study, 3 (7.5%) patients have presented with orolabial herpes and 2 (5%) with herpes zoster. It is in the conformity with other studies done in different parts of the world that Han et al. [1] from China reports 4.6% patients with herpes zoster whereas Chopra S [16] from India announces 13.33% patients. In HIV-infected patients, herpes zoster and herpes simplex virus mucocutaneous infections are more frequent, chronic and progressive than in immunocompetent persons [25]. The cutaneous lesions of zoster in HIV-positive adults can be dermatomal, multidermatomal or disseminated [26]. Patients in this study had only localized dermatomal disease at all stages during the course of HIV infection.

In this study, we record a patient (2.5%) with molluscumcontagiosum (MC), who is dangerously ill and admitted in patients' department (IPD). Umoru D et al. [27] from Nigeria also reports 3 (2.5%) patients with MC in their study group. Although the typical lesions are pearly papules with central umbilication, atypical lesion such as giant Mollusca have been reported in advanced HIV disease [28].

In the current study, non-infective mucocutaneous disorders account 21 (52.5%). Among non-infectious mucocutaneous disorders generalized pruritus is the most common 6 (15%) followed by prurigo simplex 4 (10%), psoriasis 4 (10%), eczema 3 (7.5%), pruritic papular eruption (PPE) 1 (2.5%), sebrrhoeic dermatitis (SD) 1 (2.5%), urticaria 1 (2.5%) and xerosis 1 (2.5%). In a study from Thailand by Sivayathorn A et al. [29] finds that PPE is 32.7%, SD 21% and psoriasis 6.5%. The incidence of PPE is also observed by Indian and Chinese studies as 7.77% and 5.75% respectively. A PPE is a unique dermatosis associated with the advanced HIV infection, which is characterized by sterile papules, nodules, or pustules with a hyperpigmented, urticarial appearance and pruritus [30]. The underlying etiology probably reflects a hypersensitivity reaction to insect bites in the susceptible patients [31]. The prevalence rate of SD in HIV patients ranges 8% to 21% in India reported by Chopra [16], while Han et al. [1] from China reports only 1.15%.

In the present study, 2 (5%) patients presented with paronychia, 1 (2.5%) with melanonychia and 1 (2.5%) with nail dystrophy. The paronychia and nail dystrophy is associated with candidalonychomycosis in PLWHA due to immunosuppression and also for life style of frequent hand wash as housewives. The melanonychia could be due to use of ZDV. This is also supported by other studies [12, 32].

This study also reveals that dermatological findings are more frequent and more severe as the immune status worsened. A significant proportion of subjects with immunosuppression presented commonly with more than one mucocutaneous lesion concurrently. The notable differences, however, emerge from this study: i) High prevalence of infective dermatoses, ii) the high prevalence of generalized pruritus and iii) the absence of Kaposi's sarcoma in the study population.

The major limitation of the study is that it is a hospital based study of cross-sectional design and there is lack of a non HIV-infected comparison group. The sample size is not large enough. Due to their low educational level, some patients were not clear about the previous skin diseases prior to HAART. Thus the HIV/AIDS patients who are included in this study may not reflect the true national scenario of Bangladesh. We recommend further multi-center study of cutaneous manifestations of HIV/AIDS patients.

Conclusion:

A different clinical pattern is noted in this study than reported previously. A wide range of dermatological disorders is observed in Bangladeshi HIV/AIDS patients and HAART had an impact on the spectrum of HIV/AIDS associated mucocutaneous disorders. They are seen at every stage of HIV/AIDS and are often the initial presentation in most instances within our environment. Early detection of HIV

optimizes the chemoprophylaxis for many opportunistic mucocutaneous infections. The presence of recurrent, chronic and recalcitrant skin diseases should be regarded as a strong indication for HIV testing. Our findings stress the necessity to incorporate geographic aspects in future guidelines for classification of HIV/AIDS-related mucocutaneous diseases. There is a need for increased attention to the diagnosis and treatment of skin diseases affecting the quality of life of HIV/AIDS patients.

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