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Original Research Article

Dermatological manifestations in PLHIV visiting link ART centre at rural medical college hospital in Western Tamilnadu, India

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ABSTRACT

Background: Ever since the early reports of human immuno deficiency infection, it presented as wide range of infectious and non-infectious dermatoses which correlate with the degree of immunodeficiency. Skin assessment remains a vital tool in the diagnosis and management of HIV infection due to relative easiness of examination. Most of skin diseases are amenable to diagnosis by inspection and biopsy. In this descriptive study, we have enumerated in detail the dermatological manifestations of Link ART centre clients.
Methods: To analyze the dermatological manifestations in people living with HIV, we undertook a prospective observational study of all PLHIV on ART visiting IRT Perundurai Medical College Hospital link anti- retroviral therapy centre (LAC) during July 2015 to August 2016 with focus to skin manifestations.
Results: Among the 140 clients, 22 in 2010, 12 in 2011, 6 in 2012, 51 in 2013, 36 in 2014, and 9 in 2015, 3 up to June 2016 enrolled for follow up. 31 were transferred to nearby ART, Link ART centres during this period as per their request, 4 lost for follow up and 6 deceased after enrolment, finally ninety-nine (39 male; 60 female) were utilizing our centre during the study period. Majority of participants were on ZLN (zidovudine, lamivudine, and nevirapine) regimen, hailing from rural zones, belonged to low or low middle income group, were undertaking farming, cattle rearing. CD4 counts of the asymptomatic clients in the ZLN group noted increase and decrease in the ZLE (zidovudine, lamivudine, and efavirenz), TLN (tenofovir, lamivudine, and nevirapine) group. In the symptomatic clients, decline in the individual and the mean counts except in female ZLN subset. 70% were clinically asymptomatic and 30 % were having some dermatological manifestations. Multiple manifestations were seen in 5 clients during the study period. Dermatological manifestations observed commonly were fungal and viral infections, xerosis/ichthyoses, adverse drug reactions like lipodystrophy, and discoloration of nails.
Conclusions: Skin manifestations observed in this study were due to aging and long term cosmetic side effects of highly active antiretroviral therapy (HAART). Lipodystrophy posed significant aesthetic distress in HAART clients. Hence, early management would decrease the most offending cosmetolgical side effects of the disease and drugs. Therapy yields the declining trend in the inflammatory, infectious dermatoses.

Keywords: Human immunodeficiency virus infection, Link antiretroviral therapy centre, Mucocutaneous manifestations

INTRODUCTION

Human immunodeficiency virus (HIV) infection remains a worldwide health problem. HIV/AIDS remains to anguish the entire continent's reproductive age group, who are important for socio economic development. Ever since the early reports of human immuno deficiency infection, skin conditions have become worrying stigma

for the seropositives. It is a challenging task for physicians to diagnose and manage them due to the severe and refractory nature. Skin lesions may be the first indicator of HIV infection. Dermatologic indicators proved to be visual markers of disease diagnosis and progression. They may at times establish as presenting symptoms and are seen at every stage of the diseases. Atypical and more complicated manifestations of co-infections also occur. Although these disorders may be seen in general healthy population, they are not so typical, severe and less or not responsive to treatment. More than 90% of PLHIV develop skin lesions at some time throughout the course of illness. More often diagnosis is missed or made late in the disease progression.

Skin assessment remains a vital tool in the diagnosis and management of HIV infection due to relative easiness of examination. Mucocutaneous manifestations remain the first-recognized clinical manifestations of AIDS. In advanced nations, CD4 lymphocyte count, viral load and viral culture are used in the management of HIV; want of these facilities in developing nations requires need of reliable clinical markers. Most of skin diseases are amenable to diagnosis by inspection and biopsy. HIV produces a wide range of infectious and non-infectious dermatoses which correlate with the degree of immunodeficiency. The development of highly active antiretroviral therapy (HAART) is one of the most dramatic developments in the history of medicine. It changes the course of HIV into a chronic manageable illness with improved quality-of-life. After HAART, there has been a dramatic reduction in the incidence of HIV-associated dermatoses but various cutaneous adverse drug reactions, and other non-infectious skin conditions have increased. The skin is not only a target organ for drug reactions but is also had bothersome cosmetic changes in the affected. However, studies pertaining to mucocutaneous manifestation in HIV are well explained in the Western literature, but there is a dearth of information from the southern India.[1-3]

National AIDS Control Organization (NACO) implementing programmes to reduce new infections and provides comprehensive care, treatment and support to all People Living with HIV (PLHIV); ensuring the universal access to comprehensive free services in health facilities across the country. It provides free highly active anti-retroviral therapy (HAART), psychosocial support, prevention and treatment of opportunistic infections including tuberculosis and facilitating home based care and impact mitigation in stigma free environment by service delivery points like ART centres, Link ART Centres (LAC), Link ART plus Centre.[4, 5]

Aim and objective of the study

To analyse dermatological manifestations in People Living with HIV visiting IRT Perundurai Medical College Hospital link anti- retroviral therapy centre.

METHODS

Study design and period

This is a prospective observational study conducted during July 2015 to August 2016. We undertook a prospective analysis of all PLHIV on HAART from our centre with key focus to skin manifestations. The study protocol was approved by the institutional ethical committee.

Inclusion criteria

All PLHIV on HAART from LAC, in IRT Perundurai Medical College hospital Perundurai, Erode District, Tamilnadu, India have been included, during the study period. In this period expired, transferred to other LAC/ART centre and lost for follow up more than 6 months were excluded from study.

Methods

IRT Perundurai Medical College hospital provides HAART care, follow up and continuum of care through LAC by ICTC staff from September 2010. In ICTC, we are documenting PLHIV data in Link ART registry as per the NACO guidelines, which are frequently studied by Tamilnadu State AIDS Control Society. People are visiting the LAC once in a month for free drugs and clinical follow-ups as per the guidelines. During the visit, all the recruitees had counselling, clinical assessment, opportunistic infections screening, need based laboratory investigations, and guidelines based CD4 count from Erode district headquarters hospital ART centre. In this study, we planned to analyse dermatological manifestations among PLHIV visiting the LAC.

Study data were evaluated by using computer software, Statistical Package for Social Sciences (SPSS16v).

RESULTS

There were a total of 140 clients; 22 in 2010, 12 in 2011, 6 in 2012, 51 in 2013, 36 in 2014, and 9 in 2015, 3 up to June 2016 were registered in the study centre (Table 1).

Table 1: Link ART Centre clients' details during the study period.

Client details	Male	Female	Total
Presently on ART	39	60	99
Transferred out	18	13	31
Lost for follow up	3	1	4
Deceased	5	1	6
Grand total	65	75	140

Of that, 31 were transferred to nearby ART, link ART centres during this period as per their request. During the study period, 99 (39 male; 60 female) were utilizing this

centre. Transferred out denotes peoples referred or opted out to other LACs or ART centres. In lost for follow up group, patients not reporting to our centre for last 6 months, we were unable reach them by land line and mobile phones, home visits by counsellors, outreach workers, various other health care workers, they are also not reached any other LAC or ART centres. In terms of treatment, majority of patients were on ZLN (zidovudine, lamivudine, and nevirapine) followed by TLE (tenofovir, lamivudine, and efavirenz), ZLE (zidovudine, lamivudine, and efavirenz) and TLN (tenofovir, lamivudine, and nevirapine) regimen (Table 2).

Table 2: Gender, age group, regimen wise distribution of clients on HAART.

Gender	Years	TLE	TLN	ZLE	ZLN	Total
Male-39 (39.4%)	Below 25	0	0	0	1 (100.0%)	1
	26-50	6 (16.7%)	1(2.8%)	1(2.8%)	28 (77.8%)	36
	Above 50	0	0	0	2 (100.0%)	2
Total		6 (15.4%)	1(2.6%)	1(2.6%)	31 (79.5%)	39
Female -60(60.6%)	Below 25	0	0	0	1 (100.0%)	1
	26-50	10 (18.2%)	0	5(9.1%)	40 (72.7%)	55
	Above 50	2 (50.0%)	0	0	2 (50.0%)	4
Total		12 (20.0%)	0	5(8.3%)	43 (71.7%)	60

In this, female clients were more than male, 26-50 years' age group was predominant than any other group and ZLN is the favoured regimen in both genders.

The socio demographic factors of the study group were exhibited in Table 3. Most of them were coming from rural zones and few from nearby Erode municipality. All of them belonged to low or low middle income group. Majority were undertaking farming, cattle rearing. Most of the women were housewives. In this study group 9 couples, 81 were single (legally separated, widowed, and 2 children). The average age in present study was 38.3 years. The immunological status of the study population was Tabled in 4 and 5.

Since we studied the clients for one year, all had minimum two CD4 count reports in six months' interval as per guidelines. In asymptomatic clients, noted increase in the ZLN group of either gender, decline in the ZLE, TLN group (Table 4).

Table 3: Socio demographic factors of clients.

Social demographic factors	Male-39	Female-60	Total-99
Residence			
Rural	37	58	95
Urban	2	2	4
Socioeconomic class			
Low	33	55	88
Middle	4	3	7
Occupation			
Agricultural workers	15	16	31
Daily wagers / Coolie	10	10	20
Business persons	8	5	13
Office workers	4	2	6
Unemployed	2	10	12
House makers	2	27	29
Family status			
Couple	9	9	18
Unmarried / divorced	30	51	81

Table 4: CD4 correlation in asymptomatic clients.

Drug regimen	Total	*CD4 1st	*CD4 2nd	Male	*CD4 1st	*CD4 2nd	Female	*CD4 1st	*CD4 2nd
ZLN	51	1310, 308, 620.451	1677, 302, 656.471	23	1218, 308, 576.391	1677, 302, 634.348	28	1310, 354, 656.643	1418, 362, 674.643
ZLE	4	1554, 167, 755	1442, 227, 692.250	1	167	227	3	1554, 391, 951	1442, 391, 847.333
TLN	1	282	272	1	282	272			
TLE	13	1200, 310, 634.077	1213, 325, 634.077	6	789, 310, 495.667	919, 325, 524.333	7	1200, 515, 752.714	1213, 424, 728.143
	69			31			38		

(*Maximum, minimum, mean in CD4 1st and CD4 2nd).

Table 5: CD4 correlation in symptomatic clients.

Drug regimen	Total	*CD4 1st	*CD4 2nd	Male	*CD4 1st	*CD4 2nd	Female	*CD4 1st	*CD4 2nd
ZLN	23	1319, 284 678.03	1181, 266 666.53	8	1076, 284 553.75	956, 266 510.25	15	1319, 470 747.267	1181, 412 762.333
ZLE	2	1053, 694 873.5	884, 643 763.5	0			2	1053, 694 873.5	884, 643 763.5
TLN									
TLE	5	906, 362 591	748, 347 590.4	0			5	906, 362 591	748, 347 590.4
	30			8			22		

(*Maximum, minimum, mean in CD4 1st and CD4 2nd).

Table 6: Mucocutaneous manifestation and regimen wise distribution of clients on HAART.

Diagnosis	TLE	TLN	ZLE	ZLN	Total
Asymptomatic	13 (72.2%)	1 (100.0%)	4 (66.7%)	51 (68.9%)	69 (69.7%)
Symptomatic subtotal	5 (27.8%)	0	2 (33.3%)	23 (32.1%)	30 (30.3%)
DLS onychomycosis	0	0	0	1 (1.4%)	1 (1.0%)
Seborrhoeic dermatitis	0	0	0	1 (1.4%)	1 (1.0%)
Tinea corporis	1 (5.6%)	0	0	1 (1.4%)	2 (2.0%)
Herpes zoster and post herpetic neuralgia	1 (5.6%)	0	1 (16.7%)	0	2 (2.0%)
Xerosis	0	0	0	4 (5.4%)	4 (4.0%)
Pruritic papular eruption	0	0	0	1 (1.4%)	1 (1.0%)
Photo dermatitis	1 (5.6%)	0	0	0	1 (1.0%)
Nail discoloration	0	0	0	2 (2.7%)	2 (2.0%)
Lipodystrophy	2 (11.1%)	0	1 (16.7%)	7 (9.5%)	10 (10.1%)
Lipodystrophy and tinea versicolor	0	0	0	1 (1.4%)	1 (1.0%)
Lipodystrophy and HSV	0	0	0	1 (1.4%)	1 (1.0%)
Xerosis and tinea corporis	0	0	0	1 (1.4%)	1 (1.0%)
Xerosis and prurigo nodularis	0	0	0	1 (1.4%)	1 (1.0%)
Xerosis and diffuse hair loss	0	0	0	1(1.4%)	1(1.0%)
Total	18 (100.0%)	1 (100.0%)	6 (100.0%)	74 (100.0%)	99 (100.0%)

In TLE group, total and male subset had increased counts female declined. CD4 counts of symptomatic clients analysed, there were decline in the individual counts and the mean counts except in female ZLN subset (Table 5).

Figure 1: Herpes zoster.

Figure 2: Herpes zoster and post herpetic neuralgia resolving.

The dermatological manifestations of study clients were enumerated in Table 6. Around 70% were clinically asymptomatic, 30 % had dermatological manifestations. Among those, 5 had multiple diseases among the study

period. Infections were either viral or fungal. We observed herpes viral infections with or without complications, superficial fungal infections predominantly. Xerosis was alone or with other dermatoses were often concern to the study group. Adverse reactions like lipodystrophy, nail discoloration was noted more frequently. Lipodystrophy was annoying to the clients due to cosmetic apprehensions.

Figure 3: Lipodystrophy in male.

Figure 4: Lipodystrophy in female.

DISCUSSION

Skin manifestations in HIV / AIDS have become an arduous stigma and a challenging task for clinicians. Dermatologic manifestations can act as markers of disease progression. The pathogenesis of skin lesions is directly correlated with a waning in the CD4+ T cell count, which ultimately lead to skin disorders, such as seborrhoeic dermatitis, atopic dermatitis, psoriasis and eosinophilic folliculitis.[6]

Western world physicians experienced dermatoses in PLHIV such as in the general public, though often in a more recalcitrant or earlier presentation. Cutaneous disease continues to be an important comorbidity and can affect the quality of life even with latest advancement in HIV management. Immunosuppression continues to represent a risk factor for infections and increased risk of malignancy, risk for SJS/TEN is significantly increased and might be associated with the decrease in cutaneous regulatory T cells.[7]

In the antiretroviral therapy era some dermatologic diseases have declined noticeably, other remains common. Psoriasis, photodermatitis, prurigo nodularis, molluscum, and adverse drug reactions were commonly seen among PLHIV with low immunological status who are not on or not adherent to antiretroviral therapy. Eczema, xerosis, warts, and Kaposi's sarcoma were relatively common regardless of HAART. Acne, staphylococcal infections, and erythema nodosum were concomitant with immune reconstitution.[8]

In Sharma A et al study 60% had non-infectious cutaneous manifestations, like pruritic papular eruption 35.8%, pigmentary changes 8.3%, seborrhoeic dermatitis 4.2% and psoriasis 3.3%, frequently in symptomatic PLHIV.[9] In present study we also observed the similar trend but in lesser percentage.

Naswa S et al recognized refractory eczematous dermatitis with severely pruritic papular eruptions and evidence of growth failure and delayed milestones in an adolescent as presenting illness of HIV.[10] In this study the adolescent clients did not revealed these signs and symptoms.

Moumita Samanta et al Calcutta, noted that papular pruritic eruption has high sensitivity, specificity and positive predictive value; as a clinical marker for progressive HIV disease in children.[11] We also noted papular pruritic eruption in the older age group refractory to topical and systemic agents.

According to one Turkey based study, dermatologic manifestations were identical to those styled in most studies from Asia, 36.2% had at least one dermatologic disease. Statistically significant correlation ($P<0.05$) with low CD4 cell counts was found for oral candidiasis, folliculitis, herpes zoster, hyperpigmentation, xerosis, and Kaposi's sarcoma.[12] In present study population, we noticed 30% symptomatic clients with fungal infections, post herpetic neuralgia, hyperpigmentation, xerosis, adverse drug reactions. Kaposi's sarcoma was not seen in our clients so far as it is rarely reported elsewhere.

Clinical study from North India documented, 30.9% of the WHO clinical stage 1 clients had related dermatoses paralleled with 93.6% of the WHO clinical stage 4 clients. There was a statistically noteworthy variance between prevalence of seborrhoeic dermatitis, adverse drug reaction, nail pigmentation, xerosis and patients with diffuse hair loss according to the WHO clinical stage of HIV infection. Proportion of patients having dermatoses increased with immunological worsening;

58.4% of PLHIV with CD4 count >500/mm^3 had adermatoses compared with 83.2% of PLHIV with CD4 count <200/mm.^{3} There was a statistically important association among immunological stages and dermatophytosis.[13] In current study also have 30% symptomatic in WHO clinical stage 1 client, whose mean CD4 cell count varies from 590 to 873 c/mm^3.

In Amritsar study, for any dermatologic complaints of PLHIV in respect to gender, majority were male population (75.6%), female 24.4%. In contrast, here female (60.6%) outnumbered male.[14]

Prabhakaran et al documented, 69.41% with at least one mucocutaneous lesion, fungal, viral, and bacterial infections were observed in 17.6%, 10.6%, and 9.4% respectively.[1] A noteworthy reduction of oral/genital candida infections were seen in HAART than non-HAART group. Candidiasis and human papillomavirus infection occurred more commonly with CD4 count <200 cells/mm^3. Inflammatory dermatoses like fungal infections (17.6%) were more commonly observed at recruitment followed by adverse cutaneous drug reactions (16.5%) and neoplasms (5.3%). We also had similar results but in lesser percentage.

Lokhande AJ et al noticed considerably increased incidence of NVP induced cutaneous ADRs was 9.03% -(old 4.64%), in patients with higher CD4 counts.[15] PLHIV who completed the anti-tuberculosis treatment tends to have more drug reactions as against reintroduction to NVP as compared to ATT naïve patients. Such observations were not noticed in present study period.

Marfatia YS et al recognized mitochondrial toxicities in 30% of their study population; peripheral neuropathy and lipodystrophy were more common in stavudine regimen.[16] In the study clients, common lipodystrophy pattern noticed were sunken cheeks and buttocks due to lipoatrophy; swollen neck, nape and upper trunk secondary to lipohypertrophy. Swollen neck mimicking massive thyromegaly was more distressing to the women population in the study group. Gluteal fat atrophy was noted in both genders. Even after switch over to the zidovudine or tenofovir based regimens the lipodystrophy was persistent, progressing and annoying to the affected clients.

Three years study on adverse drug reactions with 110 patients on NVP-based regimen from Vadodara, noticed rash 11.8%, 3 with Steven Johnson syndrome.[17] We did not observe similar trend and it may be attributed to clients on long term therapy.

Reynaud Mendel et al documented kaposi's sarcoma, oral hairy leukoplakia, molluscum contagiosum, xerosis and oral candidiasis were statistically associated to 200-300 CD4+/mm^3; p<0.001 in their prospective study with emphasis on CD4+ cell count.[18] In present study, CD4+ cell count was in raising trend in the asymptomatic and decreasing in symptomatic clients. In the symptomatic clients' xerosis, hyperpigmentation were more than others.

Limitations of the study

Since this was an observational study with limited only to participants from Link ART centre, its result cannot be generalized. We request the avid researchers to scale up similar one in all ART centres to document better pattern of skin manifestations in the present scenario.

CONCLUSION

Clients on regular antiretroviral therapy showed the declining trend in the inflammatory and infectious dermatoses. In the link ART centres, clients were on regular follow up; 30% of them had skin manifestations, mostly due to ageing and long term cosmetic side effects of HAART. So, early dermatological screening would be beneficial for PLHIV to avert the complications.

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