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A Study of Mucocutaneous Manifestations Seen In People Living With Hiv/Aids (Plhas) In Correlation with Cd4 Count

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Abstract:
Background: *The most common cause of Human Immunodeficiency virus (HIV) disease throughout the world is HIV-1 virus.HIV infection is predominantly transmitted sexually; can also be transmitted through infected blood and body fluids, and vertically from mother to child.CD4 cells are the main target of HIV and progressive destruction of these cells is characteristic of all stages of HIV infection.*
Skin is the largest organ of the body and mucocutaneous manifestations are among the earliest signs of HIV in the body. They are often viewed as markers for the disease's progression.
Materials and Methods: *The present study dealt with 250 HIV seropositive patients attending the outpatient department of Dermatology,Venereology and Leprosy (DVL), Guntur Medical College, Guntur General Hospital, Guntur District, Andhra Pradesh, India. Study design: it was a prospective study and was undertaken from January 2013 to June 2014.*
Results : *In the present study, males were affected more than females.74.4% of the patients were married. In 60% of the patients,CD4 count was between 200cells/µl to 500 cells /µl. 54% of the dermatological diseases were infectious and 46% were non-infectious. Infectious dermatoses had CD4 count ranging from 35 cells/µl to 640 cells/µl. Non infectious dermatoses had a CD4 count ranging from 55 cells /µl to 631cell/µl. Among the infectious dermatoses, viral infections were the commonest and among the non-infectious dermatoses, pruritic papular eruption was the commonest dermatosis observed. Oral leukoplakia was seen in two cases with CD4 count 58 cells/µl & 256 cells/µl respectively.*
Conclusion: *The dermatologic complications of HIV/AIDS are distressing to the patients. Skin manifestations give a clue to the underlying infection and also serve as prognostic markers to assess the underlying immune status in resource poor countries. The dermatologists have an important and responsible role in the care of these patients because patients turn to them with a great hope. A person who is diagnosed with HIV infection before the disease is far advanced and who gets and stays on antiretroviral therapy can live a nearly normal life span. This in turn will help the future generations.*

I. Introduction

HIV virus is a RNA containing virus belonging to the class retrovirus and family Lenti viridae. There are two recognised types of the viruses : HIV-1 and HIV-2. HIV-1 is prevalent worldwide. HIV-2 is predominantly found in West Africa.The virus contains viral enzymes, reverse transcriptase, integrase and protease which are essential for viral replication and maturation.HIV can infect multiple cells of the human body including brain cells,but its main target is the CD4 lymphocyte. A normal CD4 cell count in a healthy, HIV-negative adult varies but is usually between 500 and 1500cells/µl.

HIV Disease Staging And Classification: Two major classification systems currently are in use : the U.S. centers for disease control and prevention (CDC) classification system and the World Health Organisation (WHO) clinical staging and disease classification system.

The CDC disease staging system assesses the severity of HIV disease by CD4 cell counts and by the presence of specific HIV –related conditions. The definition of AIDS includes all HIV -infected individuals with CD4 counts of <200cells/µl (or CD4 percentage <14%) as well as those with certain HIV –related conditions and symptoms.

In contrast to CDC system, the WHO clinical staging and disease classification system can be used readily in resource-constrained settings without access to CD4 cell count measurements or other diagnostic and laboratory testing methods. The WHO system classifies HIV disease on the basis of clinical manifestations that can be recognised and treated by clinicians in diverse settings, including resource constrained settings, and by clinicians with varying levels of HIV expertise and training.

CDC classification system for HIV infection : is based on the lowest documented CD4 cell count and on previously diagnosed HIV-related conditions. For example, if a patient had a condition that once met the criteria for category B but now is asymptomatic, the patient would remain in category B. Patients in categories

A3, B3, and C1-C3 are considered to have AIDS.
CDC classification system for HIV –infected Adults and adolescents;

CD4 cell count	Clinical categories		
	A	B	C
	Asymptomatic Acute HIV,or PGL	symptomatic conditions not A or C	AIDS –indicator conditions
≥500cells/µL	A1	B1	C1
.200-499cells/ µL	A2	B2	C2
<200cells/ µL	A3	B3	C3

PGL =persistant generalised lymphadenopathy

WHO Clinical Staging of HIV/AIDS and Case Definition: this staging does not recquire CD4 cell count. Clinical stages are categorised as 1 through 4, progressing from primary HIV infection to advanced HIV/AIDS. These stages are defined as specific clinical conditions or symptoms. For the purpose of WHO staging system, adolescents and adults are defined as individuals aged ≥15 yrs.
WHO clinical staging of HIV /AIDS for adults and adolescents.

Clinical stage:	Clinical conditions or symptoms
Primary HIV infection	asymptomatic , acute retroviral syndrome
Clinical stage 1	asymptomatic, persistent generalised lymphadenopathy
Clinical stage 2	moderate unexplained weight loss(,10% of presumed or, measured body weight),recurrent respiratory infections, (sinusitis, tonsillitis, otitis media and pharyngitis), Herpes zoster, angular cheilitis, recurrent oral ulceration, Papular pruritic eruptions, seborrheic dermatitis, fungal, Infections
Clinical stage 3	unexplained severe weight loss (>10%of presumed, Or measured body weight),unexplained chronic, Diarrhoea for >1month, unexplained persistent fever, For>1month(.37.6^0 C, intermittent or constant), Persistent oral candidiasis, oral hairy leukoplakia, pulmonary, Tuberculosis, severe presumed bacterial infection, (eg; pneumonia, empyema, pyomyositis, bone or joint, Infection, meningitis, bacteremia),acute necrotising, ulcerative stomatitis, gingivitis, or periodontitis, Unexplained anemia(Hb<8g/dl), neutropenia (neutrophils< <500cells/ µL),chronic thrombocytopenia (platelets, <50,000cells/µL)
Clinical stage 4	HIV wasting syndrome,as defined by the CDC, Pneumocystis pneumonia,recurrent severe bacterial, Pneumonia,chronic herpes simplex infection(oro labial, Genital, or anogenital sitefor >1month,or visceral herpes, at any site),esophageal candidiasis (or candidiasis of trachea, bronchi, or lungs), extrapulmonary TB, kaposi sarcoma, cytomegalovirus infection(retinitis or infection of other, organs),central nervous system toxoplasmosis, HIV encephalo-pathy, cryptococcosis, extrapulmonary, disseminated non tuberculosis mycobacterial infection, progressive multifocal leukoencephalopathy, chronic cryptosporidiosis, (with diaorrhea, chronic isosporiasis, disseminated mycosis(eg; histoplasmosis, coccidioido mycosis, pencilliosis), recurrent nontyphoidal salmonella bacteremia, lymphoma, (cerebral or B-cell non-Hodgkins), invasive cervical carcinoma, Atypical disseminated leishmaniasis, symptomatic HIV –associated nephropathy and cardiomyopathy,reactivation of American trypanosomiasis(meningoencephalitis or myocarditis).

Skin is the first organ to be affected during the course of HIV disease.

Pathogenesis in relation to skin disorders: Viral replication occurs in lymphoid organs during the course of HIV infection .There is progressive exhaustion of the immune response. Destruction of lymphoid tissue results in impairment of the ability to maintain an effective ongoing HIV -specific immune response and to generate immune responses against new pathogens. Epidermal langerhans cells may become infected by HIV, and decreased langerhans cell function could account for some of the cutaneous manifestations of HIV disease.
Skin disorders in HIV- infected patients in India are infections,inflammatory disorders,adverse cutaneous drug reactions and neoplasms.

Infections: Most of these represent overgrowth of resident flora (Candida albicans) ,extension beyond sites of colonisation (dematophytosis),reactivation of latent infection (human herpes viruses),and transformation of subclinical infection (human papilloma virus infection, molluscum contagiosum).

Fungal infections may be superficial or deep. They frequently give a clue to the underlying HIV infection. There is increased incidence of candidal, dermatophytic and pityrosporum infections following progressive immunedeficiency in HIV infection. They are more extensive, atypical and progressive .

Oropharyngeal candidiasis occurs in as many as 90% of HIV patients at some point during the course of HIV infection. It is a sign of transition to AIDS. Candidal esophagitis is the second most common AIDS-defining disease after pneumocystis jiroverci (carini) pneumonia.

Dermatophytosis: dermatophytic infections occur in one-third of HIV –infected patients. The severity and variability of presentation are increased.

Viral infections are one of the major pathogens causing opportunistic infections (OIs) in HIV-infected patients. When accompanied by risk factors for HIV infection, both herpes simplex virus and varicella zoster virus infections are markers for HIV infection and should prompt counselling for HIV serologic testing.
Oral hairy leukoplakia is caused by Epstein –Barr virus. It may temporarily disappear when patients commence antiretroviral therapy or high doses of acyclovir, but its reappearance indicates clinical failure.

Bacterial Infections: Amongst the various bacterial infections bacillary angiomatosis represents the first clinical sign of HIV infection. Staphylococcal aureus is the most common pathogen in cutaneous infections such as ecthyma,cellulitis,necrotising fasciitis and systemic bacterial infections occurring in HIV-infected individuals. Syphilis, chancroid, granuloma inguinale, and lymphogranuloma venereum are sexually transmitted diseases.

Mycobacterial Diseases: Tuberculosis (TB) is the commonest opportunistic infection in HIV positive patients in India. HIV-related TB shows a higher prevalence of extrapulmonary and disseminated TB and adverse events because of antituberculous treatment.HIV positive patients should be regularly screened for tuberculosis.

Parasitic Infestations: Scabies is a common cutaneous manifestation in HIV –infected patients. In untreated patients and in patients with advanced disease, the more contagious and fulminant forms of scabies such as Norwegian scabies become apparent.

Inflammatory Disorders: The spectrum of erythematous scaling diseases in HIV-positive patients includes seborrheic dermatitis, psoriasis, Reiter's syndrome and icthyosis. Seborrheic dermatitis appearing de novo or exacerbation of mild seborrheic dermatitis in a known HIV-positive patient could indicate activation of disease from latency state to the symptomatic state.

Pruritus Associated With HIV : Pruritus is a marker of HIV infection, occurring in upto 30% of patients. It is related to inflammatory dermatoses associated with the disease. The pruritic eruptions are subdivided into follicular and nonfollicular eruptions. In tropical and semitropical regions, where biting insects are prominent, nonfollicular eruptions are most common and probably represent insect bite hypersensitivity. In temperate regions, follicular pruritic eruptions are more common. Follicular pruritic eruptions can be caused by eosinophilic folliculitis,demodex folliculitis, and pityrosporum folliculitis.

Adverse Cutaneous Drug Reactions: The incidence of adverse cutaneous drug reactions (ACDRs) ,especially due to antimicrobial agents ,is high in HIV disease and these eruptions tend to become severe than in the non HIV - infected. The pattern of cutaneous reactions include morbilliform reactions, fixed drug reactions, Stevens-Johnson syndrome(SJS), and toxic epidermal necrolysis (TEN).The commonest drugs causing reactions are sulfonamides. Antiretroviral agents have a significant incidence of ACDRs including hypersensitivity reactions, lipodystrophy syndrome and drug interactions. Drug hypersensitivity commonly occurs with nonnucleoside reverse transcriptase inhibitors (NNRTIs) nevirapine, efavirenz and delaverdine; the nucleoside reverse transcriptase inhibitor (NRTI) abacavir, and the protease inhibitor (PI) amprenavir.History of drug allergy,lower body weight and higher CD4 cell count are the risk factors for nevirapine associated rash.Initiation of nevirapine in patients with these risks needs monitoring. Due to increased risk of hepatitis ,avoid starting nevirapine in women with CD4 >250cells /µl and men with CD4 >400cells/µl.Risk of hepatitis for women with CD4>250 cells/µl does not apply to single dose nevirapine. Protease inhibitors and some NRTs, especially, stavudine causes lipodystrophy and premature ageing .Stavudine is no longer a recommended drug in guidelines used in developed countries,and no longer a preferred agent in resource –limited settings(WHO guidelines).Abacavir hypersensitivity reaction is more common in persons with HLA-B^{+}5701 haplotypes. Genetic testing for HLA-B^{+}5701 eliminates risk of hypersensitivity reaction,though patients should still be counselled about hypersensitivity before initiation.

The dermatologist should remember that azole derivatives, retinoids, and drugs that are metabolised via the p450 pathway frequently interact with antiretrovirals.

Neoplasms: Common HIV-associated neoplasms are kaposi's sarcoma, lymphoma and squamous cell

carcinoma. They have been rarely recorded in India. Immune reconstitution inflammatory syndrome(IRIS) describes a collection of inflammatory disorders associated with paradoxical worsening of pre existing infections following the initiation of highly active antiretroviral therapy(HAART) in HIV-infected individuals attributable to the recovery of the immune system. These exacerbations have been noted in dermatological diseases such as chronic anogenital herpes simplex, reactivation of herpes zoster, cutaneous warts, acute multifocal cutaneous ulceration owing to CMV, mycobacterial infections, lepra reactions in leprosy and papular urticaria.[1]

Clinical Markers of Disease Progression: Lymphadenopathy is an important clinical marker of disease progression so also candidiasis, oral pigmentation and gingivitis.

Skin is accessible for thorough and complete examination. Skin lesions are easily visible to the naked eye and may cause a social stigma. Moreover, people have become more conscious cosmetically .so, dermatologic complaints are a common reason for presentation to a general practitioner or to a dermatologist. It is needed to determine if the complaint may be a manifestation of a more serious underlying systemic disease. The skin has a potential to provide a window into the patient and aid in the diagnosis of diseases of all organ systems.

Keeping these trends in view that the present study was conducted in the outpatient department of DVL, Guntur General Hospital, Guntur.

II. . Materials And Methods.

After obtaining clearance and approval from the institutional ethical committee, a total of 250 HIV seropositive patients were included in the study. The study was undertaken from January 2013 to June 2014.

Study Design: This was a prospective study.

Inclusion Criteria: Persons who were HIV positive and who had details of CD4 count reports were included in the study irrespective of whether they were receiving antiretroviral therapy(ART) or not.

Exclusion Criteria: Patients who were not willing for investigations, chronically ill and immobile patients.
Informed and written consent was taken from all the patients included in the study.

In the selected patients, detailed history regarding the epidemiological aspects of the disease and the dermatological symptoms was taken and thorough physical examination of the patients was performed with emphasis on mucocutaneous manifestations and their correlation with CD4 count.

The clinical diagnosis of skin lesions was supplemented with relevant laboratory investigations such as 10% KOH mount, gram's staining, Tzanck smear, leishman' staining and VDRL test. Skin biopsy was done in selected cases. The data thus collected was compiled and analysed.

III. Results

A total of 60,760 patients attended the outpatient department of DVL, Government General Hospital, Guntur, during the period January 2013 and June 2014, out of which 327 persons were infected with HIV infection. Out of 327 HIV positive persons, only 250 persons gave their consent to be included in the study. All the 250 patients were HIV-I positive.

TABLE-I Sex distribution of the patients

Sex	No of patients
Males	135 (54%)
Females	115 (46%)

Out of 250 cases , 135 (54%) were males and 115 (46%) were males .

TABLE-2: Age distribution of the patients.

Age	Male	Female	Total
0-10	2 (0.8%)	3 (1.2%)	5 (2.0%)
11-20	3 (1.2%)	3 (1.2%)	6 (2.4%)
21-30	29 (11.6%)	34 (13.6%)	63 (25.2%)
31-40	55 (22.6%)	47 (18.8%)	102 (40.8%)
41-50	37 (14.8%)	24 (9.6%)	61 (24.4%)
51-60	6 (2.4%)	4 (1.6%)	10 (4%)
61-70	3 (1.2%)	0	3 (1.2%)

Majority of the patients,102 (40.8%) were in the age group 31-40 yrs . 63(25.2%) patients were in 21-30 yrs age group, 61 (24.4%) patients in 41-50 yrs age group,11 patients (4.4%) were <20 yrs of age and 13

patients (5.2%) were >50 yrs of age in the study group.

The oldest male patient was 72 yrs old and oldest female was 55yrs old. The youngest was 5 yrs old in both males and females.

TABLE-3: Marital status of the study group

Marital status	Male	Female	Total
Married(M)	97	89	186 (74.4%)
Unmarried(UM)	14	0	4 (5.6%)
Widow/Widower (W)	11	17	28(11.2%)
Separated (S)	6	7	13(5.2%)
Not applicable (NA)	5	4	9(3.6%)
Total	133	117	100%

Out of 250 patients, 186(74.4%) patients were married, 14 (5.6%) patients were unmarried, 28 were widow/widowers and 13 (5.2%) were separated from their partners.

Out of the 133 male patients, 97 (72%) were married, 14(10.5%) patients were unmarried and 11(8%) were widowers and 6(4%) male patients were separated from their spouses.

Out of the 117 female patients, 89(76%) were married, none of them were unmarried, 17 (14.5%) were widows and 7 (6%) of the women were separated from their husbands.

Table-4: Distribution of Urban and Rural HIV population

Locality	Number
Rural	155 (62%)
Urban	95 (38%)

In the present study, majority of the patients 155 (62%) were from rural background and 95 (38%) patients were from urban area.

Table-5: Mode of Transmission

Mode of transmission	Number
Heterosexual	216 (86.4%)
Mother to child transmission	7(2.8%)
Blood transfusion	2 (0.8%)
Homosexual	3(1.2%)
Not known	22 (8.8%)

In the present study 216 (86.4%) patients possibly acquired the infection through Hetero-sexual route of transmission,3(1.2%) through homosexual route,7(2.8%) through vertical transmission and 2(0.8%) through blood transfusion.The mode of possible route of transmission of HIV infection could not be determined in 22(8.8%) patients.

Table 6: Literacy

Literacy	Number
Illiterates	136 (54.4%)
Having primary education	50 (20%)
Having secondary (or) education	64 (25.6%)

In the present study, majority of the patients 136(54.4%) were illiterates. 64 (25.6%) patients had secondary and higher education and 50(20%) patients had primary education.

Table 7: Occupational distribution

Occupation	Number
Agricultural workers & other daily wage labourers	123 (49.2%)
House wives	51 (20.4%)
Drivers	21 (8.4%)
Private job	36 (14.4%)
Govt job	7 (2.8%)
Students	8 (3.2%)
Others	4 (1.6%)

In the present study 123(49.2%) patients were agricultural labourers, 51(20.4%) patients were house wives,36(14.4%) were doing private jobs,21(8.4%) were drivers,8 (3.2%),were students, 7 (2.8%) were government employees and 4(1.6%) were others ,which included Commercial sex workers (CSW) & sales men.

Table -8: Socioeconomic status of the study group

Socioeconomic status	Number
Low	162 (64.8%)
Medium	82 (32.8%)
High	6 (2.4%)

In the present study, majority of the patients were from the lower income group 162(64.8%), 82(32.8%) patients were from medium income group and 6(2.4%) patients were from high income group.

Table -9: Spouse HIV status in the study group

Spouse	Number
Positive	116 (51%)
Negative	78 (34.3%)
Not tested	33 (14.6%)

227 patients were analysed for the HIV status of their spouses after excluding 23 unmarried patients. 116(51%) patients had spouses who were positive for HIV, 78(34.3%) patient's spouses were negative for HIV and 33(14.6%) patient's spouses were not tested.

Table-10: CD4 count of the study patients

CD4counts (cells/µl)	Number
<200	65 (26%)
201-500	150 (60%)
>500	35 (14%)

Majority of the patients 150(60%) of the study group had CD4 counts in the range of 200-500 cells/µl followed by 65 (26%) patients whose CD4 count was < 200 cells /µl . 35 (14%) patients had their CD4 count > 500 cells/µl.

Table-11:Grouping of dermatological diseases seen in the study

	Number
Infectious	135 (54%)
Non-infectious	115 (46%)

The dermatological disorders seen in the study group were broadly classified into two groups: infectious and non-infectious groups.135(54%) disorders were infectious in nature and 115(46%) were of non-infectious group.

Table -12: Infectious Diseases in the study.

Etiology	No.of patients
Viral infections	63 (25.2%)
Fungal infections	38 (15.2%)
Bacterial infections	23 (9.2%)
Parasitic infestations	11 (4.4%)

The 148 infectious disorders were further sub divided based on their etiology into viral, fungal, bacterial and parasitic diseases. Viral infections were the most common 63(25.2%), followed by fungal infections 38(15.2%), and bacterial infections 23(9.2%).Parasitic infestations were few (4.4%) in this study.

Table -13: Viral Infections

Type of infection	Number	CD4 cell range		
		<200	200-500	>500
Herpes genitalis	16 (6.4%)	6	9	1
Herpes simplex labialis	4 (1.6%)	2	1	1
Herpes zoster	23 (9.2%)	8	13	2
Molluscum contagiosum	9 (3.5%)	3	6	-
Warts	9 (3.5%)	1	8	-
Oral hairy leukoplakia	2 (0.75%)	-	2	-

There were 63 patients (25.2%) with viral infections. Most common among them was Herpes zoster, seen in 23 patients (9.2%) This was followed by Herpes genitalis in 16 patients (6.4%), Molluscum Contagiosum in 9 patients (3.5%), Verrucae vulgaris in 9 patients (3.5%), Herpes labialis in 4(1.6%) and oral hairy leukoplakia in 2 (0.75%) patients

Table-14:Fungal Infections

Type of infection	Number	CD4 count		
		<200	200-500	>500
Candidiasis (oral+genital)	12 (4.8%)	3	8	1
Tinea infections(T. Unguium, cruris, pedis, capitis, manum, tinea at multiple sites)	26 (10.4%)	3	16	7

Fungal infections were seen in 38 patients. It accounted to 15.2% of the total skin disorders. Tinea infections (T.unguium, cruris, faciei, pedis, capitis, Tinea at multiple sites, and T.manum) were most common, seen in 26 patients (10.4%),and majority of the patients (64%) had CD4 count between 200-500cells/cmm. 12(4%) cases of candidiasis both oral and genital were seen.

Table-15:-Bacterial Infections

Number	Number	CD4cell count range		
		<200	200-500	>500
Staphylococcal infections(folliculitis, furuncles,ecthyma, impetigo)	14 (5.6%)	1	8	5
Mycobacterial infections (scrofuloderma and Hansen's disease)	5 (2%)	1	4	-
Secondary syphilis, LGV, Chancroid	4 (1.6%)	-	3	1

There were 23 patients with bacterial infections of which staphylococcal infections (folliculitis, furuncles, ecthyma, impetigo) constituted 9.2% of the total mucocutaneous disorders associated with HIV. Folliculitis was the most common bacterial infection. Mycobacterial infection was seen in 5 patients(2casesof scrofuloderma and 3cases of Hansen'disease). There were 2 cases of secondary syphilis, one case of Lymphogranuloma venereum (LGV) & one case of chancroid.

Table-16: Parasitic infections

Type of infection	Number	CD4 cell count range		
		<200	200-500	>500
Scabies	10 (4%)	2	7	1
Pediculosis capitis	1(0.4%)	-	-	1

Parasitic infestations were seen in 11 patients(4.4%),out of which scabies was seen in 10 patients(4%) and pediculosis in 2 patients(4%).

Table-17: Non-infectious dermatoses.

Type of infection	Number	CD4 count range		
		<200	200-500	>500
Pruritic papular eruption	49	15	25	9
Adverse cutaneous drug reactions	29	9	18	2
Nail changes excluding infections	5	2	2	1
Hair changes	5	1	3	1
Psoriasis	5	1	4	-
Eczemas	2	-	1	1
Xerosis	3	1	2	-
Oral changes excluding infections	5	1	4	-
Malignancy	2	-	2	-
Seborrheic dermatitis	14	2	8	2

Out of total 115 non-infectious diseases present in the study group, the most common was Pruritic Papular Eruptions(49 patients). This was followed by 29 cases of adverse cutaneous drug rashes such as exanthematous rash, urticaria, & Stevens-Johnson syndrome. There were 14 cases of seborrheic dermatitis, 2 cases of flexural eczemas, 5 cases of psoriasis vulgaris, 3 cases of xerosis, 2 cases of malignancy, 5cases of hair changes,5 cases of nail changes & 5 cases of oral changes excluding infections.

Table-18: Oral lesions in the study.

Type of lesion	Number	CD4 count range		
		<200	200-500	>500
Candidiasis	7	1	6	-
Herpes simplex labialis	4	2	1	1
Aphthous ulcers	4	-	4	-
Oral hairy leukoplakia	2	-	2	-
Pigmentation of tongue	1	1	-	-

Oral lesions were found in 18 patients. Oral candidiasis was the most common & was seen in 7 patients. Oral aphthae were seen in 4 patients, oral pigmentation in 1, H.labialis in 4, & oral hairy leukoplakia in 2 patients.

Table-19: Genital disorders in the study.

Disorder	Number	CD4 count		
		<200	200-500	>500
Herpes genitalis	16	6	9	1
Genital warts	4	1	3	-
Molluscum contagiosum lesions	3	1	2	-
Sphilis	2	-	2	-
Lymphogranuloma venereum(LGV)	1	-	1	-
Chancroid	1	-	-	1

Among genital disorders majority had Genital herpes (16 patients), 4 had genital warts, 3 had molluscum contagiosum, 2 had syphilitic ulcers and LGV & Chancroid one in each.

Table-20: Nail infections

Disorder	Number	Cd4 count		
		<200	200-500	>500
onychomycosis	6	2	3	1
paronychia	3	1	2	-
pigmentation	3	1	2	-

Nail changes were seen in 12 patients, and pigmentation of nails in 3 patients especially in those who were on anti-retroviral therapy. Onychomysis was seen in 3 & paronychia in 3 patients.

Table-21: Adverse cutaneous drug reactions

Type of lesion	Number	Cd4 count		
		<200	200-500	>500
Maculopapular rash	17	2	13	2
Urticaria	4	1	3	-
stevens-johnson syndrome	3	-	3	-
Erythema multiforme	3	1	2	-
Musculodystrophy, lipoatrophy	2	1	1	-

Adverse drug reactions were seen in 29 patients. Maculopapular rash was seen in 17 patients, majority of which were due to Nevirapine. Urticaria was seen in 4 patients & Erythema multiforme and Stevens-Johnson syndrome were seen in 3 patients each. Musculo dystrophy & lipoatrophy were seen 1 in each.

IV. Discussion

In the present study majority (66%) of the patients were in the age group 21-40yrs.This is similar to the study done by Jing et al [2](66.3%), Zancanaro et al[2](51.45%) & Sen et al[4](73.7%).This shows that majority of the affected persons belong to the most sexually active group of the population and it is also the major part of working population which causes a lot of economic burden to the family & society.

Children <10 yrs age were only 5 in the present study. This might be due to early intiation of ART. Irrespective of the CD4 count ART is initiated in children <5yrs age, whereas in children >5yrs, ART is started when the CD4 count is<500cells/µl. There were only 13 patients in the age group between 51-70 yrs. If majority of the young people who are the earning members of the family are affected leaving behind children and elderly, helpless in the family, this will have tremendous medical, psychosocial and economic consequences on the family and to the country.

Male to female ratio in the present study was 1.17:1.This was similar to observations made by Sen et al [4] (1.6:1), and Jindal et al [5] (0.9:1).It was lower when compared to the study done by Kumaraswamy et al[6] (2.4:1). Men out numbered females may be because, men are more exposed to high risk behaviour when compared to females.

The incidence of HIV infection in unskilled workers in the present study was 49.2% which was almost similar to the study of Jindal et al[5](39%).House wives made up for 20.4% of the patients in the present study which was lower than that in the study done by Jindal et al[5] (47.4%).Drivers who are at a higher risk of developing HIV infection are only 8.4% in the present study whereas they are 5.3% in Jindal et al study. People from all walks of life are susceptible to HIV infection and it is not exclusive to one group of population.

Rural population (62%) is affected more than urban (38%) population in the present study which is similar to Jindal et al study (rural 71% & urban 29%).The factors responsible for this probably are illiteracy, lack of

awareness about the disease & condom usage.

In the present study 54.4% of the patients were illiterates which is similar to Jindal et al study (52.6%).This is to stress the importance of literacy in the control of the infection & prevention of mucocutaneous manifestations with knowledge of skin & genital hygiene.

In the present study 74.4% of patients were married which is higher when compared to study done by Jindal et a l(63.5%) and Jing et al (46.2%). 51% of spouses of patients in the present study were HIV positive which is slightly higher(47.2%) than in the study done by Jindal et al. Males outnumbered females in the present study in comparison to female predominance in Jindal et al study. This difference between the two studies can be possibly due to better preventive measures like condom use & STI treatment which vary from region to region.

Majority of the patients (64.8%) were from low income group in the present study who are deprived of nutritious diet, lack of proper clothing & healthy surroundings which make them vulnerable for many skin manifestations.

History Of Exposure To The Risk Of Sexually Transmitted Diseases (Stds) :

125 (50%) patients in the study group gave positive history of exposure to the risk of STDs. 110 out of 125 patients who gave a positive history of exposure to the risk of STDs were men. This shows that men are the main source of infection to their spouses as they acquire it through their high risk behaviour. Creating awareness regarding safe sexual practices is very important to curb the spread of HIV infection.

In the present study, CD4 count was <200 cells/µl in 26% of patients, in 60% of patients CD4 count was between 200-500 cells/µl and in 14% of patients the count was >500 cells/µl.In the study by Munoz-Peroz et al [7] 53% of patients had CD4 cell count <200 cells/µl, 26% patients had CD4 cell count between 200-500cells/µl and in 21% patients it was >400 cells/µl. In the study done by Raju et al [8], 77.5% of the patients had CD4 cell count <500 cells/µl. In the study by Jing et al [2] CD4 cell count was <200cells/µl in 89% of patients. Majority of people had CD4 count between 200-500cells/µl .This may be because of intake of ART.

Non-infectious inflammatory dermatoses like seborrheic dermatitis and psoriasis (46%) are nearly equal to infectious lesions (54%).This may be due to immune disturbances associated with HIV infection.

The range of CD4 count was between 35cells/µl to 542cells/µl in patients with viral infections. Viral infections were more, probably because of the persistent and recurrent nature of viral infections.CD4 count range was between 54cells/µl to 640cells/µl in fungal infections. In bacterial infections the range was between 104cells/µl to 680 cells/µl.The bacterial infections usually occur at an advanced stage of HIV infection, but present study indicates bacterial infection can occur at any CD4 count but the severity changes.

Correlation Of Viral Infections In Various Studies : In the present study Herpes zoster was most common among viral infections seen in 23(9.2%) patients with CD4 count range between 80 cells/µl to 541 cells/µl.One child had H.zoster ophthalmicus with CD4 count 242cells/µl.The lesions of H.zoster in some patients were disseminated, recurrent & had multidermatomal and aberrant involvement which were similar to the studies of Mandal[8]and Cohen et al[10.] It is important to recognise the wide & varied spectrum of H.zoster in HIV patients which may occur at any CD4 count but usually at 350 cells/µl.Ther is a strong association between occurrence of H.zoster and HIV infection, for this reason all patients with H.zoster should be screened for HIV infection. The recurrence of H.zoster in HIV infection may be an indication of more advanced stage of HIV infection.

In one patient with H.labialis CD4 count was 58 cells/µl and in one patient with oral hairy leukoplakia, CD4 count was 256 cells/µl. In patients with H.genitalis CD4count range was between 48cells/µl to 502 cells/µl. Genital herpes was the main etiology of chronic genital ulcer in patients with HIV infection[11]. Herpetic ulcers persisting for more than one month are the hall mark of active AIDS status[11]. Aggressive treatment of H.simplex virus infection in combination with ART provides a significant benefit. Male circumcision in addition to decreasing the incidence of HIV infection, significantly reduces the incidence of HSV-2 infection and the prevalence of HPV infection[11] .

There were 9 (3.6%) patients with molluscum contagiosum &range of CD4 count was between 89cells/µl to 356cells/µl.Out of 9 patients 3 had genital molluscum contagiosum lesions and they might have acquired the infection through sexual route.

Warts were present in 9 (3.6%) patients out of which 4 had genital lesions.CD4 count was between 81 cells/µl to 364 cells/µl.Munoz Peroz [7] in their study mentioned HIV infection itself predisposes to an increased risk of human papilloma virus (HPV) infection that is not directly related to the degree of immunosupression.

Correlation of fungal infections in various studies: Hot and humid environment of Guntur district may be one of the factors predisposing the patients to fungal infections. Tinea infection were most common & CD4 count was between 94 cells/µl to 640 cells/µl.This was similar to study done by Rosatelli et al (17.5%)[12] but lower than that of study done by Singh et al(32.9%)[13] & greater than study done by Kumaraswamy et al (8%)[6].Goodman et al[14] observed several cases of tinea capitis in their study but in the present study only one case was observed. In the present study in patients with oral candidiasis CD4 count between 64 cells/µl to 351 cells/µl & in patients

with genital candidiasis CD4 count between 102 cells/µl to 323 cells/µl.

Correlation of bacterial infections in various studies: The percentage of patients with bacterial infections(15.2%) were more in the present study when compared to that of done by Kumaraswamy et al(2.9%)[6] but lower than the study done by Golstein et al [15] (20.1%) and Nicholas et al[16](54%).Occurrence of bacterial infections in HIV infection varies from place to place. In the present study staphylococcal infections were most common (CD4 range between 88cells/µl to 510 cells/µl.

Mycobacterial Infections: There were 2 patients with scrofuloderma with CD4 count 104cells/µl & 220cells/µl respectively. There were 2 patients with boderline tuberculoid(BT) leprosy with CD4 count 230cells/µl & 430 cells/µl respectively. One patient had neuritic leprosy with claw hand and CD4 count was 300 cells/µl. Tuberculides, atypical mycobacterial infections can occur as a manifestation of immune reconstitution syndrome, however there were no such cases in our study.

There were 2 patients with secondary syphilis & CD4 count was 221 cells/µl & 390 cells/µl respectively. It is recommended that all patients with newly diagnosed syphilis should be counselled for HIV testing & serologic tests for syphilis should be done in newly diagnosed patients with HIV.[17] In the present study one case with Lymphogranuloma venereum and one case with Chancroid was seen with CD4 count 372cells/µl & 299cells/µlrespectively. Bacterial infections could be attributed to poor hygiene & low socioeconomic status in the study group.

Parasitic Infestations: 10 patients with scabies (CD4 count between 39cells/µl to 550 cells /µl) and one patient with pediculosis (CD4 count 622cells/µl) were seen in the present study. Out of 10 patients with scabies 4 had norwegian scabies (crusted scabies).Because the infection is related to cutaneous immune response, crusted scabies could be considered as an opportunistic infection of AIDS [6]. Scabies can be accounted for, by poor hygiene, over-crowding & lowered body resistance.

Non-Infectious Disorders:

Pruritic Papular Eruption (PPE) : In the present study out of 115 patients with non infectious diorders,49(19.6%) had PPE with CD4 range 55 cells/µl to 631cells/µl. Kumaraswamy et al[6] and Mniar et al [18] reported PPE in 7.7% & 48% cases respectively. Some researchers reported that PPE shows good response to antiretroviral therapy & they have suggested that PPE to be added to the list of conditions qualifying for specific therapy.

Seborrheic Dermatitis: In the present study 14 patients (5.6%) patients had seborrheic dermatitis with CD4 range 72 cells/µl to 526 cells/µl.Goldstein et al found seborrheic dermatitis in 7.4% of their HIV patients which is closer to the present study. Xerosis was seen in 3 patients (1.2%) with CD4 range between 65 cells/µl to 272cells/µl. Xerosis was seen in advanced stage of the disease. In the present study 5 patients had psoriasis (2%) with CD4 count from 56 cells/µl to 349 cells/µl.Knowledge of both the common & atypical presentations of HIV – associated dermatoses may be helpful in arousing suspicion of HIV, especially in patients with no reported risk factors.

Two cases of eczema were seen in the present study with CD4 counts 520cells/µl & 469 cells/µl respectively. 2 patients with squamous cell carcinoma were seen (CD4 count 278cells/µl & 400 cells/µl respectively. There were no cases of Kaposi's sarcoma, possibly due to low number of cases reporting homosexual behaviour in contrast to reports from Europe and the United states.

Adverse Drug Reactions: Maculopapular rash was seen in 17 (6.8%) patients with CD4 count range between 81 cells/µl to 580 cells/µl; majority of them(5.6%) were due to nevirapine followed by efavirenz and carbamazepine. Patel et al [19] reported nevirapine induced rash in 6.6% cases which is nearer to the present study. Kohlbrenner et al [20] attempted to analyze the risk factors that may contribute to development of nevirapine rash. They reported that CD4 cell count <100cells/µl & concurrent use of fluconazole increase the risk of nevirapine rash. To minimise adverse drug reactions, a clinician should always start a 2 week nevirapine lead –in- dose (200mg once daily) & closely monitor patients on nevirapine –based regimen especially during the first 2 months of therapy. If nevirapine is interrupted due to any reason for > 14 days then the drug should be restarted with lead in dose. Starting with full dose of nevirapine without lead in dose results in higher serum concentration of the drug, which increases the risk of hepatotoxicity & rash.

In 4 patients with urticaria CD4 count was between 78 cells/µl to 412 cells/µl. Nevirapine was the cause of Stevens'Jhonson syndrome in 2 patients. In the present study stavudine caused muscle atrophy and lipoatrophy in 2 cases. In majority of patients rashes occurred within the first 4-6 weeks of treatment.

16 (6.4%) patients had genital herpes with CD4 count between 48 cells/µl to 502 cells. Among them 10 (4%) had recurrent Herpes genitalis. Genital infections indicate an important portal of entry of HIV. Herpes

simplex virus type – 2 causing genital ulcerative disease acts as main risk factor for acquisition of HIV infection. Chronic mucocutaneous ulcers persisting for more than one month are the hallmarks of active AIDS status. Aggressive treatment of HSV in combination with HAART therapy provides a significant benefit.[10] In patients with genital warts CD4 count was between 187 cells/µl to 392 cells/µl.In the present study in patients with molluscum contagiosum CD4 count was between 89cells/µl to 456 cells /µl.

In 2 patients with secondary syphilis CD4 count was 221 cells/µl & 390 cells/µl respectively. One patient with LGV had CD4 count of 229 cell/µl and another patient with chancroid had CD4 cell count 674 cells/µl.

Nail changes: 3 patients had paronychia & CD4 count was between 194 cells/µl to 410 cells/µl.Three patients with Pigmentation of nails had CD4 count range between 181 cells/µl to 264 cells and these patients were on ART .

In the present study 6 patients had onychomycosis & CD4 count was between 76 cells /µl to 526 cells/µl; among them 2 had toe nail involvement and 4 had finger nail involvement. onychomycosis in HIV infection commonly involves toe nails [21].

In the present study oral candidiasis was seen in 7 patients with CD4 count between 64 cells/µl to 351cells/µl. Oral candidiasis is a major sign of disease progression.

CD4 count was between 48cells/µl to34 cells/µl in patients with aphthous ulcers in the present study. 4 patients with H.labialis had cd4 count between 89cells/µl to 236 cells/µl.

Hair Changes: in the present study 4 patients had diffuse alopecia and one had alopecia areata. Chronic, diffuse hair loss in HIV –infected patients has been attributed to chronic HIV -1 infection itself & recurrent secondary infections, nutritional deficiencies, immunologic and endocrine dysregulation and exposure to multiple drugs. Many cytokines including IL-1, IL-6 &TNF-alpha increase in the mid to late stages of HIV-1 disease and these may have an effect on the follicle.

Oral Infections: Oral candidiasis was most common finding(7 patients) observed with CD4 counts ranging from 64cells/µl to 351cells/µl.The most common HIV related oral disorder is candidiasis which occurs in 17-43% cases with HIV infection & in more than 90% of cases with AIDS.

Oral aphthous ulcers were seen in 4 patients with CD4 counts ranging from 48 cells/µl to 342cells/µl.Major aphthae occur due to immune dysregulation in seropositives. Pigmentation was found in 1 patient & H. labialis in 4 patients with CD4 counts ranging from 89 cells/µlto 236cells/µl.The lesions of recurrent oral herpes simplex in HIV infected patients present with ulceration and pain of longer duration, which can result in reduced intake of food with resultant weight loss, which worsens the morbid condition.

Oral hairy leukoplakia was seen in 2 patients with CD4 counts 256cells/µl & 340 cells /µl respectively. It should be differentiated from oral candidiasis as the treatment differs.

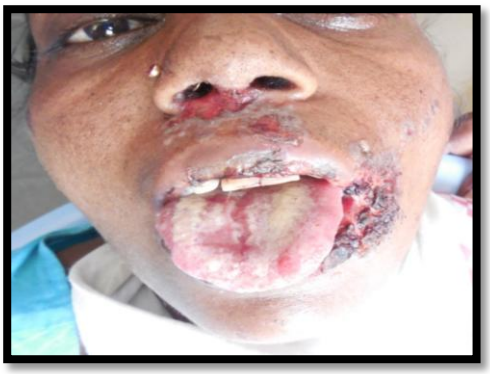
Limitations Of The Study: 1.As the ART centre is far from our department, patients are not attending our department unless they have severe mucocutaneous manifestations. 2.Some of the patients with muscle atrophy and lipoatrophy are not reporting back as they are not aware that these changes can occur due to drugs.

V. Conclusion

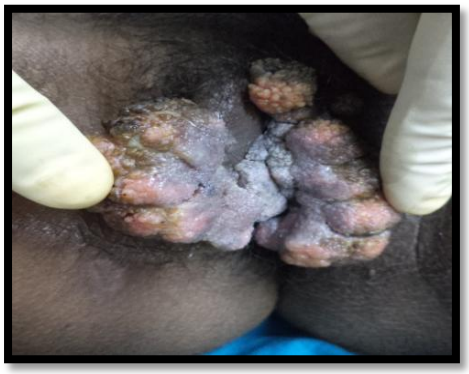
Skin conditions are among the earliest signs of the presence of HIV in the body. A low CD4 count is associated a higher number of skin disorders. Majority of patients are in reproductive age group so, all HIV infected patients should be screened for sexually transmitted infections (STIs). Education should include safer sex practices and skin care to avoid infections. There should be universal access to the treatment of STIs and other opportunistic infections which will decrease the HIV burden and improve the quality of life in those who are already infected. The dermatologist's role in the care of HIV infected patients is to be familiar with HIV associated mucocutaneous manifestations, their diagnosis and management. Antiretroviral drugs can help prevent and manage the skin conditions. Patients should be well counselled before the start of ART regarding the side effects and also regarding the cosmetic disfigurement which they can cause. Standard treatment regimens for mucocutaneous disorders may be inadequate in HIV infected patients and the treatment should be given for extended periods and intensified. HIV and AIDS are life threatening conditions. It is advisable to counsel the Patients to change their behaviour that people disapprove of and improve their morality to live peacefully.

Infections

Herpes Zoster Ophthalmicus Involving The Cornea

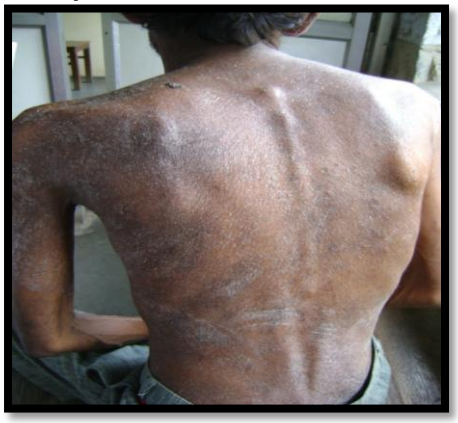


Herpe stomatitis With idiasis

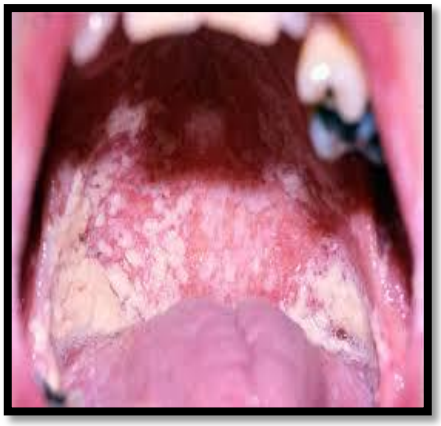


COndyloma Accuminata

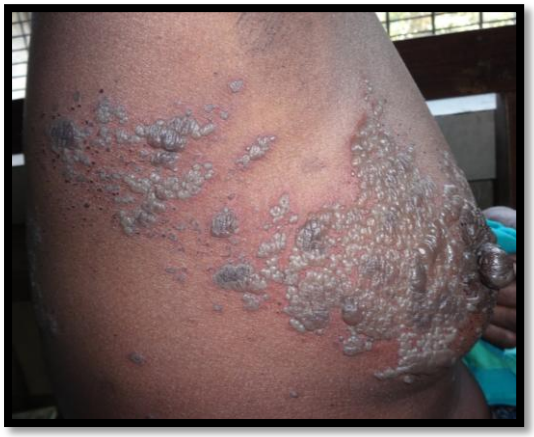
Norwegian Scabies



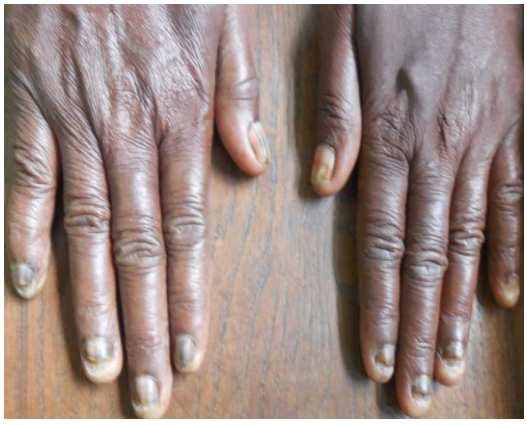
Extensive Tinea Corporis



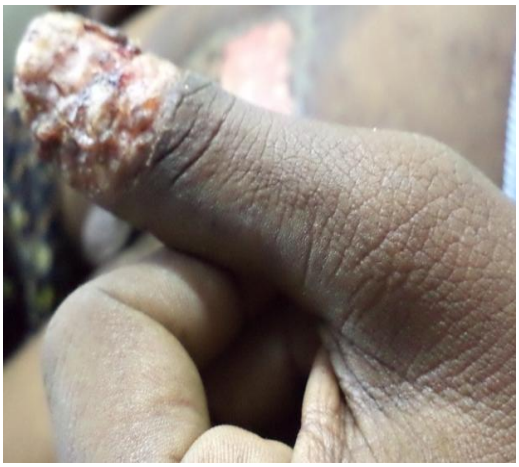
Oral Candidiasis

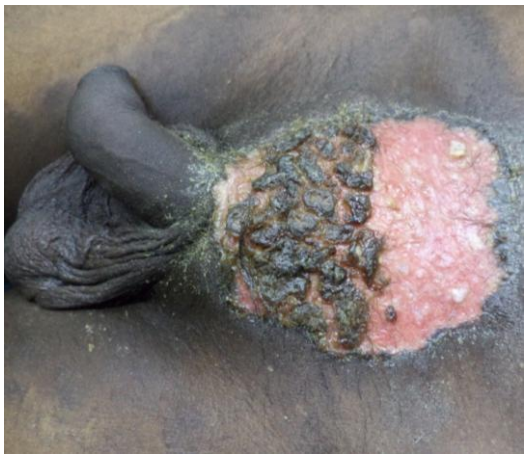


Multi Dermatomal Herpes Zoster

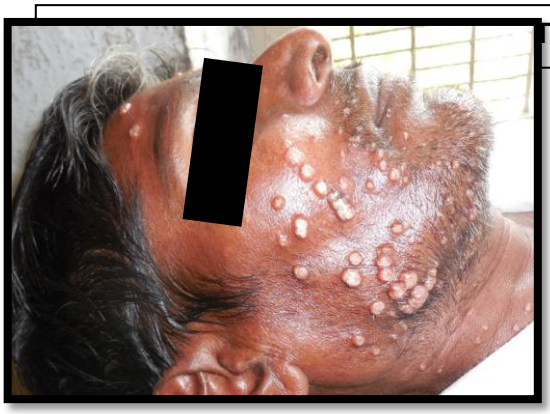


Tinea Mannum

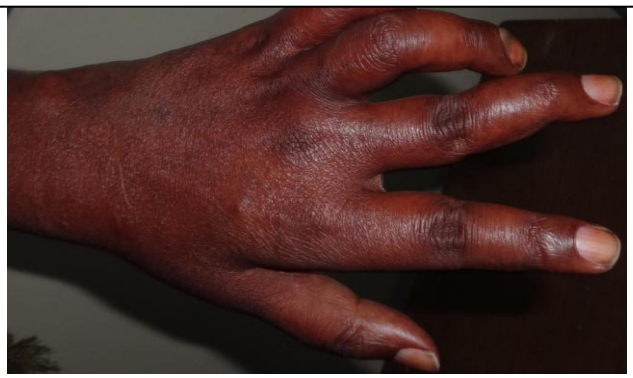




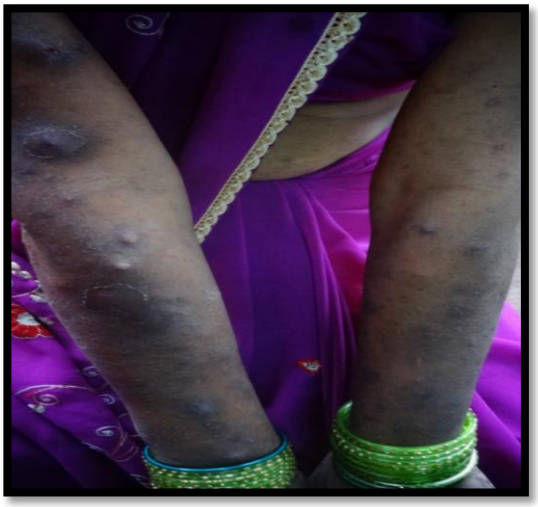
TIC WHITLOW OF HAND OF THE SAME PATIENT



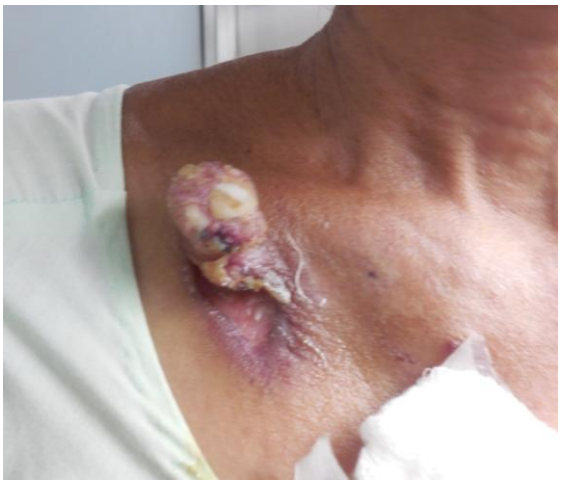
Molluscum Contagiosum On The Face



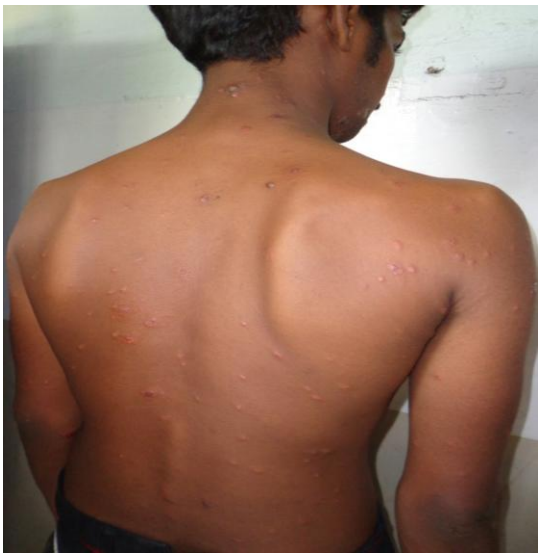
ULNAR CLAW HAND IN A Patient With Leprosy

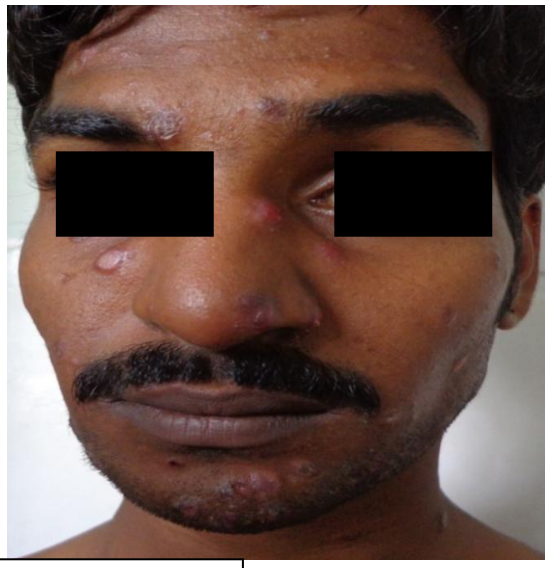


FURUNCULOSIS



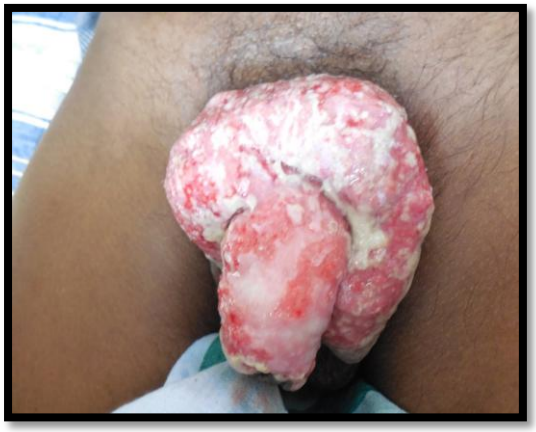
SCROFULODERMA OF THE NECK



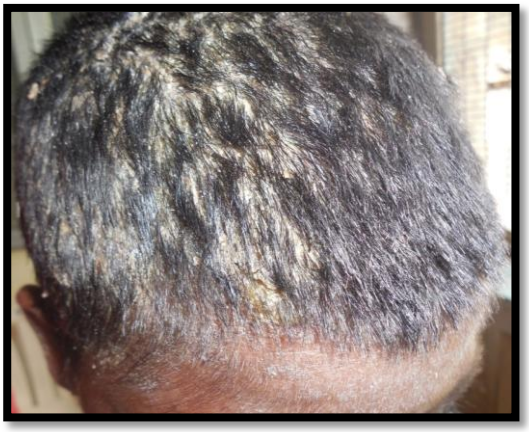


SECONDARY SYPHILIS

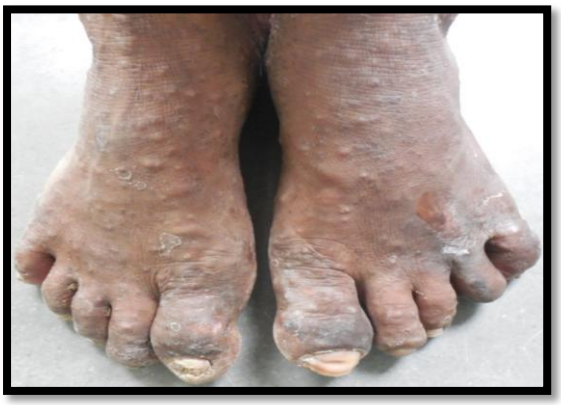
NON- INFECTIONS

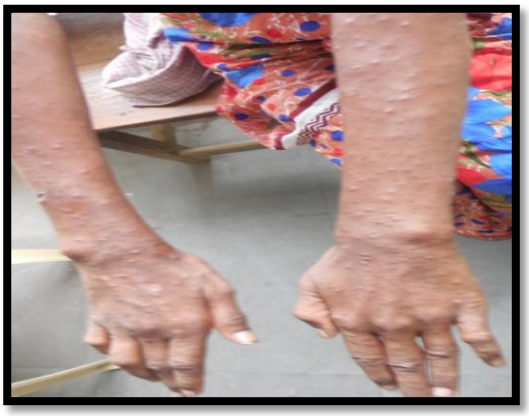


SQUAMOUS CELL CARCINOMA



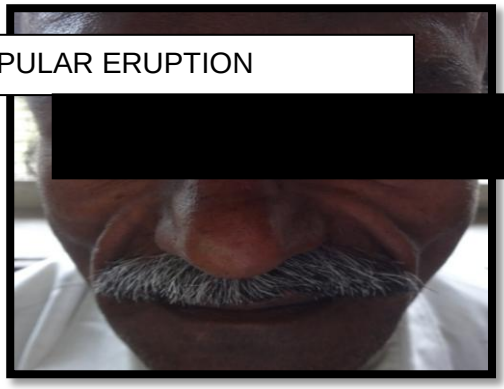
SEBORRHEIC DERMATITIS



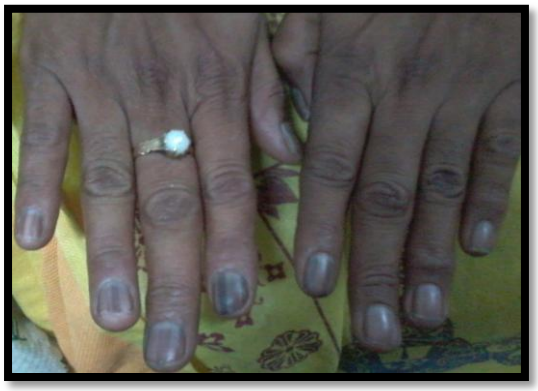


STEVENS JOHNSON SYNDROME WITH NEVIRAPINE –RESOLVING STAGE

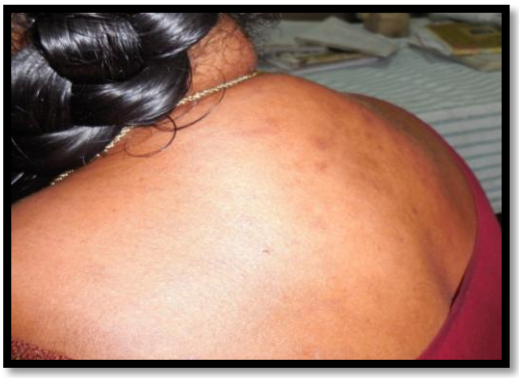
PRURITIC PAPULAR ERUPTION



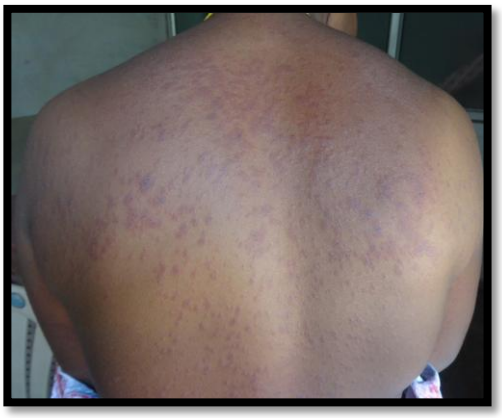
LIPOATROPHY OF THE FACE



ZIDOVUDINE INDUCED NAIL PIGMENTATION



BUFFALO HUMP DUE TO STAVUDINE



NEVIRAPINE INDUCED MACULOPAPULAR RASH

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