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CD4 Cell Counts, Lipid Profile, and Oral Manifestations in HIV-Infected and AIDS Patients

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A B S T R A C T

Objectives: The present study aimed to evaluate CD4 cell counts, lipid profile, and oral manifestations in human immunodeficiency virus (HIV)-infected and acquired immune deficiency syndrome (AIDS) patients and their correlation with seronegative controls.

Materials and Methods: In this cross-sectional, hospital-based study, there were three groups of subjects: group A consisting of 500 healthy patients (controls), group B composed of 500 HIV-infected patients, and group C comprised of 500 AIDS patients based on their CD4 cell counts. CD4 cell counts were assessed using the CyFlow counter. Lipid profile was evaluated with the Erba EM 360 analyzer.

Results: The results were statistically significant for CD4 cell counts ($P<0.001$). The levels of total cholesterol (TC) and low-density lipoproteins (LDLs) were significantly decreased while triglycerides (TGs) and very-low-density lipoproteins (VLDLs) were significantly increased in AIDS patients compared to the controls and HIV-infected patients. Various results were obtained regarding oral manifestations with different levels of significance.

Conclusion: CD4 cell counts, TC, LDLs, TGs, and VLDLs were significantly changed in HIV-infected and AIDS patients compared to the controls.

Keywords: CD4 Cell Counts; Lipids; Oral Manifestations; HIV Infections; Acquired Immunodeficiency Syndrome

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INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is caused by a retrovirus called human immunodeficiency virus (HIV), which impairs the body's immune system and leaves the patient susceptible to life-threatening opportunistic infections, neurological disorders, and malignancies [1]. The two known forms of this

virus are HIV-1 and HIV-2 from a family of lentiviruses [2]. HIV is a spherical virus enveloped by a lipid bilayer (90-120 nm). The nucleocapsid comprises an outer icosahedral shell and an inner cone-shaped core, encompassing the ribonucleoproteins. The virus core contains the major capsid protein p24, nucleocapsid protein p7/p9, two copies of genomic RNA, protease, reverse transcriptase, and integrase [2]. A matrix protein called p17, which lies underneath the virion envelope, surrounds the viral core. Studding the viral envelope are two viral glycoproteins, namely gp120 and gp41 [2,3]. According to estimates by the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS), 35 million people were living with HIV at the end of 2013 [4]. Based on the HIV Sentinel Surveillance (2008-09), it is estimated that 23.9 lakh people are infected with HIV in India (39% females and 4.4% children) [4]. The first AIDS case in India was detected in 1986 [4]. HIV is transmitted by homosexual and heterosexual contact, blood, infected mothers via intrapartum or perinatal routes or breast milk, and by occupational transmission. To date, there is no evidence that HIV can transmit because of exposure to saliva, tears, sweat, and urine [5]. The immune system and the central nervous system (CNS) are two major targets of HIV infection. The hallmark of AIDS is immunosuppression, affecting the cell-mediated immunity (CMI) [5]. HIV enters the body through mucosal tissues and blood, infecting the T-cells, dendritic cells, and macrophages. The infection is established in the lymphoid tissue and remains latent for long periods. Active viral replication is associated with cell infection and progression to AIDS. The nervous system is a major target for HIV infection. Macrophages and microglial cells in the CNS are the main cell types in the brain that are infected with HIV [3]. The frequency and severity of common cutaneous diseases increase in HIV patients, correlating with the number of CD4 T-helper cell counts [3]. Cutaneous manifestations are prognostic indicators for the development of AIDS [6]. India bears the third-largest number of HIV-infected patients worldwide following South Africa and Nigeria [7]. In India, the highest prevalence of HIV/AIDS has been observed in Nagaland followed by Mizoram, Manipur, and Andhra Pradesh (0.59%) according to the latest national AIDS statistics (NACO, HIV Sentinel Surveillance 2012-13) [8]. HIV infection causes the depletion of CD4 cells in peripheral blood and lymphoid tissues, leading to CD8 cell dysfunction [9]. Quantification of CD4 helper lymphocytes is necessary for staging and observing HIV-infected patients [9]. The oral cavity has a key role in defining the history of HIV/AIDS. Oral manifestations of HIV are present in about 30%-80% of the patients, and the predisposing factors include <200/mm^3 CD4 cell counts, viral load, xerostomia, poor oral hygiene, and smoking [9]. Although the most common oral lesion is candidiasis, normal microbial flora or commensals of the oral mucosa present in the saliva, dental plaque, gingival crevice, tonsils, and pharynx may become invasive because of the weakened immune system [10].

Granulocytopenia occurs with reduced CD4 cell counts in HIV infection. When the counts of granulocytes fall beneath 500/mm^3, in the presence of anatomical barrier damage, invasion of the bloodstream by microorganisms is facilitated, leading to sepsis and death [10]. The periodontal tissues in the mouth provide a weak barrier through which bacteria can enter the connective tissues and the systemic circulation [10]. The oral manifestations may be of predictive value, indicating the progression from HIV seropositivity to AIDS [11]. HIV-associated periodontal diseases have been reported in HIV-infected persons, which include linear gingival erythema, necrotizing ulcerative gingivitis (NUG), and necrotizing ulcerative periodontitis (NUP) [11]. The CD4+ T lymphocytes are the primary target of HIV infection because of the affinity of the virus to the CD4+ cell surface marker. HIV infection causes a gradual decline of CD4+ T lymphocyte levels in peripheral bloodstream, leading to increased susceptibility to opportunistic, viral, bacterial, protozoal, and fungal infections as well as certain malignancies [11]. Infection can increase plasma triglyceride (TG) levels by decreasing the clearance of circulating lipoproteins as a result of reduced lipoprotein lipase (LPL) or by stimulating hepatic lipid synthesis through an increase in hepatic fatty acid (FA) synthesis or re-esterification of FAs derived from lipolysis [1].

Hypertriglyceridemia was the first dyslipidemia reported in HIV-infected patients. HIV has been associated with hypertriglyceridemia, low levels of total cholesterol (TC), low levels of low-density lipoprotein cholesterol (LDLC), and low levels of high-density lipoprotein cholesterol (HDLC) [1]. Different studies have been conducted on the lipid profile in HIV-infected patients in Nigeria, Brazil, Thailand, Switzerland, and Ghana. In India, few reports are available from Uttar Pradesh, Chandigarh, Karnataka, Tamil Nadu, and Manipur. Few studies have been conducted correlating these parameters with oral manifestations in the Indian population. The present study was conducted to evaluate the CD4 cell counts, lipid profile, and oral manifestations in HIV-infected and AIDS patients and to correlate them with seronegative controls.

MATERIALS AND METHODS

The present study was a cross-sectional, hospital-based study, conducted between January 2014 to September 2014 to assess the CD4 cell counts and lipid profile in the HIV infected and AIDS patients and to compare the parameters with the healthy controls. The study population included 1500 subjects reporting to the Outpatient Department divided into 3 groups including:

Control Group (A): consisting of 500 individuals who were healthy controls without any systemic illness

HIV Group (B): consisting of 500 patients who were diagnosed as HIV infected, and

AIDS Group (C): consisting of 500 patients diagnosed as AIDS patients, depending on their CD4 cell counts.

A written, informed consent was obtained from the patients forming the study sample to participate in the study. Also, the study was sent for approval to the Ethical Committee of the Institution and permission was obtained before the start of the study. The patients at the extremes of ages, pregnant women and those on chemotherapy were excluded from the study because of possible weakened immune status. The patients who did not agree to give consent and were not willing to participate in the study were, also, excluded from the study.

Materials for patient examination (Fig. 1A): Mouth mask, sterile gloves, mouth mirror, explorer, kidney tray and torchlight for artificial illumination.

Fig. 1. (A) Armamentarium for sample collection and (B) the phlebotomy procedure

Methodology:

All subjects of groups A and B were informed about the study and written signed informed consents were obtained A detailed history was taken followed by clinical examinations, which were performed according to the protocols of the Universal Precautions. All group C patients were similarly informed about the study, and the same procedure was followed. The findings were recorded according to the WHO Collaborating Center on Oral Manifestations of the Immunodeficiency Virus protocols. All patients were then subjected to phlebotomy.

Phlebotomy procedure (Fig. 1B)

After adequate explanation, the patients' forearms were rested on the laboratory table comfortably. The ante-cubital fossa was exposed, and the tourniquet was applied about half an inch to two inches above the ante-cubital fossa. The area was disinfected with 70% ethyl alcohol. Using a sterile disposable syringe and a 23-gauge needle, a needle puncture was made and maneuvered to enter the ante-cubital vein, and 2 ml of blood was drawn. The tourniquet was relieved, and the needle was removed.

Dry cotton was placed on the site of the needle puncture, and instructions were given to apply pressure for about five minutes and then to dispose of the cotton. The blood was transferred immediately into tubes containing EDTA.

Biochemical analysis:

Fifty µl of EDTA anti-coagulated blood was added to 10 µl of the monoclonal antibody, and after 15 minutes of incubation, one ml of no lyse dilution buffer (Partec, Münster, Germany) was added. The sample tube was attached to the CyFlow counter (Sysmex Partec GmbH, Am Flugplatz, Goerlitz, Germany; Fig. 2, left) for the evaluation of CD4 cell counts.

Fig. 2. The Partec CyFlow cell counter for the evaluation of CD4 cell counts (left) and the Erba EM 360 analyzer for the evaluation of lipid profiles (right).

Lipid profile was evaluated using the Erba EM 360 analyzer (ERBA Diagnostics Mannheim GmbH, Mallaustrasse, Mannheim, Germany; Fig. 2, right). The device was powered by a diffraction grating photometer. It was packed with the power of analyzing 360 tests per hour.

Statistical analysis:

One-way analysis of variance with post-hoc Games-Howell test was used for comparison of the parameters. $P<0.05$ was considered statistically significant.

RESULTS

The distribution of patients according to age and gender as well as the distribution of male and female patients according to age are presented in Tables 1 to 3 and Graph 1.

Table 1. Patient distribution according to age groups

Age groups (years)	Control N (%)	HIV N (%)	AIDS N (%)
10-20	40 (8)	31 (6.2)	16 (3.2)
21-30	127 (25.4)	193 (38.6)	150 (30)
31-40	99 (19.8)	161 (32.2)	181 (36.2)
41-50	126 (25.2)	79 (15.8)	102 (20.4)
51-60	73.(14.6)	21.(4.2)	38 (7.6)
61-70	35 (7)	15 (3)	13 (2.6)

HIV: human immunodeficiency virus, AIDS: acquired immune deficiency syndrome

Table 2. Distribution of the patients based on gender

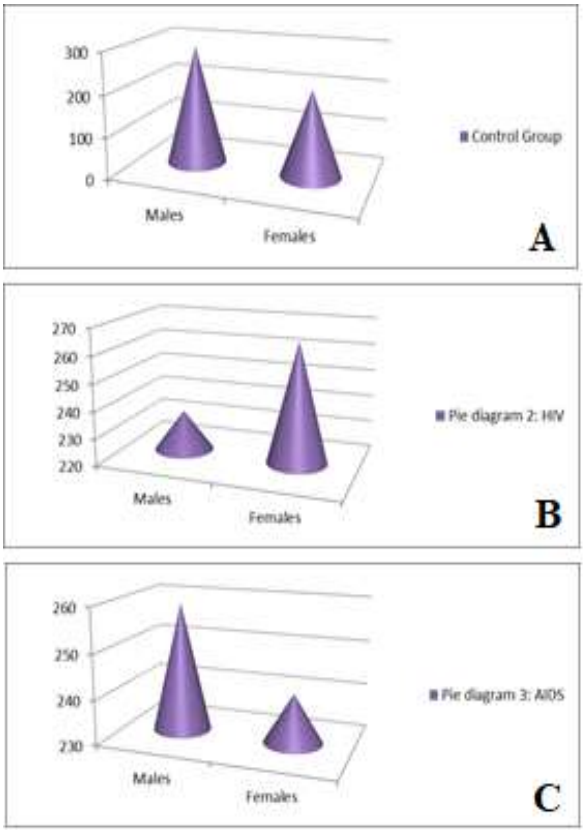
Gender	Control	HIV	AIDS
Male	291	235	259
Female	209	265	241

HIV: human immunodeficiency virus; AIDS: acquired immune deficiency syndrome

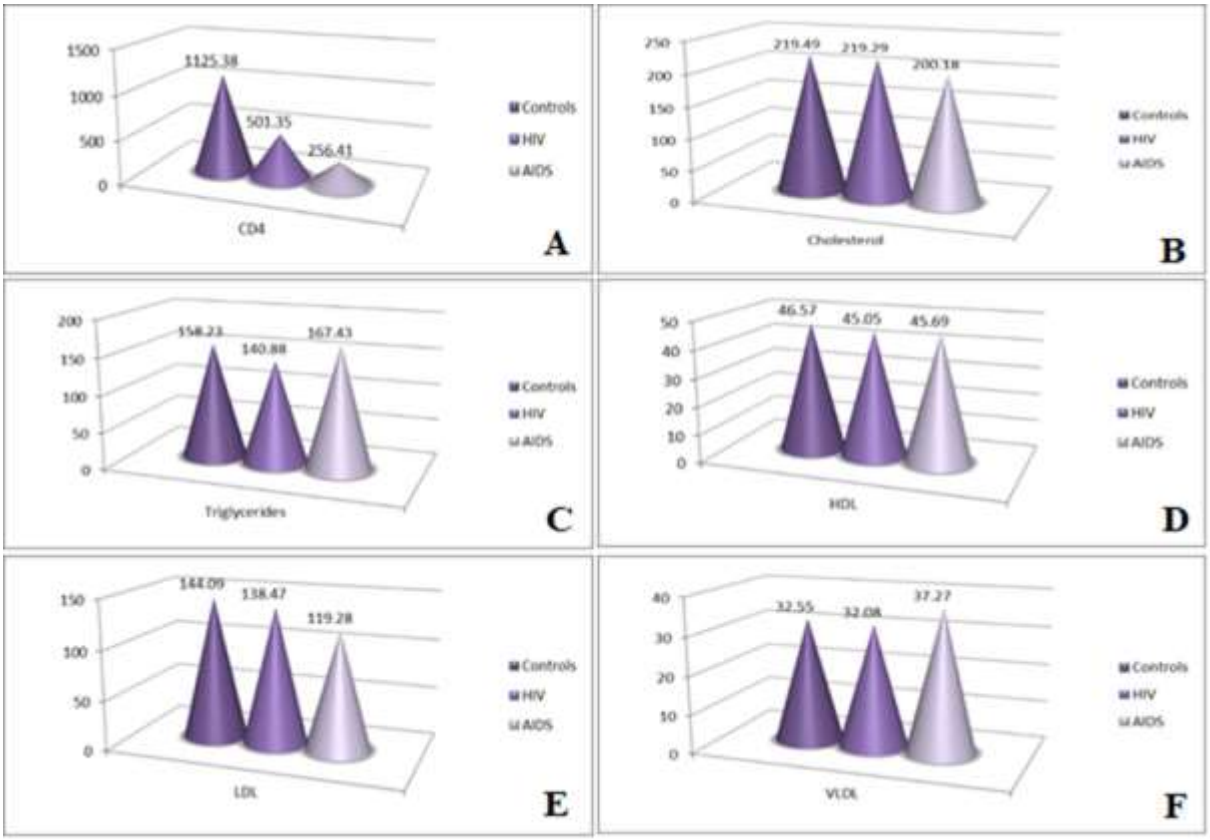
Table 3. Distribution of male and female patients according to age groups

Age group (years)	Control		HIV		AIDS	
	M	F	M	F	M	F
10-20	29	11	11	20	06	10
21-30	79	48	79	114	70	80
31-40	52	47	81	80	90	91
41-50	71	55	41	38	55	47
51-60	38	35	14	07	31	07
61-70	22	13	09	06	07	06

M: Male; F: Female; HIV: human immunodeficiency virus; AIDS: acquired immune deficiency syndrome



Graph 1. (A) Distribution of male and female patients in the control group. (B) Distribution of male and female patients in the human immunodeficiency virus (HIV) group. (C) Distribution of male and female patients in the acquired immune deficiency syndrome (AIDS) group.



Graph 2. (A) Comparison of mean CD4 cell counts between the groups. (B) Comparison of mean total cholesterol (TC) between the groups. (C) Comparison of mean triglycerides (TGs) between the groups. (D) Comparison of mean high-density lipoproteins (HDLs) between the groups. (E) Comparison of mean low-density lipoproteins (LDLs) between the groups. (F) Comparison of mean very-low-density lipoproteins (VLDLs) between the groups.

CD4 cell counts in HIV-infected and AIDS patients:

The mean CD4 cell counts was 1125.38± 154.73 in the controls, 501.35±140.20 in the HIV group, and 256.41±67.05 in the AIDS group. The results were statistically significant (P<0.001; Table 4 and Graph 2A).

Lipid profile, TC, TG, HDLs, LDLs, and VLDLs in HIV-infected and AIDS patients:

The mean cholesterol level was 219.49±37.46 in the controls, 219.29±43.01 in the HIV group, and 200.18±39.36 in the AIDS group. The results were statistically significant (P<0.001; Table 5 and Graph 2B). The mean TG level was 158.23±49.20 in the controls, 140.88±67.79 in the HIV group, and 167.43±75.40 in the AIDS group. The results were statistically significant (P<0.001; Table 5 and Graph 2C). The mean HDL level was 46.57±22.54 in the controls, 45.05±17.84 in the HIV group, and 45.69±14.70 in the AIDS group.

The results were not statistically significant

Table 4. Evaluation of CD4 cell counts in the control (C), HIV (H) and AIDS (A) groups

	Groups						P-value	Post-hoc test
	Control		HIV		AIDS			
	Mean	SD	Mean	SD	Mean	SD		
CD4 cell counts	1125.38	154.73	501.35	140.20	256.41	67.05	<0.001; Sig	C>H>A

HIV: human immunodeficiency virus; AIDS: acquired immune deficiency syndrome; SD: Standard Deviation

Table 5. Inter-group comparisons of lipid profile in the control (C), HIV (H) and AIDS (A) groups

Lipid Profile	Group Control		HIV		AIDS		P-value	Post-hoc test
	Mean	SD	Mean	SD	Mean	SD		
TC	219.49	37.46	219.29	43.01	200.18	39.36	<0.001	C,H>A
TG	158.23	49.20	140.88	67.79	167.43	75.40	<0.001	C>H; A>H
HDL	46.57	22.54	45.05	17.84	45.69	14.70	0.497	-
LDL	144.09	43.44	138.47	46.48	119.28	27.89	<0.001	C,H>A
VLDL	32.55	8.62	32.08	10.30	37.27	11.09	<0.001	A>C,H

HIV: human immunodeficiency virus; AIDS: acquired immune deficiency syndrome; TC: total cholesterol; TG: triglycerides; HDL: high-density lipoproteins; LDL: low-density lipoproteins; VLDL: very-low-density lipoproteins; SD: Standard Deviation

(Table 5 and Graph 2D). Mean LDL level was 144.09±43.44 in the controls, 138.47±46.48 in the HIV group, and 119.28±27.89 in the AIDS group. The results were statistically significant (P<0.001; Table 5 and Graph 2E). Mean VLDL level was 32.55±8.62 in the controls, 32.08± 10.30 in the HIV group, and 37.27±11.09 in the AIDS group. The results were statistically significant (P<0.001; Table 5 and Graph 2F).

The levels of TC and LDLs were significantly decreased while TG and VLDLs showed significant increase in AIDS patients compared to the control group and HIV-infected patients (Table 5 and Graph 2).

Oral manifestations in HIV-infected and AIDS patients:

The prevalence of angular stomatitis (Fig. 3A) was 0.8% in the controls, 1.6% in the HIV group, and 3.8% in the AIDS group. The prevalence of aphthous ulcer (Fig. 3B) was 1.0% in the controls, 5.6% in the HIV group, and 4.4% in the AIDS group. The prevalence of dry mouth was 0.2% in the controls, 2.8% in the HIV group, and 5.8% in the AIDS group. The prevalence of herpes zoster infection (Fig. 3C) was 0.6% in the AIDS group while the prevalence of herpes labialis (Fig. 3D) was 0.6% in the controls, 2.2% in the HIV group, and 3.4% in the AIDS group.

Table 6. Prevalence of oral manifestations in the three groups

Oral manifestations	Groups Control N (%)	HIV N (%)	AIDS N (%)
Nil	479 (95.8)	371 (74.2)	318 (63.6)
Angular stomatitis	04 (0.8)	08 (1.6)	19 (3.8)
Aphthous ulcer	05 (1.0)	28 (5.6)	22 (4.4)
Dry mouth	01 (0.2)	14 (2.8)	29 (5.8)
Herpes zoster	00 (0.0)	00 (0.0)	03 (0.6)
Herpes labialis	03 (0.6)	11 (2.2)	17 (3.4)
Oral candidiasis	00 (0.0)	21 (4.2)	58 (11.6)
Oral hairy leukoplakia	00 (0.0)	06 (1.2)	15 (3.0)
Other oral findings	08 (1.6)	41 (8.2)	19 (3.8)

HIV: human immunodeficiency virus, AIDS: acquired immune deficiency syndrome

The prevalence of oral candidiasis (Fig. 3E and F) was 4.2% in the HIV group and 11.6% in the AIDS group. The prevalence of oral hairy leukoplakia (Fig. 3G) was 1.2% in the HIV group and 3% in the AIDS group.

Other oral findings, including frictional keratosis, oral submucous fibrosis (OSF), oral lichen planus (OLP), oral leukoplakia, and traumatic ulcers, were cumulatively seen in 1.6% of the controls, 8.2% of the HIV-infected patients, and 3.8% of the AIDS patients (Table 6).

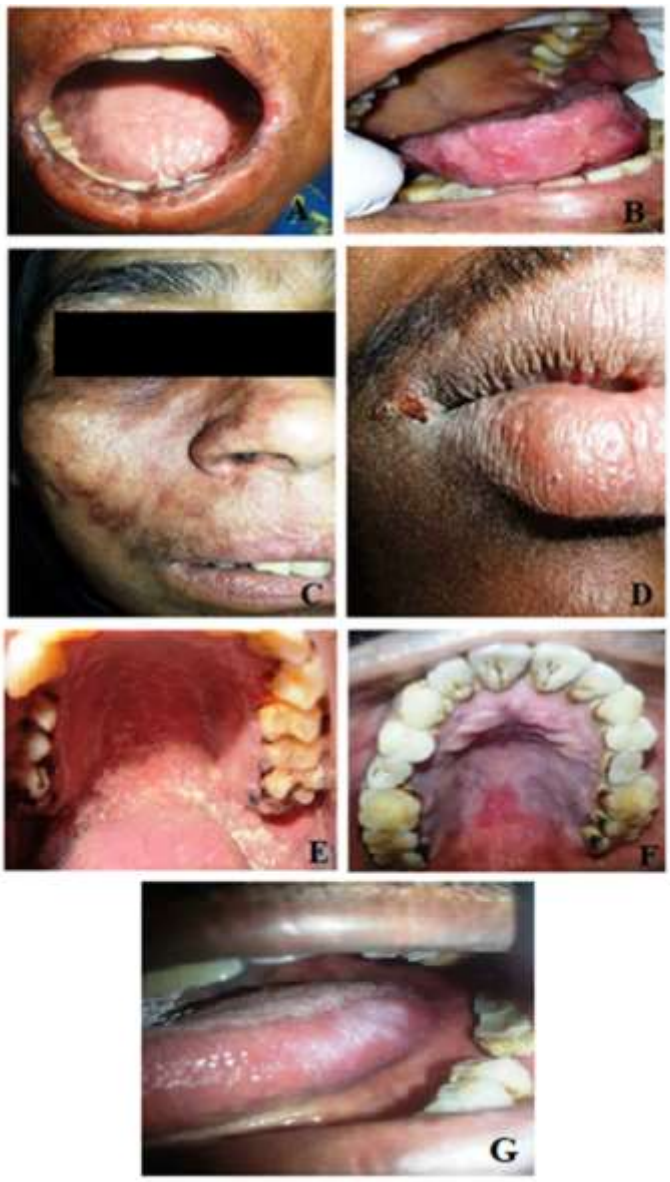


Fig. 3. (A) Angular stomatitis in an acquired immunodeficiency syndrome (AIDS) patient. (B) Aphthous ulcers in a human immunodeficiency virus (HIV)-infected patient. (C) Herpes zoster in an AIDS patient. (D) Herpes labialis in an HIV-infected patient. (E) Acute pseudo-membranous candidiasis in an AIDS patient. (F) Erythematous candidiasis in an AIDS patient. (G) Oral hairy leukoplakia in an AIDS patient.

DISCUSSION

HIV/AIDS damages the body by affecting the host's immune system [12]. The pathogenesis of HIV infection is mostly attributed to the decrease in the number of T-cells with CD4 cell surface receptors (CD4+) [12]. The immune status of an HIV patient can be assessed by measuring the absolute number (per mm3) or percentage of CD4+ cells, which is considered as the standard method to assess the severity of HIV-related immunodeficiency [12].

Progressive diminution of CD4+ T-cells is associated with the progression of HIV disease and an increased risk of opportunistic infections as well as death. The normal absolute CD4 cell counts in adolescents and adults range from 500 to 1500 cells/mm^3 of blood. CD4 counts progressively decrease as the disease advances. In children, assessing the CD4 cell counts over time is more useful. The CD4 cell counts usually increase in response to an effective combination antiretroviral therapy

(ART) although this might take many months. Opportunistic infections and other HIV-related conditions are expected with falling CD4 cell counts, especially to below 200 cells/mm^3 of blood [12]. Individuals starting ART with advanced immunodeficiency (CD4 cell counts >200-350/mm^3) gain better outcomes than those who start with more severe immunodeficiency [12]. Adults starting ART with CD4 cell counts below 50/mm^3 are at a greater risk of death. On the contrary, adults who begin ART with mild immunodeficiency do not gain any additional benefits. Pregnancy influences the CD4 cell counts although the importance of these changes is not well understood [12]. The present study was conducted to evaluate the CD4 cell counts, lipid profile, and oral manifestations in HIV-infected and AIDS patients and to correlate them with seronegative controls.

CD4 cell counts are necessary for the assessment of immune status in HIV-infected patients. The pathogenesis of AIDS is attributed to a decrease in CD4 cell counts [13]. Different methods have been implemented in evaluating the CD4 cell counts by different authors. Chanarat et al [14] used the Coulter manual CD4 kit for evaluating the CD4 cell counts. Ghate et al [15] estimated the CD4 cell counts using a formula. Pasupathi et al [16] and Srirangaraj and Venkatesha [17] estimated the CD4 cell counts using the Fluorescence-Activated Cell Sorter (FACS) count system. Sharma et al [11] estimated the CD4 cell counts using flow cytometry. Angelo et al [18] estimated the CD4 cell counts using an automated flow cytometry software. Tiwari et al [19] estimated the CD4 cell counts using the absolute flow cytometry system. Mbanya et al [20] estimated the CD4 cell counts by conventional flow cytometry using the BD FACSCount system. Sen et al [21] estimated the CD4 cell counts using the FACS Counter. Edathodu et al [22] estimated the CD4 cell counts by standard flow cytometry using the BD FACSCalibur. Pranitha and Kulkarni [13] estimated the CD4 cell counts using the BD FACSCalibur flow cytometer. In the present study, the Partec CyFlow counter was used to estimate the CD4 cell counts because it is relatively small and easy to use. In the present study, the mean CD4 cell counts was 1125.38±154.73 in the controls, 501.35±140.20 in the HIV group, and 256.41±67.05 in the AIDS group. The results were statistically significant. The gradual decrease in the CD4 cell counts observed in HIV-infected and AIDS patients in the present study was still higher than the mean values observed in studies by Pasupathi et al [16,23], recording a mean CD4 cell count of 394 and 375 in HIV-infected and 191 and 150 in AIDS patients. Our results were in accordance with the results obtained in research conducted by Tiwari et al [19], reporting a mean value of 281 cells/mm^3, and Sharma et al [24] that observed a mean CD4 cell count of 622.4 in HIV-infected and 245.39 in AIDS patients against 798.81 in the control group. The values obtained in the present study were slightly higher than the values obtained in the study conducted by Sharma et al [24]. They divided the patients based on their CD4 cell counts into three groups and obtained a mean of 163.43 in group 1, 325 in group 2, and 502.33 in group 3 [24]. The reason for the higher values obtained in the present study might be the difference in the classification of the patients into HIV-infected and AIDS patients based on the CD4 cell counts. In the present study, HIV-infected and AIDS patients were categorized based on their CD4 cell counts with 10-350 and 350-500 cells/mm^3 of blood. Tiwari et al [19] stated that the CD4 cell counts decreases because of cell membrane disruption; they proposed apoptosis as an additional mechanism for CD4 cell loss in HIV infection.

The present study showed that the lipid profile was altered in HIV-infected and AIDS patients. Alteration in the lipid profile occurred even during the early stages of HIV infection. Different methods have been implemented in evaluating the lipid profile by various authors. Khiangte et al [1] estimated the lipid profile using the enzymatic methods and observed a decrease in HDL and LDL fractions and an increase in VLDL and serum TG with the progressing disease. Nery et al [25] estimated the lipid profile by measuring the TC, HDLC, and TG using an automated

enzymatic method. LDLC was calculated using Friedwald's equation [25]. Pasupathi et al [16] estimated the lipid profile by measuring the serum TC, TG, HDL, and LDL by a fully automated clinical chemistry analyzer. VLDLC was calculated by Friedewald's equation. They observed a significant decrease in TC, HDL, and LDL and a significant increase in TG and VLDL in the AIDS patients compared to the HIV-infected patients and the controls [16]. Anastos et al [26] estimated the lipid profile by measuring the serum TC, TG, HDL, and LDL using an automated clinical chemistry auto-analyzer. Adewole et al [27] estimated the lipid profile by measuring TC using the ferric perchlorate method while HDL was determined after precipitation of the LDL fraction with the phosphotungstate-magnesium precipitation method. VLDLC was calculated according to Friedwalds's equation. TGs were measured using the colorimetric enzymatic method. They observed a significant increase in the mean LDL and TG levels with a significant decrease in the mean HDL and TC levels in the HIV-infected patients compared to the controls [27]. In the present study, the Erba EM 360 automated analyzer was used for the evaluation of the lipid profile because it is more reliable, accurate, and less time consuming than the conventional methods.

The results of the present study showed that the levels of TC and LDL were significantly decreased while the levels of TG and VLDL were significantly increased in the HIV-infected and AIDS patients compared to the controls although the results were not statistically significant for HDL in the three groups. Hypertriglyceridemia and a decrease in TC and HDLC in advanced phases of HIV infection are considered as markers of a chronic inflammatory process as proposed by Grunfeld [28] and Shor-Posner et al [29]. However, highly active antiretroviral therapy (HAART) leads to lipid changes with increases in both TG and TC [30,31]. Other factors that might contribute to dyslipidemia in HIV infection are transformed cytokine profile, decreased lipid clearance, and increased hepatic synthesis of VLDLs. Cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), appear to promote lipid peroxidation besides endothelial and platelet cell activation and the production of reactive oxygen species (ROS) [31]. An increase in serum TG levels is observed in HIV-infected patients as the disease progresses, particularly in the presence of opportunistic infections due to an increase in the levels of inflammatory cytokines [TNF-α, ILs, and interferon-alpha (IFN-α)] and steroid hormones [31]. The CD4+ lymphocyte levels in peripheral blood have an inverse correlation with TG levels and a direct correlation with TC and LDLC levels. On the contrary, HIV-infected patients show lower levels of LDLC, irrespective of the CD4+ T lymphocyte counts [31].

Different antiretroviral drugs might be associated with abnormalities in the lipid profile. Various studies have shown an association between the use of protease inhibitors (PIs) and dyslipidemia. The prevalence and the degree of lipid abnormalities might vary between different drugs within a single class and possibly with the duration of treatment [32]. Young et al [33] reported increased HDLC levels and decreased TG levels after exposure to non-nuclear reverse transcriptase inhibitors (NNRTIs)-based therapy. However, TG levels increase with exposure to PI-based therapy. This might be one of the possible reasons for the patients in the present study to have increased TG levels as they were on PIs.

Different studies on lipid profiles in different countries show variations in their results. A study by Crook [34] showed that HIV infection is normally associated with hypo-cholesterolemia, hypertriglyceridemia, and low plasma HDLC levels. Another study by Pynka et al [35] showed that there was no significant difference in TC and LDL levels between HIV-infected and healthy controls. The results of the present study were in accordance with the results reported by Iffen et al [36]. They reported an increase in TG and VLDLC in HIV-infected patients compared to the controls. The probable reason given by Iffen et al [36] for the increase in TG and VLDLC levels was that increased TNF and other cytokines increase lipolysis and insulin

resistance. Insulin regulates the uptake of glucose into the skeletal muscle tissue and other cells in the body. As insulin sensitivity decreases with a reduction in CD4 cell counts, uptake of glucose is reduced, which leads to increased free FAs in the circulation and reduced storage of TG in the adipose tissues [36]. These free FAs return into the circulation as TGs. Therefore, very high TG levels are seen in HIV seropositive cases compared to seronegative controls. VLDLs are composed predominantly of TG; this is the reason for VLDL elevation when the levels of TG are increased.

According to El-Sadr et al [37], CD4 cell counts below 200/mm^3 of blood were associated with an elevation in VLDLC and TG levels. This observation agreed with the findings of the present study. VLDLC carries fats around the body; elevation of this cholesterol can increase the risk of heart disease. Grunfeld [28] observed decreased TC levels in both HIV-infected and AIDS patients. The results of the present study were in accordance with the results of the study conducted by Pasupathi et al [16]. They observed a decrease in serum levels of TC and LDLC and an increase in TG and VLDLC levels in HIV-infected and AIDS patients compared to the controls. This is against the results obtained in the study conducted by Akpa et al [38], which reported increased mean TC and LDL but decreased TG and HDL levels. Adewole et al [27] observed increased TC, TG, and HDL levels in HIV positive patients compared to HIV negative patients. The probable reason for this lack of association might be the similarity in CD4 cell counts as most patients were in the CD4 cell count range of 50-220 cells/mm^3 of blood.

Rogowska-Szadkowska and Borzuchowska [39] and Ducobu and Payen [40] determined the levels of plasma TG, TC, and HDLC in HIV-infected patients by the level of immunological deficiency according to the CD4 cell counts. They concluded that with an increase in the immunological deficiency and clinical development of HIV infection, lipid profile disorders were indicated by an increase in TG levels and decreased concentrations of HDLC. Ducobu and Payen [40] and Crook and Mir [41] reported that patients with AIDS had increased levels of LDLC, which contraindicated the results obtained in the present study. Shor-Posner et al [29] reported similar findings, indicating significantly low levels of TC, HDL, and LDL in HIV-infected patients.

Oral lesions play an important role in the early diagnosis and management of HIV-infected and AIDS patients. Oral lesions have been associated with increased risk of progression of HIV disease. They are predictive markers for immune weakening [42-44]. In the present study, a high prevalence of oral candidiasis was observed followed by dry mouth, aphthous ulceration, angular stomatitis, herpes labialis, oral hairy leukoplakia, herpes zoster, in addition to other oral findings, including frictional keratosis, OSF, OLP, oral leukoplakia, and traumatic ulcers, which were cumulatively seen in 1.6% of the controls, 8.2% of the HIV-infected patients, and 3.8% of the AIDS patients.

Oral candidiasis was the most common manifestation and was seen in 4.2% of the HIV-infected patients and 11.6% of the AIDS patients, in accordance with the findings reported by Jain et al [6]. They observed oral candidiasis in 14% of the HIV-infected patients [6]. Rao et al [45] noted oral candidiasis in 16.4% of the HIV-infected patients. The percentage of patients with oral candidiasis was less than that observed in the study by Shobhana et al [46]. The lower incidence of oral candidiasis in the present study might be explained by the fact that the relative number of patients with CD4 cell counts below 200/mm^3 might be less than that in other studies. The salivary immunoglobulin A (IgA) affects the adherence of candida to buccal epithelial cells in AIDS patients while the levels of candida-specific IgAs increase in the saliva of healthy patients with oral candidiasis [46,47]. Kolokotronis et al [48] observed that oral candidiasis and oral hairy leukoplakia in correlation with low circulating CD4 cell counts and the lack of anti-p24 antibodies and secretory anti-p24 antibodies might serve as prognostic markers for the progression of HIV infection to AIDS.

Agbelusi and Wright [32] found that 43% of the patients had oral candidiasis, which is much higher than that reported in the present study. The majority of oral candidiasis patients had CD4 cell counts below 200/mm^3 in the present study. Similar results were found in the study conducted by Ranganathan et al [49].

Kerdpon et al [50] observed a strong association between oral candidiasis and CD4 cell counts below 200/mm^3. The lower incidence of oral candidiasis observed in the present study might be explained by the fact that the relative number of patients with CD4 cell counts below 250/mm^3 was less than that seen in other studies. The average levels of TC, TG, LDL, and VLDL in AIDS patients having oral candidiasis were 212.5, 182.3, 139.8, and 38.1, respectively, while in the HIV-infected patients, the values were found to be 222.5, 131, 144.6, and 34.6, respectively. The fungi-like candidiasis contains several compounds with the most abundant being lovastatin, which acts as an HMG-CoA reductase inhibitor. Researchers have reported that naturally occurring unsaturated FAs appear to promote lower TG levels in these patients [51].

Dry mouth was observed in 5.8% of the AIDS patients and 2.8% of the HIV-infected patients. The relative percentages were found to be low when compared to the study conducted by Sow et al [10]. They observed a 14.3% prevalence of dry mouth in the HIV-infected and AIDs patients [10]. The possible reason for dry mouth in HIV-infected and AIDS patients might be the decreased immune levels and the adverse effect of the ART drugs. The average levels of TC, TG, LDL, and VLDL in AIDS patients with dry mouth were 203.3, 246.9, 118.4, and 41.3, respectively, and 237.21, 161.9, 163.9, and 36.7 in the HIV-infected patients, respectively. Increased TG and decreased LDL levels were observed in AIDS patients with dry mouth. The probable reason for this might be the long-term and highly potent ART drugs used in AIDS patients along with an increased rate of declination in immune levels when compared to the HIV-infected patients.

Oral hairy leukoplakia was seen in 3% of the AIDS patients and 1.2% of the HIV-infected patients in the present study, in accordance with the results reported by Agbelusi and Wright [32]. This prevalence was higher than that found in the study by Rao et al [45] and lower than that observed in studies conducted by Sharma et al [24] (17.5%), Lourenço and Figueiredo [52] (11.8%), and Pedreira et al [53] (9%). The average levels of TC, TG, LDL, and VLDL in AIDS patients with oral hairy leukoplakia were 216.7, 180.5, 129, and 36.1, respectively, and 220.6, 175.1, 151.3, and 36.6, respectively, in the HIV-infected patients. In the present study, no significant variations in the lipid profile were observed in HIV-infected patients with oral hairy leukoplakia compared to AIDS patients; this might be attributed to the increased percentage of younger individuals in both HIV and AIDS groups in the present study.

Herpes labialis was observed in 3.4% of the AIDS patients and 2.2% of the HIV-infected patients in the present study, which was higher than the results found in the study by Jain et al [6]. The average levels of TC, TG, LDL, and VLDL in AIDS patients with herpes labialis were 241.8, 156, 147.5, and 39.5, respectively, and 204.8, 178, 140.5, and 35.6, respectively, in the HIV-infected patients.

In the present study, aphthous ulcerations were observed in 4.4% of the AIDS patients and 5.6% of the HIV-infected patients. The observation in the present study was slightly higher than that of Glick et al [44] and Rao et al [45]. The average levels of TC, TG, LDL, and VLDL in AIDS patients having aphthous ulcers were 213.6, 193.3, 149.3, and 29.6, respectively, and 209.7, 171.1, 147.2, and 28.1, respectively, in the HIV-infected patients.

Other significant oral findings, including frictional keratosis, OSF, OLP, oral leukoplakia, and traumatic ulcers, were cumulatively seen in 8.2% of the HIV patients and 3.8% of the AIDS patients, which was higher than the findings reported by Rao et al [45]. No oral warts were observed in the present study, similar to the findings of other studies conducted in Asia. The probable enhanced anti-viral effect of the ART drugs on human papillomavirus (HPV)-related lesions could be the reason for the absence of warts in Asian countries [6]. No case of Kaposi's sarcoma was

noted in the present study, in accordance with the results of previous studies [6]. The present study supports the fact that skin is the most common organ affected in HIV-infected patients, and mucocutaneous manifestations are important clinical prognostic markers [6]. Furthermore, NUP was not reported in any of the cases in the present study. NUP is significantly more common among homosexuals. One of the reasons for the absence of NUP in the present study might be the very low prevalence of homosexuality in the present region [11].

CONCLUSION

CD4 cell counts, TC, LDLs, TGs, and VLDLs were significantly changed in HIV-infected and AIDS patients compared to the controls. Further studies are required to achieve valid conclusions and to use the common oral manifestations as diagnostic and prognostic indicators to manage HIV-infected and AIDS patients.

CONFLICT OF INTEREST STATEMENT

None declared.

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