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ORIGINAL PAPER

IMPACT OF DISEASE STAGE AND ORAL HYGIENE ON ORAL MANIFESTATIONS IN NEWLY DIAGNOSED HIV/AIDS PATIENTS: AN ALBANIAN PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Introduction. Oral manifestations are among the most common clinical complications of HIV infection and are closely associated with immune decline. While disease stage is a known factor, the independent effect of oral hygiene practices has not been thoroughly studied.

The objective of the study was to assess the impact of HIV disease stage and oral hygiene practices on the occurrence of oral pathologies in newly diagnosed, antiretroviral treatment (ART)-naïve HIV-infected patients.

Material and methods. This prospective observational study included 160 newly diagnosed HIV-infected patients. The patients were categorized into HIV infection without acquired immunodeficiency syndrome (AIDS) (stages 1–3) (87 patients) and AIDS stage (73 patients). Standardized oral examinations assessed mucosal lesions, dental, and periodontal status (decayed, filled, and missing teeth index (DMFT), community

Résumé

Impact du stade de la maladie et de l'hygiène bucco-dentaire sur les manifestations orales chez les patients nouvellement diagnostiqués avec le VIH/SIDA: une étude observationnelle prospective albanaise.

Introduction. Les manifestations orales figurent parmi les complications cliniques les plus fréquentes de l'infection par le VIH et sont étroitement associées au déclin immunitaire. Bien que le stade de la maladie soit un facteur reconnu, l'effet indépendant des pratiques d'hygiène bucco-dentaire n'a pas été suffisamment étudié.

L'objectif de l'étude a été d'évaluer l'impact du stade clinique de l'infection par le VIH et des pratiques d'hygiène bucco-dentaire sur la survenue de pathologies orales chez des patients nouvellement diagnostiqués comme infectés par le VIH et n'ayant pas encore débuté un traitement antirétroviral (ART).

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periodontal index (CPI), loss of attachment (LOA)). Multivariate logistic regression identified independent predictors of oral pathology.

Results. At least one oral pathology was found in 83.6% of AIDS patients compared to 59.8% of non-AIDS patients (p=0.02). Oral candidiasis (52.1% vs 27.6%, p=0.002), periodontal disease (63.0% vs 42.5%, p=0.01), and ulcerative lesions (37.0% vs 8.1%, p=0.0001) were significantly more common in AIDS patients. In multivariate analysis, AIDS stage (adjusted OR 18.86; 95% CI 2.48–143.29; p=0.004) and brushing teeth less than once a day (adjusted OR 12.98; 95% CI 1.51–111.92; p=0.020) were independent predictors of oral pathology.

Conclusions. Advanced HIV stage and poor oral hygiene independently raise the risk of oral pathology. Incorporating oral health strategies into HIV care could lower morbidity.

Keywords: HIV/AIDS, oral pathology, periodontal disease, oral hygiene, CD4+ lymphocytes.

List of abbreviations

ART – antiretroviral treatment
AIDS – acquired immunodeficiency syndrome
HIV – human immunodeficiency virus
HAART – highly active anti-retroviral therapy
DT – decay teeth
FT – filled teeth
MT – missing teeth
DMFT – decayed, filled, and missing teeth index
CPI – community periodontal index
LOA – loss of attachment

Materiel et méthodes. Cette étude observationnelle prospective a inclus 160 patients nouvellement diagnostiqués comme infectés par le VIH. Les patients ont été classés en deux groupes: VIH sans SIDA (stades 1–3) (87 patients) et stade SIDA (73 patients). Des examens bucco-dentaires standardisés ont permis d'évaluer les lésions muqueuses ainsi que l'état dentaire et parodontal (DMFT, CPI, LOA). Une régression logistique multivariée a été réalisée afin d'identifier les prédicteurs indépendants des pathologies orales.

Résultats. Au moins une pathologie orale a été observée chez 83,6% des patients atteints du SIDA, contre 59,8% chez les patients sans SIDA (p=0,02). La candidose orale (52,1% vs 27,6%, p=0,002), la maladie parodontale (63,0% vs 42,5%, p=0,01) et les lésions ulcéreuses (37,0% vs 8,1%, p=0,0001) étaient significativement plus fréquentes chez les patients atteints du SIDA. Dans l'analyse multivariée, le stade du SIDA (OR ajusté 18,86; IC 95% 2,48–143,29; p=0,004) ainsi que le brossage des dents moins d'une fois par jour (OR ajusté 12,98; IC 95% 1,51–111,92; p=0,020) ont été identifiés comme des prédicteurs indépendants des pathologies orales.

Conclusions. Le stade avancé de l'infection par le VIH et une mauvaise hygiène bucco-dentaire augmentent indépendamment le risque de pathologie orale. L'intégration de stratégies de santé bucco-dentaire dans la prise en charge du VIH pourrait réduire la morbidité associée.

Mots-clés: VIH/SIDA, pathologie orale, maladie parodontale, hygiène bucco-dentaire, lymphocytes CD4+.

Introduction

Human immunodeficiency virus (HIV) infection remains a major global public health challenge, affecting approximately 40.8 million [37.0 million–45.6 million] people worldwide in 2024[1]. Albania registered 125 new HIV cases in 2025, and the total number of HIV cases recorded in the country from 1993 to October 2025 has reached 1973[2]. Despite significant advances in antiretroviral therapy (ART), HIV-related complications still significantly contribute to morbidity, especially in patients with advanced immunosuppression.

The oral cavity is one of the earliest and most affected sites in HIV infection. Oral symptoms can indicate immune decline and disease progression. Historically, oral candidiasis, hairy leukoplakia, Kaposi sarcoma, periodontal disease, and ulcerative lesions have been closely associated with declining CD4 counts and advanced clinical stages[3-5].

Disease stage, as classified by clinical and immunological criteria, remains one of the most reliable predictors of oral pathology. Progressive depletion of CD4+ T-cells weakens mucosal immunity, allows opportunistic infections like *Candida albicans*, and leads to destruction of periodontal tissue[6-8].

While immunosuppression plays a key biological role, behavioral and environmental factors can also affect the burden of oral disease[9]. Oral hygiene habits, especially how often people brush their teeth and control plaque, are increasingly recognized as modifiable factors influencing periodontal inflammation and mucosal susceptibility[10]. Poor oral hygiene may worsen microbial imbalance and boost inflammatory responses in immunocompromised individuals, thus increasing their risk of oral pathology[11,12].

Despite increasing evidence linking immune status to oral disease, fewer studies have simultaneously examined the combined effect of clinical stage and oral hygiene behaviors on the presence and

severity of oral pathologies in HIV-infected populations. Understanding this relationship is clinically important, as oral hygiene is a potentially modifiable factor within comprehensive HIV care.

The objective of the study was to assess the impact of disease stage and oral hygiene practices on the presence and severity of oral pathologies among HIV-infected patients, and to compare these findings with international data.

Materials and methods

Study Design and Setting

This prospective observational study was carried out at the University Dental Clinic in collaboration with the Infectious Diseases Service at the University Hospital Center "Mother Teresa" in Tirana, Albania. The study period spanned from February 2024 to June 2025. It was conducted in accordance with the Declaration of Helsinki and received approval from the Ethics Committee of Tirana University of Medicine (approval number: 11, dated March 18, 2024). Informed consent was obtained from each patient who underwent a dental examination.

Study Population

A total of 160 patients diagnosed with HIV infection at the Infectious Diseases Service of the University Hospital Center "Mother Teresa" were included in the study. All patients underwent an oral examination at the University Dental Clinic to evaluate oral pathologies.

Inclusion Criteria

All consecutive patients who presented to the Infectious Diseases Service and met the following criteria were included:

1. First-time diagnosis of HIV infection confirmed by standard serological testing protocols.
2. No prior use of ART.
3. Age 18 years or older.
4. Provided written informed consent.

Exclusion Criteria

1. Previous ART.
2. Other immunosuppressive conditions (e.g., chemotherapy, organ transplantation).
3. Pregnancy.
4. Incomplete clinical or laboratory data.
5. Declined participation.

Clinical Group Classification

HIV infection was classified according to the World Health Organization (WHO) clinical staging system[13]. The patients were categorized into:

- HIV without AIDS (WHO stages 1–3): Patients in the acute and chronic phases of infection without AIDS-defining conditions.
- AIDS group (WHO stage 4): Patients presenting with AIDS-defining clinical conditions.

Patients with CD4 <200 cells/mm^3 or WHO stage 4 conditions were classified as having AIDS, in line with CDC criteria. The CD4/CD8 ratio was also recorded as an additional marker of immune dysfunction.

Oral Examination Protocol

All participants underwent a standardized oral exam at the University Dental Clinic, conducted by calibrated dental professionals. The exam included assessment of all oral manifestations diagnosed based on established clinical criteria described by the EC Clearinghouse on Oral Problems Related to HIV infection[14]. The number of oral pathologies per patient was recorded. The following indices were documented: Decayed, Missing, Filled Teeth index (DMFT), Community Periodontal Index (CPI), and Loss of Attachment (LOA). The methodology for measuring these indices has been previously described in an earlier publication[15].

Oral Hygiene Assessment

Oral hygiene behavior was assessed through a structured patient interview. Tooth-brushing frequency was categorized as less than once per day, once per day, or more than once per day. Poor oral hygiene was defined as brushing less than once daily.

Laboratory Evaluation

Blood samples were collected before ART initiation. Parameters recorded included CD4+ T-cell count, CD4/CD8 ratio, complete blood count, and other relevant biochemical markers.

Statistical Analysis

Data was analyzed using SPSS Version 21.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean±standard deviation and compared with Student's t-test. Categorical variables were expressed as frequencies and percentages and analyzed using Chi-square or Fisher's exact test, as appropriate.

Multivariable logistic regression analysis was performed to identify independent predictors of oral pathology. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. Point–Biserial correlation (r) was performed to assess the association between CD4+ cell count and oral pathology. A p-value < 0.05 was considered statistically significant.

Table 1. Baseline characteristics of HIV (non-AIDS) and AIDS patients

Variable	*HIV (No AIDS) (n=87) n, (%)*	*AIDS (n=73) n, (%)*	*p-value**
Age, mean (SD)	38.56 (14.19)	42.25 (12.87)	0.09
Male sex, n (%)	62 (71.3%)	53 (72.6%)	0.74
Smoking	36 (41.4%)	32 (43.8%)	0.82
Cardiovascular disease	1 (1.1%)	0 (0.0%)	0.36
Type 2 diabetes	0 (0.0%)	1 (1.4%)	0.27
Neoplastic disease	1 (1.1%)	1 (1.4%)	0.90
Hypertension	14 (16.1%)	13 (17.8%)	0.97
Pulmonary disease	13 (14.9%)	12 (16.4%)	0.98
Hepatic insufficiency	1 (1.1%)	1 (1.4%)	0.90
Anemia	6 (6.9%)	8 (11.0%)	0.37
Renal insufficiency	0 (0.0%)	2 (2.7%)	0.12
Weight loss	30 (34.5%)	34 (46.6%)	0.15
Diarrhea	14 (16.1%)	22 (30.1%)	0.04
Seborrheic dermatitis	18 (20.7%)	39 (53.4%)	0.0003
Drug use (transmission)	3 (3.5%)	2 (2.7%)	0.80
Blood transfusion	2 (2.3%)	3 (4.1%)	0.66
Heterosexual transmission	62 (71.3%)	48 (65.8%)	0.45
Homosexual transmission	10 (11.5%)	11 (15.1%)	0.50
Bisexual transmission	1 (1.1%)	0 (0.0%)	0.36
Occupational exposure	0	0	NA
Unknown transmission	9 (10.3%)	9 (12.3%)	0.69
Tooth brushing <1/day	42 (48.3%)	47 (64.4%)	0.04
Tooth brushing once/day	37 (42.5%)	21 (28.8%)	0.07
Tooth brushing >1/day	8 (9.2%)	5 (6.9%)	0.59
CD4 count (cells/mm^3), mean (SD)	411.99 (179.81)	189.04 (171.19)	0.0001
CD4/CD8 ratio, mean (SD)	21.88 (9.56)	11.67 (8.63)	0.0001

** To determine statistical significance for the comparison regarding each characteristic, variables were summarized using mean ± SD for continuous variables, compared using t-tests, and frequency and percentage for categorical variables, compared using chi-squared tests. Legend; AIDS – acquired immunodeficiency syndrome, HIV – human immunodeficiency virus; SD – standard deviation*

Results

Baseline Characteristics

Baseline characteristics of HIV (non-AIDS) and AIDS patients are shown in Table 1. A total of 160 patients were included: 87 with HIV infection without AIDS and 73 with AIDS. There were no statistically significant differences in the mean age between the groups (38.6±14.2 vs. 42.3±12.9 years, p=0.09), nor in sex distribution (male 71.3% vs. 72.6%, p=0.74), demonstrating demographic comparability.

Most comorbidities did not differ significantly between groups, including cardiovascular disease, diabetes, hypertension, pulmonary disease, hepatic insufficiency, anemia, and renal insufficiency (all p>0.05). However, diarrhea was significantly more common in the AIDS group (30.1% vs 16.1%, p=0.04), and seborrheic dermatitis was markedly higher in AIDS patients (53.4% vs 20.7%, p=0.0003).

No statistically significant differences were observed across transmission routes (heterosexual, homosexual, drug-related, transfusion-related), indicating that disease progression is not linked to the mode of transmission in this cohort.

A poor oral hygiene (<1 tooth brushing/day) was significantly more common among AIDS patients (64.4% vs 48.3%, p=0.04). Brushing once daily showed a trend toward lower frequency in AIDS patients (28.8% vs 42.5%, p=0.07), while brushing more than once per day did not differ significantly.

AIDS patients exhibited significantly lower CD4 counts (189.0±171.2 vs 412.0±179.8 cells/mm^3; p=0.0001) and lower CD4/CD8 ratios (11.67±8.63 vs 21.88±9.56; p=0.0001). These findings confirm the expected immunological decline associated with AIDS classification.

Prevalence of Oral Manifestations

The prevalences of oral manifestations are presented in Table 2. Oral candidiasis was significantly more common among AIDS patients (52.1%) compared to non-AIDS HIV patients (27.6%)

Table 2. Oral manifestations and dental parameters in HIV infected (non-AIDS) and AIDS patients

Variable	*HIV (no AIDS), n=87*	*AIDS, n=73*	*p-value**
Oral Diseases			
Oral candidiasis	24 (27.6%)	38 (52.1%)	0.002
Hairy leukoplakia	4 (4.6%)	6 (8.2%)	0.35
Kaposi sarcoma	0 (0.0%)	1 (1.4%)	0.27
Non-Hodgkin lymphoma	3 (3.5%)	4 (5.5%)	0.51
Periodontal disease	37 (42.5%)	46 (63.0%)	0.01
Ulceration (NOS)	7 (8.1%)	27 (37.0%)	0.0001
Xerostomia	23 (26.4%)	28 (38.4%)	0.11
Oral mucosal pigmentation	28 (32.2%)	34 (46.6%)	0.06
Parotitis	0 (0.0%)	1 (1.4%)	0.27
≥1 Oral disease (per patient)	52 (59.8%)	61 (83.6%)	0.02
Mean number of oral lesions per patient (SD)	1.46 (1.49)	2.53 (1.83)	0.0001
Dental Indices			
Decayed teeth (DT), mean (SD)	1.61 (3.09)	2.42 (3.22)	0.44
Filled teeth (FT), mean (SD)	2.72 (3.79)	5.53 (5.52)	0.08
Missing teeth (MT), mean (SD)	2.06 (2.90)	3.37 (3.71)	0.24
DMFT index, mean (SD)	0.27 (0.31)	0.51 (0.34)	0.03
Community Periodontal Index (CPI), mean (SD)	2.17 (1.10)	2.95 (0.97)	0.03
Loss of Attachment (LOA), mean (SD)	2.11 (1.02)	3.00 (1.00)	0.01

* To determine the statistical significance of each characteristic comparison, variables were summarized using mean ± SD for continuous variables and analyzed with t-tests, while frequencies and percentages for categorical variables were analyzed with chi-squared tests.
Legend: AIDS – acquired immunodeficiency syndrome, HIV – human immunodeficiency virus, DT – decayed teeth, FT – filled teeth, MT – missing teeth, DMFT – decayed, filled, and missing teeth index, CPI – community periodontal index, LOA – loss of attachment SD – standard deviation.

Table 3. Oral pathology presence: univariate logistic regression

Variable	*Crude OR*	*95% CI*	*p-value*
HIV clinical stage 1	0.15	0.06 – 0.40	0.0002
HIV clinical stage 2-3	1.00	0.49 – 2.02	0.989
AIDS stage	3.81	1.76 – 8.28	0.0007
Tooth brushing <1/day	10.76	1.41 – 82.39	0.022
Tooth brushing once/day	0.66	0.15 – 2.87	0.577
Tooth brushing >1/day	1.22	0.24 – 6.29	0.810

Legend: Crude OR (Odds Ratio) represents the unadjusted association between each independent variable and the outcome. An OR >1 indicates increased odds of the outcome, whereas an OR <1 indicates a protective association. The 95% Confidence Interval (CI) reflects the precision of the estimate; associations are considered statistically significant when the CI does not include 1. A p-value <0.05 was considered statistically significant.

(p=0.002). Likewise, periodontal disease occurred more frequently in the AIDS group (63.0% vs 42.5%, p=0.01). Ulcerative lesions (NOS) showed a notably higher prevalence in AIDS patients (37.0% vs 8.1%, p=0.0001). No statistically significant differences were found for hairy leukoplakia, Kaposi sarcoma, non-Hodgkin lymphoma, xerostomia, or parotitis. Overall, 83.6% of AIDS patients exhibited at least one oral manifestation compared to 59.8% in the non-AIDS group (p=0.02). The average number of oral lesions per patient was significantly higher in AIDS patients (2.53±1.83) than in HIV patients without AIDS (1.46±1.49; p=0.0001).

Dental and Periodontal Parameters

The data on dental and periodontal parameters are shown in Table 2. The DMFT index was significantly higher in AIDS patients (0.51±0.34 vs. 0.27±0.31; p=0.03). Although decayed, filled, and missing teeth individually did not reach statistical significance, the overall DMFT index indicates a greater cumulative dental burden in advanced disease. Periodontal parameters were also significantly worse

Table 4. Oral pathology presence multivariate logistic regression (adjusted OR)

Variable	*Adjusted OR*	*95% CI*	*p-value*
Sex	0.70	0.26 – 1.89	0.479
Age	1.02	0.99 – 1.05	0.259
Cardiovascular disease	3.66	0.01 – 2916.93	0.704
Diabetes mellitus	1.00	–	–
Malignancy	23.04	0.02 – 22329.00	0.371
Hypertension	0.07	0.00007 – 66.95	0.443
Pulmonary disease	2.18	0.59 – 7.98	0.241
Anemia	5.97	0.62 – 57.94	0.123
Substance use (history)	0.46	0.0006 – 366.70	0.819
Renal insufficiency	2.10	0.003 – 1600.33	0.827
HIV clinical stage 1	1.39	0.17 – 11.42	0.759
HIV clinical stage 2-3	8.62	1.19 – 62.42	0.033
AIDS clinical Stage	18.86	2.48 – 143.29	0.004
Drug exposure	8.58	0.007 – 11116.79	0.557
Blood transfusion	0.81	0.04 – 14.91	0.886
Heterosexual transmission	1.01	0.38 – 2.69	0.988
Homosexual transmission	3.22	0.48 – 21.77	0.230
Bisexual transmission	77.21	0.08 – 74100.91	0.215
Tooth brushing <1/day	12.98	1.51 – 111.92	0.020
Tooth brushing once/day	1.00	0.16 – 6.37	0.996
Tooth brushing >1/day	4.23	0.59 – 30.39	0.152

Legend: Adjusted OR (Odds Ratio) represents the association between each independent variable and the outcome after adjustment for all other variables included in the multivariate logistic regression model. An OR >1 indicates increased odds of the outcome, whereas an OR <1 indicates a protective effect. The 95% Confidence Interval (CI) reflects the precision of the estimate; associations are considered statistically significant when the CI does not include 1. A p-value <0.05 was considered statistically significant.

in AIDS patients, with CPI: 2.95 vs. 2.17 (p=0.03) and LOA: 3.00 vs. 2.11 (p=0.01).

Univariate analysis for the presence of at least one oral pathology

In univariate logistic regression analysis, HIV clinical stage and poor oral hygiene were identified as significant predictors of oral pathology. Patients classified as AIDS Stage had significantly higher odds of oral disease compared to the reference category (OR 3.81; 95% CI 1.76–8.28; p=0.0007). Conversely, HIV clinical stage 1 was strongly protective (OR 0.15; 95% CI 0.06–0.40; p=0.0002), indicating a substantially lower risk of oral manifestations in early-stage disease. Poor oral hygiene (<1 brushing/day) was associated with a more than 10-fold increase in the odds of oral pathology (OR 10.76; 95% CI 1.41–82.39; p=0.022).

No statistically significant associations were found for age, sex, systemic comorbidities, transmission route, or substance use. Anemia showed a borderline association (OR 5.79; p=0.095), suggesting a possible trend that needs further study in larger cohorts.

Multivariate logistic regression analysis for the presence of at least one oral pathology

After adjusting for demographic variables, systemic comorbidities, transmission routes, and oral hygiene practices, advanced HIV clinical stage and poor oral hygiene remained independent predictors of oral pathology (Table 4 and Figure 1).

Patients classified as having AIDS showed a significantly higher likelihood of oral pathology (OR 18.86; [2.48–143.29]; p=0.004). Similarly, HIV clinical stages 2-3 were independently linked to oral disease (OR 8.62; p=0.033). In contrast, earlier stages (stage 1) did not show independent significance (OR 1.39; p=0.759). Among behavioral factors, brushing teeth less than once per day was independently associated with oral pathology (OR 12.98; [1.51–111.92]; p=0.020). No statistically significant associations were found for other variables.

CD4+ Levels According to Oral Pathology Status

The analysis of CD4+ T-cell counts demonstrated a clear difference between patients with and without oral pathology (Figure 2). Patients without

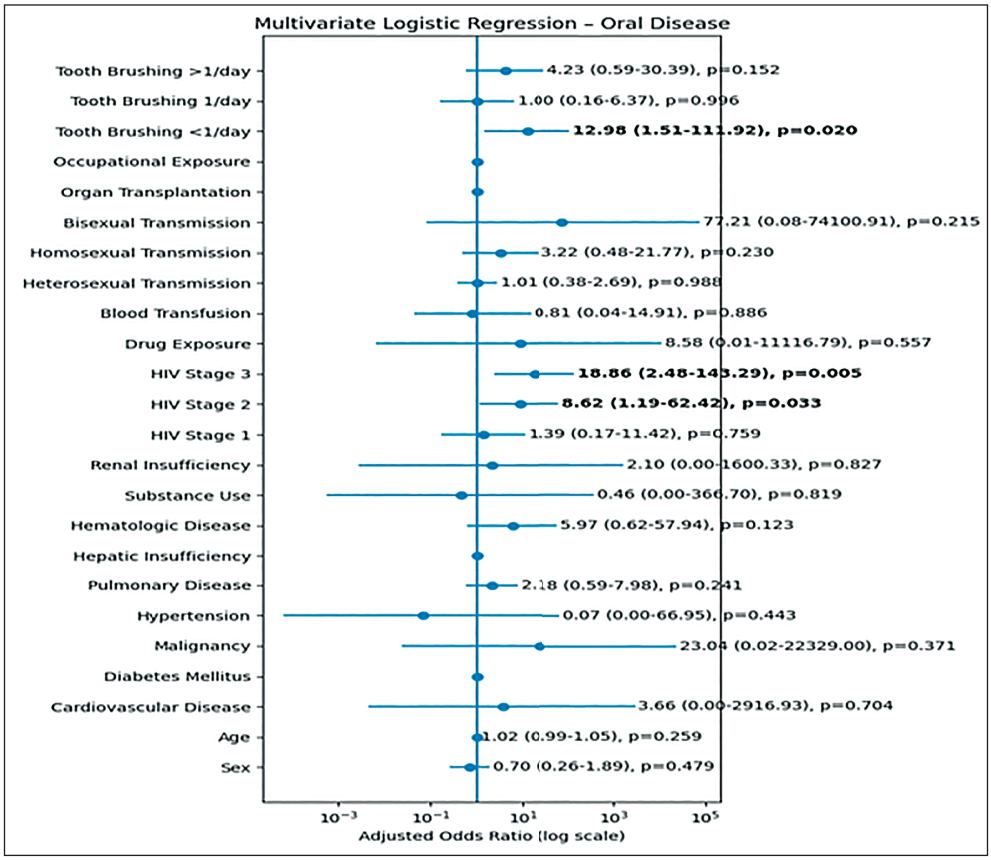


Figure 1. Multivariate logistic regression analysis of predictors of oral pathology in HIV-infected patients.
Legend: Forest plot displaying adjusted odds ratios (AOR) with 95% confidence intervals (CI) for the association between demographic factors, systemic comorbidities, HIV clinical stage, transmission routes, oral hygiene practices, and the presence of oral pathology. The vertical reference line indicates an odds ratio (OR) of 1.0 (no effect). Points represent adjusted ORs, and horizontal bars show 95% CIs on a logarithmic scale. Variables with statistically significant associations ($p < 0.05$) are highlighted in bold

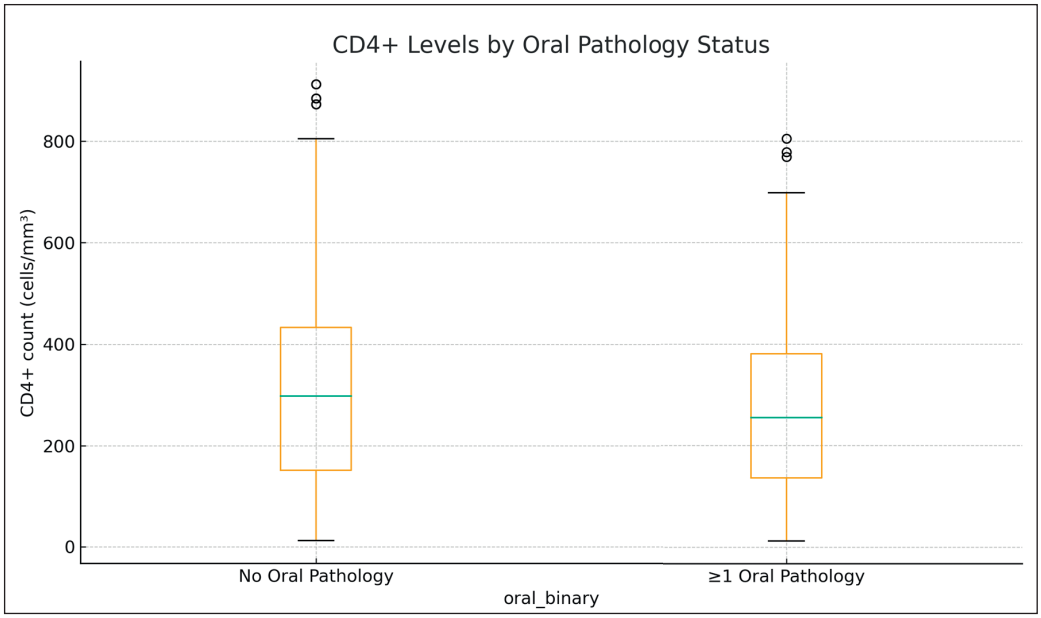


Figure 2. CD4+ T-cell levels according to oral pathology status.
Legend: Boxplot showing the distribution of CD4+ cell counts (cells/mm³) among HIV-infected patients stratified by the presence or absence of at least one oral pathology. The median CD4+ count is lower in patients with ≥1 oral lesion compared to those without oral pathology. Boxes represent the interquartile range (IQR), horizontal lines indicate medians, whiskers represent the range excluding outliers, and circles denote extreme values.

oral pathology had higher median CD4+ levels compared to those with at least one oral lesion. The distribution in the oral pathology group shifted toward lower CD4+ values, indicating greater immunosuppression. The interquartile range (IQR) was broad in both groups, indicating variation in immune status; however, the central tendency consistently remained lower in patients with oral manifestations. Although some overlap between groups was observed, the overall trend ($r = -0.110$, $p = 0.051$) indicated a clinically meaningful association between decreased CD4+ count and the presence of oral pathology. This finding suggests that while immune suppression is a major determinant, additional local or behavioral factors may also contribute to the expression of oral disease.

Discussion

This prospective observational study assessed the effect of HIV disease stage and oral hygiene practices on the presence of oral pathologies in newly diagnosed HIV-infected patients prior to starting antiretroviral therapy. We found that: 1) there was a significantly higher prevalence of at least one oral pathology, especially among patients with advanced disease (in the AIDS group compared to the non-AIDS group); 2) oral candidiasis occurred significantly more often in AIDS patients than in non-AIDS patients; 3) AIDS patients showed significantly higher DMFT index values, along with higher CPI and LOA scores, indicating worse periodontal attachment loss and increased dental burden; 4) Patients classified as AIDS stage had nearly a 19-fold higher likelihood of presenting with at least one oral lesion, while stage 2-3 patients exhibited about an 8-fold increase compared to HIV stage 1; 5) A poor oral hygiene (less than one tooth brushing per day) was independently linked to oral disease, emphasizing the impact of modifiable behavioral factors on HIV-related oral pathology; 6) The immune deterioration, as measured by CD4+ T-cell count (lower CD4+ level) was associated with the presence of oral manifestations in newly diagnosed HIV-infected patients.

Prevalence of Oral Manifestations

The overall prevalence of at least one oral pathology was high, particularly among patients with advanced disease. In the AIDS group, 83.6% of patients presented with ≥1 oral lesion, compared with 59.8% in the non-AIDS group.

These results are consistent with historical pre-ART studies reporting oral lesion prevalence exceeding 70% among untreated HIV populations[16]. With the introduction of the highly active anti-retroviral therapy (HAART), the prevalence declined in treated cohorts but remains high in untreated or late diagnosed individuals[17,18].

Similarly, Patton documented oral disease prevalence of 50–80% in advanced HIV cohorts in the United States[8], while Asian cohorts report 45–70% prevalence in untreated patients[19]. In Sub-Saharan Africa, reported prevalence ranges from 50% to 65% among patients with advanced stage disease[20].

Specific Oral Lesions

The prevalence of oral candidiasis in AIDS patients (52%) aligns with global estimates ranging between 40–70% in advanced HIV[3,5]. Patton reported rates of 50–80% in advanced U.S. cohorts and ORs of 3.5–6.0 for candidiasis in advanced disease[8]. The observed doubling of candidiasis prevalence in AIDS patients confirms the strong association between immune deterioration and opportunistic fungal infection. Mechanistically, CD4 depletion impairs Th17-mediated mucosal immunity, facilitating Candida overgrowth[21].

The 63% prevalence of periodontal disease in AIDS patients aligns with European and Latin American data reporting a 55–70% prevalence in advanced HIV[3,22]. Feller et al. noted that HIV-associated periodontal disease is strongly linked to immune suppression[15]. Studies from Brazil and Sub-Saharan Africa indicate a necrotizing periodontal disease prevalence of 40–65% among AIDS patients[20,22]. Recent microbiome studies demonstrate altered subgingival bacterial profiles in HIV patients, even after ART initiation[23].

The notable difference in ulcerative lesions (37% vs 8%) supports previous reports that ulcerative conditions increase significantly in advanced stages. European cohorts have reported ulcer prevalence between 20–35% in patients with CD4 <200 cells/mm^3[24].

The significantly higher average number of lesions (2.53 vs 1.46) reflects cumulative immune deterioration. A Brazilian cohort reported mean lesion counts of 2.1 in advanced HIV compared to 0.9 in early stages[22]. This pattern supports the concept of progressive mucosal vulnerability proportional to the severity of immune suppression.

Dental and Periodontal Indices

The higher DMFT index in AIDS patients indicates cumulative dental deterioration. Although DMFT values appear numerically low, the statistically significant difference suggests that disease progression affects the oral health burden. Studies from Brazil, and Thailand have reported mean DMFT values between 0.4 and 1.2 in advanced HIV populations[22,25].

CPI and LOA differences point to more severe periodontal attachment loss in advanced disease.

Similar findings were observed in Asian cohorts, where LOA scores were significantly higher in AIDS patients (mean 2.8 vs 1.9; $p<0.05$)[26]. Also, we have previously documented that DMFT, CPI, and LOA in HIV/AIDS patients are higher than in non-HIV patients[15]. These findings suggest that advanced HIV not only increases opportunistic oral lesions but also worsens periodontal tissue destruction.

Advanced HIV Stage and Oral Pathology

The strongest independent predictor identified in the multivariate model was AIDS stage (OR 18.86; 95% CI 2.48–143.29; p=0.004). Patients in stage 2-3 also exhibited a significantly elevated risk. Prior adjusted ORs reported in the international literature range from 4 to 12[4-6]. These results align with extensive international literature demonstrating that oral manifestations increase dramatically with immune deterioration. Patton documented odds ratios ranging from 3.0 to 6.0 for candidiasis and periodontal disease in advanced HIV stages[8]. The magnitude observed in our study (OR 18.86) falls within the upper range of these reports and may reflect patients' pre-ART status, as all participants were newly diagnosed and untreated.

Oral Hygiene as an Independent Behavioral Determinant

While immunosuppression is the primary biological driver, our findings demonstrate that poor oral hygiene independently increases the risk of oral pathology. One of the most clinically relevant findings was the strong association between tooth brushing less than once per day and oral manifestations (OR=12.98; p=0.019). Local factors such as plaque accumulation and microbial dysbiosis likely amplify disease expression. Greenspan et al. emphasized the synergistic interaction between immune dysfunction and oral microbiome imbalance in HIV-related oral disease[7]. Similarly, studies from Brazil and Asia have shown significant associations between plaque index and periodontal destruction in HIV-infected patients[22,26]. Our findings suggest that behavioral factors may substantially potentiate immunologically mediated vulnerability, reinforcing the importance of preventive oral health interventions in HIV care.

CD4+ Decline and Oral Manifestations

The lower median CD4+ levels seen in patients with ≥1 oral pathology are consistent with decades of clinical evidence showing that oral lesions serve as indicators of immune suppression in HIV infection.

Earlier epidemiologic data from the pre-ART era showed that oral candidiasis was one of the earliest clinical signs of CD4 decline below 200 cells/mm[37]. Similarly, Patton documented that oral candidiasis and periodontal disease occur most frequently in patients with advanced immunosuppression[8]. Pattrapornnan et al.[28], in a study including HIV-positive pregnant women, found a significant association between low CD4 levels and periodontitis (OR = 2.06, 95% CI = 1.00-4.27, p = 0.05). Additionally, we previously documented a notable negative correlation between CD4+ levels and dentition and periodontal health. A reduced CD4+ level was linked to increased DMFT ($r = -0.52$, $p = 0.01$), CPI ($r = -0.38$, $p = 0.024$), and LOA ($r = -0.37$, $p = 0.029$)[15]. Thus, the lower CD4+ levels observed in patients with oral pathology are consistent with known immunopathogenic pathways.

Clinical Implications

The findings highlight two dominant determinants of oral pathology:

1. Biological factor: advanced HIV clinical stage.
2. Behavioral factor: poor oral hygiene.

Integration of routine oral examination into HIV management protocols may facilitate early detection of immune deterioration. Additionally, a structured oral hygiene education should be incorporated into pre-ART counseling. Given the strong effect size observed for poor oral hygiene, preventive interventions may significantly reduce oral morbidity even in immunocompromised patients.

On the other side, the visual separation of CD4 distributions between groups supports the concept that oral examination may serve as a practical clinical indicator of immune deterioration. Moreover, given that some patients with moderate CD4 counts still developed lesions, integrating preventive dental care into early HIV management remains essential.

Strengths and Limitations

This study has several important strengths. First, its prospective design enhances data quality and reduces recall bias. Second, the inclusion of newly diagnosed, ART-naïve patients allowed assessment of oral manifestations in the absence of treatment-related confounding, thereby providing a clearer understanding of the natural relationship between HIV disease stage and oral pathology. Third, the simultaneous evaluation of both clinical stage and behavioral factors, particularly oral hygiene practices, enabled a more comprehensive analysis of biological and modifiable risk determinants. Furthermore, the use of multivariate logistic regression allowed identification of independent predictors while adjusting for potential confounders.

However, several limitations should be acknowledged. The single-center design may limit the

generalizability of the findings to other populations or healthcare settings. The relatively moderate sample size, particularly within certain subgroups, resulted in wide confidence intervals for some estimates and may have reduced statistical precision. Although the study was prospective in recruitment, the analysis of oral outcomes was cross-sectional, preventing evaluation of temporal progression or causal inference. Viral load data were not available, which could have provided additional stratification of immune status beyond CD4 count. Finally, oral hygiene practices were self-reported and therefore subject to potential reporting bias. Future multicenter longitudinal studies incorporating viral load measurements and ART follow-up are warranted to validate and extend these findings.

Conclusions

Advanced HIV clinical stage and poor oral hygiene are independent predictors of oral pathology in newly diagnosed HIV-infected patients. The strength of the association observed for AIDS stage highlights the strong connection between immune decline and oral disease burden. Importantly, poor oral hygiene is a changeable behavioral risk factor. Incorporating preventive oral health techniques into HIV care models can greatly lower morbidity and enhance the quality of life for affected patients. These findings emphasize the importance of multidisciplinary collaboration between infectious disease experts and dental professionals in managing HIV infection effectively.

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Conceptualization, E.S.M. and A.H.; methodology, E.S.M., A.H, L.S.; software, L.S; validation, A.H. and N. Ç.; formal analysis, L.S.; investigation, E.S.M..; resources, E.S.M., A.H, L.S.; data curation, E.S.M., A.H, L.S..; writing–original draft preparation, E.S.M..; writing–review and editing, A.H. and N.Ç.; visualization, E.S.M and L.S..; supervision, A.H and N.Ç.; project administration, E.S.M. and A.H. All the authors have read and agreed with the final version of the article.

Compliance with Ethics Requirements:

"The authors declare no conflict of interest regarding this article"

"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study"

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