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Prevalence of Periodontal Diseases in a Multicenter Cohort of Perinatally HIV-Infected and HIV-exposed and Uninfected Youth

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Abstract

Aims—To compare the prevalence and severity of periodontal diseases between 180 perinatally HIV-infected (PHIV) and 118 perinatally HIV-exposed and uninfected (PHEU) youth in a cross-sectional study conducted at 11 clinical sites in the United States and Puerto Rico from the Adolescent Master Protocol (AMP) study of the Pediatric HIV/AIDS cohort study (PHACS) network.

Methods—Several analyses were conducted, employing the current CDC/AAP classification for periodontitis and incorporating a definition of gingivitis based on a bleeding on probing threshold, and analyses based on more detailed whole mouth, intraoral regionally, site-based, and tooth-based criteria of bleeding on probing, plaque levels, pockets depths and clinical attachment levels.

Results—After adjusting for plaque control habits, and behavioral and sociodemographic factors, there were no significant differences in periodontal diseases between the PHIV and PHEU youth using any of these criteria. For PHIV youth, there was no significant association between parameters of periodontal disease and current HIV status.

Conclusions—While no significant differences in periodontal parameters were noted between the PHIV and PHEU youth, the influence of antiretroviral therapy on merits further exploration in this cohort in a longitudinal study.

Introduction

Although periodontal disease has been well described in HIV-infected adults, it has not been adequately investigated among children who acquired HIV through perinatal exposure. More

importantly, perinatally HIV-infected children are living longer into adolescence and young adulthood when periodontal disease begins to emerge as a major health problem regardless of HIV status. Among adults, several forms of periodontal diseases have been found to be associated with HIV including unusual forms of gingivitis, necrotizing gingivitis and periodontitis (Reddy, 2007). Few studies have examined periodontal health in perinatally HIV-infected (PHIV) youth with a full set of periodontal parameters, including a full-mouth assessment of clinical attachment loss (CAL)(Howell et al., 1996, Vaseliu et al., 2005, Magalhaes et al., 2001, Santos et al., 2001). The small number of studies which have been conducted did not include an adequate comparison group of uninfected children. PHIV youth may be at particular risk for disease due to exposure to sugar-containing liquid medications before and during tooth eruption and immunosuppression resulting in chronic gingival bacterial growth.

We previously published our findings comparing caries, mucosal disease, and periodontal disease (using the updated Centers for Disease Control and Prevention/ American Academy of Periodontology (CDC/AAP) classification (Eke et al., 2015, Eke et al., 2012)) between PHIV and perinatally HIV-exposed but uninfected (PHEU) youth (Moscicki et al., 2016). The comparison group of PHEU youth is unique since socioeconomic factors which are known to influence oral health are similar to those of PHIV youth. As classifications of periodontal disease for larger populations, such as the CDC/AAP classification, are based on a few sites with the highest level of specific periodontal parameters, such categorization of periodontal disease may lead to misclassification because only a fraction of periodontal measurements are considered. However, optimal statistical methods for clustered data that allow the inclusion of all measurements on all teeth have been used in the analysis of periodontal data (DeRouen et al., 1995). Thus this paper investigates not only periodontal disease assessed using the well-established CDC/AAP classification, but also detailed full-mouth periodontal parameters, in PHIV as compared to PHEU youth.

Methods

Study Design and Population

The Pediatric HIV/AIDS Cohort Study (PHACS) oral health substudy was a cross-sectional observational study that included participants currently enrolled in the PHACS Adolescent Master Protocol (AMP). AMP is a prospective cohort study designed to determine the impact of HIV infection and antiretroviral therapy (ART) on PHIV compared to PHEU youth at 15 clinical sites in the United States and Puerto Rico (Van Dyke et al., 2011). AMP eligibility criteria included perinatal HIV infection or exposure, age 7 to 16 years at enrollment as confirmed by the medical record, and engagement in medical care with available ART history for the PHIV group. Participants enrolled in AMP from March 2007 through October 2009 at 15 US clinical research sites. Regularly scheduled visits included audio-computer assisted structured interviews (ACASI), physical examination, chart reviews for medications and illnesses, and for CD4 counts and viral load assessments. Participants were recruited from 11 AMP sites with an affiliated dental school or dentist from September 2012 to January 2014 after written informed consent was obtained from both participants and their legal guardian, following a protocol approved by the Institutional Review Board of

each participating site and the Harvard T.H. Chan School of Public Health. Exclusion criteria included an inability to sit through a comprehensive oral examination due to acute systemic illness or presence of craniofacial anomalies, or a history of treatment with head or neck radiation (Moscicki et al., 2016).

Variables and Measures

Standardized dental and periodontal examinations were performed on youth at participating clinical research sites. The clinical periodontal parameters recorded included: 1) Probing depths (PD) measured for each tooth with a UNC probe on six sites rounded down to the nearest millimeter; 2) Distance from the gingival margin (GM) to the cemento-enamel junction (CEJ), for calculation of clinical attachment level (CAL); 3) Bleeding on probing (BOP) on six sites for each tooth recorded as present or absent; 4) Gingival index (GI) measured on six sites around the tooth using the standard GI of Loe and Silness (Loe and Silness, 1963); 5) The modified plaque index (PI) of Silness and Loe (Silness and Loe, 1964) for each buccal and lingual surface of each tooth.

Prior to commencing examination of participants, a periodontist/calibrator (MR) conducted a training at each of the examination centers with each of the participating dentists. The orientation included a demonstration of techniques to measure GI, BOP, PI, GM, and PD. Following this demonstration, each examiner was assessed with the calibrator (MR) on a second participant for PD, GM to CEJ to calibrate CAL, and GI. A minimum concurrence of 90% for both PD and GM position was required. If this level of concurrence was not achieved, the calibrator would review these techniques and conduct a second calibration on another patient until this minimal concurrence was met. All patients were referred for dental care if needed.

While the main outcomes of interest were the periodontal parameters used in the diagnosis of periodontitis and their association with HIV infection, other explored covariates considered to be associated with periodontal diseases included demographics (age, sex, race and ethnicity), caregiver socioeconomic characteristics (education and income), history of sex (ever had sex, ever had oral sex), drinking alcohol in the past 3 months, smoking cigarettes in the past 3 months, oral hygiene behavior (brushing frequency, flossing frequency), dental care (having a source of, cleaning in the last year), meal/snack consumption frequency per day and juice/soda consumption frequency per day. For PHIV participants, the risk factors considered also included HIV disease severity (lifetime CD4+ nadir < 200 cells/mm³, current CD4+ < 350 cells/mm³, current viral load > 400 copies/mL) and history of AIDS-defining illness.

Statistical Analyses

Summary statistics for demographics and other characteristics were compared across the two subgroups (PHIV and PHEU) with a Wilcoxon rank-sum test for continuous measures and a Fisher's Exact test for discrete measures.

Based on the periodontal parameters of CAL and PD, periodontitis was first summarized as either absent, mild, moderate, or severe using the CDC/AAP definition (Eke et al., 2015, Eke et al., 2012). Among those with no periodontitis, gingivitis was defined as having BOP on at

least 10% of the sites scored (definition adapted from (Offenbacher et al., 2008)). The extent and severity of periodontal disease of a participant was then measured by number (or percentage) of teeth and percentage of sites, respectively, of assessments exceeding various thresholds of each of the periodontal parameters. These measures were then summarized by HIV infection status using mean, standard deviation, median and quartiles.

The association between HIV infection and the prevalence of periodontal diseases at the tooth surface level was then assessed using two separate parameters: GI ≥ 2 for gingival inflammation, and CAL ≥ 3 mm for periodontitis. Taking the association among the multiple sites within each participant into account, Generalized Estimating Equation (GEE) models with a logistic link function were applied with and without adjustment for known risk factors and for the location of the site in the mouth. The analyses were conducted using Proc GLIMMIX of SAS 9.4 (METHOD=RMPL, EMPIRICAL=FIRORES) with a compound symmetry working correlation matrix (Mancl and DeRouen, 2001). Univariable logistic regression models were constructed for each covariate. The multivariable models adjusted for demographics, drinking alcohol, smoking cigarettes, oral hygiene behavior in addition to all other covariates with a p-value < 0.2 in the univariable analyses and a p-value < 0.1 in the final multivariable model after backward selection. The final model also considered the variation among multiple centers using random intercept with participants nested within center.

Another set of analyses was performed using one summary measure per participant to assess the association of HIV infection with the extent of periodontal diseases, for each of two separate parameters: the number of teeth with GI ≥ 2 at any site for gingival inflammation, and the number of teeth with CAL ≥ 3 mm at any interproximal site for periodontitis. These tooth counts were corrected for missing teeth by multiplying the ratio of 28 over the number of scored teeth. The unadjusted and adjusted regression analyses were applied directly to the tooth count whose distributions were characterized by an extra proportion of zeros and overdispersion when compared to Poisson distributions. Therefore, zero-inflated negative binomial (ZINB) regression analyses were performed to assess the association of HIV infection and other covariates with the tooth counts.

Results

Sample Characteristics

A total of 335 participants enrolled in the PHACS oral health substudy (209 PHIV and 126 PHEU). For the analysis of periodontal parameters, 37 participants were excluded (PHIV: 29, PHEU: 8) either because of the inability to complete the examination (PHIV: 4, PHEU: 1) or because they were currently taking an antibiotic, or had taken one within 90 days before the oral examination (PHIV: 25, PHEU:7). Statistically significant differences between the 180 PHIV and 118 PHEU youth were noted in that the PHIV were older, had greater physical development (Tanner stage), a greater proportion of Hispanics (Table 1), smaller proportion of caregivers being biological parent, annual income of \$30,000 or less, and had more sexual experience and marijuana use (Table 2). These differences were similar to previous research from this cohort since the PHIV youth were older and their parents with HIV were more likely to have died of AIDS. There was no significant differences between

the two groups with respect to sex, smoking, use of alcohol, oral hygiene and dental care (Tables 1 and 2). Among the 180 PHIV youth, 29% had a lifetime nadir CD4+ cell count below 200 cells/mm³, 14% had a CD4+ cell count below 350 cells/mm³, and 71% had suppressed viral load (< 400 copies/mL) at the time of the oral examination, or within 3 months prior.

Periodontal parameters by HIV Status

No significant differences in the prevalence of periodontal disease measured using the modified CDC-AAP classification were observed between the PHIV and PHEU groups (Table 3).

Table 4 shows the distribution patterns for specific periodontal parameters. Without adjusting for confounding factors, both PHIV and PHEU participants demonstrated similar patterns for periodontal parameters that primarily measure clinical inflammation and plaque levels. Specifically, no difference was seen for the overall percent of sites with BOP per participant, percent of teeth with at least one site with BOP per participant, and percent of teeth with at least four sites with BOP per participant. When we examined the severity and extent of higher levels of plaque and gingival inflammation, several differences were found. The mean percent of sites with a PI score = 3 was lower in the PHIV than the PHEU youth (2.81 versus 4.7; $p = 0.04$) and the number of teeth with at least 1 surface with a PI = 3 was also lower in the PHIV than the PHEU youth (1.46 versus 2.25; $p = 0.04$). Similarly, percent of sites with GI = 3 and number of teeth with at least 1 surface with GI = 3 were lower in the PHIV than the PHEU youth. However the actual number of sites per subject with this highest level of PI=3 or GI=3 was relatively small. By contrast, the overall measures of PD and CAL and the severity and extent of higher measures of PD and CAL were similar between the PHIV and PHEU groups (Table 4). Similar distributions patterns were observed for the prevalence of periodontal parameters when utilizing different cut-off levels (Supplementary Table 1).

Further stratified by site or region, the observed proportion of GI scores ≥ 2 among all examined tooth surfaces of the study population was lower for PHIV compared to PHEU youth regardless of sites or regions, with an overall proportion of 13.9% and 18.6%, respectively (Table 5). Regional and site variations for both PHIV and PHEU subjects were also observed, with the highest proportion of GI ≥ 2 on lower anterior teeth and on mesial buccal and distal buccal sites, and the lowest on upper posterior teeth and on lingual sites. The overall observed proportion of CAL ≥ 3 mm was similar between the PHIV and PHEU groups, with the highest proportion on mesial buccal surfaces and upper posterior teeth, and lowest proportion on lingual surfaces and anterior teeth. For PD ≥ 4 mm, the overall proportion was also similar between the PHIV and PHEU groups with a similar regional distribution pattern (Table 5).

Univariate and Multivariable analyses

In the unadjusted logistic regression model, PHIV youth had a lower risk of having a GI ≥ 2 compared to PHEU youth (Odds Ratio (OR) = 0.69, 95%CI = 0.48, 1.00) (Table 6). However, in the adjusted logistical regression model incorporating the observed higher

levels of PI in the PHEU group and the influence of variation among centers, the two groups were not different (adjusted OR (aOR) = 1.05, 95%CI = 0.73, 1.50). Other associations with having GI scores ≥ 2 were having juice/soda twice or more per day compared to once or none per day, having a higher PI and lower brushing frequency; flossing frequency was found to have a negative association. The odds of GI scores ≥ 2 showed similar regional variation and site variation with and without adjustment for other covariates. Among PHIV youth, no association was found between having GI scores ≥ 2 and low lifetime nadir CD4+, low current CD4+, or high current viral load in both unadjusted and adjusted analyses. Mild association was observed between having GI scores ≥ 2 and a history of an AIDS-defining illness in adjusted analysis.

No significant association was found between HIV infection and having interproximal CAL ≥ 3 mm (Table 7). The regional pattern stayed the same with or without adjustment for other covariates. Significant positive associations were noted between CAL ≥ 3 mm and a history of sex and PI. Having a caregiver with some college education was associated with lower odds of interproximal CAL ≥ 3 mm with marginal statistical significance; but drinking alcohol and smoking cigarettes were not associated with interproximal CAL ≥ 3 mm.

Within the PHIV cohort, no significant association was found between CAL ≥ 3 mm and lower CD4+ cell count nadir, low current CD4+ cell count, detectable current viral load or history of an AIDS-defining illness after adjusting for demographics, history of sex, education of caregiver, drinking alcohol and floss frequency, PI, site and region.

ZINB regression analyses on the extent of periodontal diseases confirmed the findings of the GEE analysis. There were no significant associations observed between HIV infection and the number of teeth with GI ≥ 2 at any site. However, these models confirmed that having juice/soda ≥ 2 per day (adjusted mean count ratio (aMR) = 1.75, 95% CI=1.26, 2.44) and high percent of teeth with visible plaque (aMR = 1.03, 95% CI=1.01, 1.04) were significantly associated with higher mean number of teeth with GI ≥ 2 at any site (Supplementary Table 2); Additionally, a history of sex (aMR= 2.17, 95% CI=1.34, 3.53). and high percent of teeth with visible plaque (aMR = 1.01 per unit, 95% CI=1.00, 1.02) were significantly associated with higher mean number of teeth with any interproximal CAL ≥ 3 mm, and caregiver had some college education was associated with lower mean tooth count of interproximal CAL ≥ 3 mm (aMR = 0.44, 95% CI=0.29, 0.67) (Supplementary Table 3).

Discussion

The general findings of the periodontal component of this oral health study were that there were no significant differences in the overall periodontal condition between the PHIV and PHEU groups. The proportion of sites with the high levels of gingival inflammation were lower in the PHIV group when compared to the PHEU group, but was not statistically significant after adjusting for factors such as plaque index and the influence of variation among centers. Nevertheless it is possible that ART may influence the ecology of the oral microbiome and/or secretion of inflammatory cytokines and chemokines. in particular as plaque and gingival inflammation tend to increase in prevalence during puberty. However to date the influence on the lifelong antiretroviral therapies on the bacterial oral microbiome

remains to be determined (Beck et al., 2015, Brito et al., 2008, Goncalves et al., 2007, Navazesh et al., 2005, Ryder et al., 2012).

The first cases of the unusual periodontal diseases and conditions associated with HIV, including linear gingival erythema (LGE), necrotizing ulcerative gingivitis (NUG) and necrotizing ulcerative periodontitis (NUP), were published 3 decades ago (Rosenstein et al., 1989, Winkler et al., 1989, Williams et al., 1990, Masouredis et al., 1992, Riley et al., 1992, EC-Clearinghouse, 1993). Furthermore, several studies demonstrated an association between periodontal disease and low CD4 cell count and progression to AIDS (Glick et al., 1994). Since that time, the prevalence of these conditions seems to have declined in part due to the advent of ART (Patton et al., 2000, Tappuni and Fleming, 2001, Ramirez-Amador et al., 2003, Ferreira et al., 2007, Vernon et al., 2011) and non-ART local and systemic antimicrobial approaches (Ryder et al., 2012). Most of these studies focused on adults, with relatively few on HIV-infected youth. One difficulty in developing such surveys on periodontal conditions in this younger population is that periodontitis in general is a slowly progressing chronic condition that does not manifest itself clinically until adulthood. Therefore, any minor changes in periodontal attachment loss that may start in childhood or adolescence are usually not clinically detectable with conventional periodontal diagnostic approaches. In addition, the classifications for the type and severity of periodontal diseases for adults may not be relevant to children (Lopez and Baelum, 2003, Albandar and Tinoco, 2002). The earliest clinical manifestations of disease may be a simple form of gingival inflammation without measurable CAL. In addition, distinguishing periodontitis from gingivitis by PD measures may be of limited value as increases in PD in this age group may more often reflect gingival enlargement from inflammation, rather than CAL.

Therefore it is understandable that when we used both the current CDC/AAP classification for periodontitis and a separately created definition for gingivitis without periodontitis using a BOP threshold (Offenbacher et al., 2008), there were no significant differences in the prevalence of mild, moderate or severe forms of periodontitis between PHIV and PHEU youth. In addition, direct comparisons using our definition to other studies, which use a range of classification systems, are difficult. However, several general observations can be made. First, the prevalence of gingivitis (including a diagnosis of gingivitis alone or periodontitis) of 80% in this PHIV/PHEU population is comparable to the range of the prevalence of gingivitis from other cross sectional studies in children (Jenkins and Papapanou, 2001). However, the 31% prevalence of mild to moderate forms of periodontitis as defined by the current modified CDC classification was higher than reported in some studies and comparable to other studies (Albandar and Tinoco, 2002, Jenkins and Papapanou, 2001)

When considering the reported lower prevalence of more severe forms of periodontal diseases in these younger populations (Howell et al., 1996, Lopez and Baelum, 2003, Albandar and Tinoco, 2002), several more extensive analysis strategies were employed in this study to determine if there were differences in the extent, severity, distribution, and intraoral geographic clustering of clinical indicators for gingivitis. These included more rigorous analyses of the extent and distribution of clinical measures of inflammation (GI) and attachment loss (CAL) by numbers of affected teeth and numbers of sites, taking into

consideration known sociodemographic, behavioral, clinical, and laboratory findings. Instead of a broad categorization by the number of interproximal sites with attachment loss or deep pockets, we directly analyzed all available data of CAL or GI from all surfaces within the entire dentition. This methodology avoids collapsing or summarizing information to only one measure per participant and makes direct use of each observation from all sites and thus is more sensitive to identify subtle differences across the entire mouth. At the same time, this method recognizes the data collected from the same participant and participants from the same institution are correlated and thus adjusts the statistical comparison to prevent exaggerated differences. These more rigorous analytical approaches did not demonstrate statistical differences between the PHIV and PHEU cohorts for periodontal measures at the time of this survey.

In conclusion, this study found that using both general disease categories and more in depth analysis, that the overall presence of periodontal disease in PHIV youth was similar to our comparison group of HIV –exposed but uninfected youth. The influence of HIV-exposure and ART, whether perinatally or through-out childhood on periodontal health and disease needs further exploration. Furthermore, microbial and inflammatory marker assessments of these two populations may show differences between these groups which in turn may affect clinical manifestations as both of these population groups grow older. Therefore, follow-up studies on the development of periodontal diseases for these PHIV and PHEU groups at selected intervals are warranted in order to assess the long-term effects of HIV infection on the periodontium in the ART era.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Conflict of Interest and Source of Funding

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Clinical Relevance of the Study

Scientific rationale for the study

To compare the periodontal health between perinatally HIV-infected (PHIV) and perinatally HIV-exposed and uninfected (PHEU) youth in a multicenter cross-sectional study.

Principle Findings

There were no significant differences in periodontal health between PHIV and PHEU youth. For PHIV youth, there was no significant association between parameters of periodontal disease and current HIV status.

Practical Implications

In the current HIV treatment era, PHIV youth and PHEU youth have similar levels of periodontal health. However the longer-term effects of antiretroviral treatment need to be monitored.

Table 1

Study Population: Demographic, Developmental Covariates, Caregiver Characteristics and Substance Use by HIV Infection Status

Characteristic	N	HIV Infection Status			P-Value*
		Infected (N=180)	Uninfected (N=118)	Total (N=298)	
Age at OH Visit (years)					
Mean (s.d.)		16.84 (2.61)	14.76 (2.53)	16.02 (2.77)	<.001
Median (Q1, Q3)		17.26 (14.88, 18.85)	14.47 (12.51, 16.48)	16.25 (13.80, 18.39)	
Min, Max		10.25, 21.71	10.63, 20.90	10.25, 21.71	
Age Category (years)					
10 to <14		30 (17%)	51 (43%)	81 (27%)	<.001
14 to <17		55 (31%)	46 (39%)	101 (34%)	
17 to <19		52 (29%)	12 (10%)	64 (21%)	
19+		43 (24%)	9 (8%)	52 (17%)	
Female Sex		88 (49%)	57 (48%)	145 (49%)	1.00
Black Race		119 (66%)	67 (57%)	186 (62%)	0.11
Hispanic Ethnicity		48 (27%)	50 (42%)	98 (33%)	0.006
Maximum Tanner Stage					
1–3		23 (13%)	33 (28%)	56 (19%)	0.001
4		35 (19%)	28 (24%)	63 (21%)	
5		122 (68%)	57 (48%)	179 (60%)	
Caregiver is Biological Parent		65 (36%)	95 (81%)	160 (54%)	<.001
Caregiver Some College		67 (37%)	36 (31%)	103 (35%)	0.26
Caregiver Income <\$30,001		93 (52%)	99 (84%)	192 (64%)	<.001
Ever Had Sex		86 (48%)	39 (33%)	125 (42%)	0.01
Drink Alcohol: Past 3 Months		44 (24%)	20 (17%)	64 (21%)	0.15
Smoke Cigarette: Past 3 Months		20 (11%)	6 (5%)	26 (9%)	0.09
Use Marijuana: Past 3 Months		43 (24%)	13 (11%)	56 (19%)	0.006

* P-value by Wilcoxon Test for continuous measures and Fisher's exact test for categorical characteristics

Missing data on 2 participants for caregiver some college, 6 for caregiver income, 6 for ever had sex, 6 for alcohol, 8 for cigarettes, and 6 for marijuana,

Table 2

Oral health behavioral characteristics by HIV Infection Status

Characteristic		HIV Infection Status			P-Value [*]
		Infected (N=180)	Uninfected (N=118)	Total (N=298)	
Brush Frequency (times/day)	<1	16 (9%)	8 (7%)	24 (8%)	0.86
	1	69 (38%)	46 (39%)	115 (39%)	
	2	95 (53%)	64 (54%)	159 (53%)	
Floss Frequency (times/day)	<1	154 (86%)	96 (81%)	250 (84%)	0.15
	1	14 (8%)	17 (14%)	31 (10%)	
	2	12 (7%)	5 (4%)	17 (6%)	
Have Source of Dental Care		144 (80%)	88 (75%)	232 (78%)	0.56
Cleaning in Last Year		116 (64%)	73 (62%)	189 (63%)	0.62
Juice/Soda Frequency (times/day)	0-1	52 (29%)	34 (29%)	86 (29%)	1.00
	2	128 (71%)	84 (71%)	212 (71%)	
Saliva Volume (mL/min)	Median (Q1, Q3)	0.72 (0.40, 1.00)	0.60 (0.40, 1.00)	0.60 (0.40, 1.00)	
	Min, Max	0.06, 3.00	0.00, 2.20	0, 3	0.08
Plaque Index: % Teeth Any Site >1	Median (Q1, Q3)	25.00 (10.71, 47.29)	32.14 (11.54, 59.26)	26.42 (10.71, 53.57)	0.14
	Min, Max	0, 100	0, 100	0, 100	

* P-value by Wilcoxon ranksum test for continuous measures and Fisher's exact test for binary characteristics.

Missing data on 4 participants for have source of dental care, 1 for cleaning in last year, and 2 for saliva volume.

Table 3
Study Population: Periodontal Disease Diagnosis Using the CDC-AAP Case Definition

Characteristic	Cohort			P-Value*
	Infected (N=180)	Uninfected (N=118)	Total (N=298)	
Periodontal Disease	37 (21%)	23 (19%)	60 (20%)	0.93
None				
Gingivitis	85 (47%)	60 (51%)	145 (49%)	
Mild Periodontitis	30 (17%)	17 (14%)	47 (16%)	
Moderate Periodontitis	28 (16%)	18 (15%)	46 (15%)	

* Fisher's Exact Test

Table 4

Summary of Extent and Severity of Periodontal Diseases by HIV Infection Status

Characteristic	HIV Infection Status			P-Value*
	Infected (N=180)	Uninfected (N=118)	Total (N=298)	
% Sites BOP	Mean (s.d.)	21.49 (18.02)	23.64 (18.61)	22.34 (18.25)
	Median (Q1, Q3)	15.77 (9.62, 30.95)	17.86 (9.52, 35.12)	16.96 (9.52, 31.55)
% Teeth BOP	Mean (s.d.)	57.32 (27.78)	60.59 (26.19)	58.61 (27.17)
	Median (Q1, Q3)	59.99 (39.29, 79.97)	61.84 (42.86, 83.33)	60.71 (39.29, 81.48)
% Teeth BOP 4-6 Sites	Mean (s.d.)	10.00 (17.84)	12.41 (18.80)	10.95 (18.23)
	Median (Q1, Q3)	0.00 (0.00, 10.71)	3.57 (0.00, 18.52)	3.57 (0.00, 14.81)
% Sites PI 1	Mean (s.d.)	64.22 (27.91)	63.17 (25.81)	63.80 (27.06)
	Median (Q1, Q3)	69.20 (41.07, 89.74)	68.30 (44.23, 82.14)	68.75 (42.86, 87.04)
% Sites PI 2	Mean (s.d.)	18.42 (17.72)	22.64 (20.45)	20.09 (18.93)
	Median (Q1, Q3)	12.50 (5.36, 26.36)	16.96 (7.14, 35.71)	14.29 (5.36, 30.77)
% Sites PI =3	Mean (s.d.)	2.81 (6.77)	4.71 (9.79)	3.56 (8.14)
	Median (Q1, Q3)	0.00 (0.00, 1.79)	0.00 (0.00, 5.36)	0.00 (0.00, 3.57)
# Teeth Max PI 1	Mean (s.d.)	21.92 (6.93)	21.69 (6.75)	21.83 (6.85)
	Median (Q1, Q3)	24 (19, 28)	24 (18, 27)	24 (19, 28)
# Teeth Max PI 2	Mean (s.d.)	8.54 (7.20)	9.97 (7.86)	9.11 (7.49)
	Median (Q1, Q3)	7 (3, 13)	9 (3, 16)	7 (3, 15)
# Teeth Max PI =3	Mean (s.d.)	1.46 (3.43)	2.25 (4.39)	1.77 (3.85)
	Median (Q1, Q3)	0 (0, 1)	0 (0, 3)	0 (0, 2)
% Sites GI 1	Mean (s.d.)	52.43 (36.66)	52.69 (35.10)	52.53 (35.99)
	Median (Q1, Q3)	53.87 (16.96, 89.38)	53.87 (17.26, 85.71)	53.87 (17.26, 87.50)
% Sites GI 2	Mean (s.d.)	13.82 (19.35)	18.76 (23.19)	15.78 (21.05)
	Median (Q1, Q3)	4.76 (0.00, 20.12)	4.85 (0.00, 31.55)	4.76 (0.00, 26.19)
% Sites GI =3	Mean (s.d.)	1.43 (4.19)	3.06 (7.43)	2.07 (5.74)
	Median (Q1, Q3)	0 (0, 0)	0.00 (0.00, 1.28)	0.00 (0.00, 0.60)
# Teeth Max GI 1	Mean (s.d.)	18.79 (10.21)	19.49 (9.42)	19.07 (9.90)
				0.99

Characteristic	HIV Infection Status			P-Value *
	Infected (N=118)	Uninfected (N=118)	Total (N=236)	
# Teeth Max GI 2	Median (Q1, Q3)	24 (10, 28)	24 (10, 28)	0.19
	Mean (s.d.)	7.84 (9.08)	8.49 (9.36)	
	Median (Q1, Q3)	4 (0, 14)	4.50 (0.00, 17.00)	
	Mean (s.d.)	1.11 (2.91)	1.47 (3.47)	
	Median (Q1, Q3)	0 (0, 0)	0 (0, 1)	
# Teeth Max GI =3	Median (Q1, Q3)	0 (0, 0)	0 (0, 1)	0.01
	Mean (s.d.)	1.11 (2.91)	1.47 (3.47)	
	Median (Q1, Q3)	0 (0, 0)	0 (0, 1)	
	Mean (s.d.)	1.11 (2.91)	1.47 (3.47)	
	Median (Q1, Q3)	0 (0, 0)	0 (0, 1)	
% Sites PD 3	Median (Q1, Q3)	22.02 (16.90)	22.32 (16.85)	0.63
	Mean (s.d.)	19.05 (7.49, 32.14)	19.57 (7.74, 32.14)	
	Median (Q1, Q3)	3.57 (5.04)	3.76 (5.90)	
	Mean (s.d.)	1.19 (0.00, 5.57)	1.19 (0.00, 5.59)	
	Median (Q1, Q3)	1.40 (0.00, 5.95)	1.19 (0.00, 5.59)	
# Teeth Max PD 4	Median (Q1, Q3)	14.83 (8.24)	15.48 (8.12)	0.51
	Mean (s.d.)	15 (8, 22)	15 (9, 22)	
	Median (Q1, Q3)	3.79 (4.78)	4.04 (5.18)	
	Mean (s.d.)	2.00 (0.00, 6.50)	2 (0, 6)	
	Median (Q1, Q3)	2.00 (0.00, 6.50)	2 (0, 6)	
% Sites CAL 2	Median (Q1, Q3)	17.03 (19.40)	17.24 (17.47)	0.47
	Mean (s.d.)	10.71 (2.68, 23.12)	11.46 (2.98, 23.21)	
	Median (Q1, Q3)	2.91 (6.17)	2.81 (5.91)	
	Mean (s.d.)	0.00 (0.00, 2.47)	0.00 (0.00, 2.47)	
	Median (Q1, Q3)	0.00 (0.00, 2.47)	0.00 (0.00, 2.47)	
% Sites CAL 3	Median (Q1, Q3)	11.46 (8.92)	11.78 (8.74)	0.37
	Mean (s.d.)	11.00 (3.50, 19.00)	12 (4, 18)	
	Median (Q1, Q3)	2.79 (4.88)	2.74 (4.77)	
	Mean (s.d.)	0.00 (0.00, 3.50)	0 (0, 3)	
	Median (Q1, Q3)	0.00 (0.00, 3.50)	0 (0, 3)	

* Wilcoxon Test

“% Sites XXX” parameter: percent of all sites examined in the entire dentition of a participant with characteristic XXX.

% Teeth BOP: percent of all teeth with at least one site with BOP per participant

% Teeth BOP 4-6 sites: percent of all teeth with at least four sites with BOP per participant

“# Teeth Max XXX” parameter: the count of teeth of a participant with at least one surface with characteristic XXX”

Table 5

Proportion of selected periodontal parameters by site or region and by HIV infection status

Group (Total number of tooth surfaces)	GI 2 Frequency (Proportion)		CAL 3 mm Frequency (Proportion)		PD 4 mm Frequency (Proportion)		
	PHIV (n=29372)	PHEU (n=19099)	PHIV (n=29301)	PHEU (n=18980)	PHIV (n=29306)	PHEU (n=19022)	
Overall	4,083 (13.9%)	3,555 (18.6%)	862 (2.94%)	502 (2.64%)	1,041 (3.55%)	755 (3.97%)	
site	distal buccal	893 (18.2%)	764 (24.1%)	261 (5.34%)	137 (4.33%)	351 (7.18%)	224 (7.06%)
	buccal	563 (11.5%)	535 (16.9%)	27 (0.56%)	28 (0.89%)	18 (0.37%)	14 (0.44%)
	mesial buccal	943 (19.3%)	782 (24.7%)	224 (4.58%)	150 (4.74%)	290 (5.93%)	244 (7.70%)
	distal lingual	683 (14.0%)	568 (17.8%)	173 (3.54%)	96 (3.04%)	211 (4.32%)	149 (4.70%)
	lingual	333 (6.8%)	369 (11.6%)	25 (0.51%)	22 (0.70%)	14 (0.29%)	17 (0.54%)
	mesial lingual	668 (13.6%)	537 (16.8%)	152 (3.11%)	69 (2.18%)	157 (3.21%)	107 (3.37%)
region	lower anterior	1,294 (20.1%)	1,160 (27.7%)	60 (0.93%)	58 (1.39%)	91 (1.41%)	76 (1.81%)
	upper anterior	828 (12.9%)	610 (14.7%)	98 (1.53%)	61 (1.47%)	106 (1.65%)	121 (2.92%)
	lower posterior	1,075 (13.0%)	1,012 (18.8%)	328 (3.98%)	192 (3.59%)	412 (5.00%)	297 (5.53%)
	Upper posterior	886 (10.7%)	773 (14.4%)	376 (4.58%)	191 (3.60%)	432 (5.26%)	261 (4.90%)

Table 6
Surface Level Logistic Regression Models for the Risk of Gingival Index 2 using GEE Methods *

Parameter	Level	Unadjusted Univariate Models			Adjusted Multivariable Model** (290 participants)		
		N****	OR (95% CI)	p-value	aOR (95% CI)	p-value	
HIV Infected		298	0.69 (0.48, 1.00)	0.05	1.05 (0.73, 1.50)	0.81	
Age Category (years)	19+	298	0.83 (0.48, 1.42)	0.50	1.04 (0.59, 1.81)	0.90	
	17 to <19	.	1.01 (0.61, 1.67)	0.98	0.93 (0.55, 1.59)	0.80	
	14 to <17	.	1.12 (0.69, 1.81)	0.66	1.09 (0.77, 1.54)	0.64	
	10 to <14	.	1		1		
Female Sex		298	0.88 (0.62, 1.27)	0.50	1.07 (0.81, 1.42)	0.62	
Black Race		298	1.00 (0.69, 1.45)	0.98	0.70 (0.41, 1.22)	0.21	
Hispanic Ethnicity		298	1.08 (0.75, 1.57)	0.67	0.83 (0.49, 1.42)	0.50	
Tanner Category	Stage 5	298	1.18 (0.69, 2.04)	0.54	--	--	
	Stage 4	.	0.96 (0.53, 1.75)	0.90	--	--	
	Stage 1-3	.	1		--	--	
Caregiver is Biological Parent		298	1.00 (0.69, 1.43)	0.98	--	--	
Caregiver has some College		296	0.82 (0.54, 1.26)	0.37	--	--	
Caregiver Income <\$30,001		292	0.83 (0.55, 1.26)	0.38	--	--	
Sex Ever		292	0.90 (0.63, 1.30)	0.59	--	--	
Oralsex Ever		292	0.88 (0.61, 1.29)	0.52	--	--	
Drink Alcohol: Past 3 Months		292	1.06 (0.69, 1.62)	0.78	1.30 (0.76, 2.21)	0.34	
Smoke Cigarette: Past 3 Months		290	0.87 (0.46, 1.64)	0.67	0.81 (0.53, 1.22)	0.31	
Use Marijuana: Past 3 Months		292	0.76 (0.47, 1.23)	0.27	--	--	
Brush Frequency (times/day)	<1	298	1.92 (1.02, 3.63)	0.04	1.76 (1.12, 2.77)	0.02	
	1	.	1.56 (1.06, 2.28)	0.02	1.02 (0.74, 1.41)	0.91	
	2	.	1		1		
Floss Frequency (times/day)	<1	298	0.81 (0.30, 2.16)	0.67	0.63 (0.43, 0.90)	0.01	
	1	.	1.01 (0.34, 3.01)	0.99	0.68 (0.40, 1.14)	0.14	

Parameter	Level	Unadjusted Univariate Models			Adjusted Multivariable Model** (290 participants)		
		N***	OR (95% CI)	p-value	aOR (95% CI)	p-value	
	2		1		1		
Have No Source of Dental Care		294	0.95 (0.61, 1.49)	0.82	--	--	
No Cleaning in Last Year		297	1.13 (0.78, 1.64)	0.52	--	--	
Meal/Snack Frequency (times/day) 5		298	1.47 (0.99, 2.19)	0.06	--	--	
Juice/Soda Frequency (times/day) 2		298	1.78 (1.12, 2.83)	0.01	1.90 (1.30, 2.79)	<.001	
Saliva Volume (mL/min)		296	1.00 (0.71, 1.40)	0.98	--	--	
Pl: 1 vs 0		298	1.81 (1.61, 2.04)	<.0001	1.70 (1.39, 2.08)	<.0001	
Pl: 2 vs 0		.	3.78 (3.14, 4.55)	<.0001	3.37 (2.26, 5.01)	<.0001	
Pl: 3 vs 0		.	8.17 (5.72, 11.7)	<.0001	7.03 (4.17, 11.8)	<.0001	
Site		298					
Distal Buccal		.	2.73 (2.32, 3.21)	<.0001	2.62 (1.68, 4.08)	<.0001	
Buccal		.	1.66 (1.42, 1.95)	<.0001	1.47 (1.13, 1.90)	<.01	
Mesial Buccal		.	2.87 (2.42, 3.41)	<.0001	2.78 (1.72, 4.48)	<.0001	
Distal Lingual		.	1.93 (1.72, 2.16)	<.0001	2.06 (1.20, 3.56)	<.01	
Mesial Lingual		.	1.84 (1.65, 2.06)	<.0001	1.95 (1.22, 3.12)	<.01	
Lingual	Reference	.	1		1		
Region		298					
Lower Anterior	Teeth 22–27	.	2.16 (1.83, 2.56)	<.0001	2.10 (1.48, 3.00)	<.0001	
Lower Posterior	Teeth 18–21, 28–31	.	1.33 (1.18, 1.50)	<.0001	1.34 (1.04, 1.74)	0.03	
Upper Anterior	Teeth 6–11	.	1.13 (0.96, 1.33)	0.15	1.24 (0.80, 1.93)	0.33	
Upper Posterior	Teeth 2–5, 12–15	.	1		1		
PHIV cohort					(n=175) [#]		
CD4+ Nadir < 200 cells/mm ³		180	1.44 (0.86, 2.41)	0.16	1.30 (0.84, 2.00)	0.23	
Current CD4+ 350 cells/mm ³		180	1.13 (0.63, 2.05)	0.68	1.30 (0.97, 1.74)	0.08	
HIV Viral Load 400		178	1.22 (0.73, 2.01)	0.45	1.13 (0.82, 1.55)	0.46	

Parameter	Level	Unadjusted Univariate Models			Adjusted Multivariable Model** (290 participants)	
		N****	OR (95% CI)	p-value	aOR (95% CI)	p-value
copies/mL						
History of AIDS-Defining illness		180	1.21 (0.70, 2.08)	0.50	1.51 (1.04, 2.20)	0.03

* Generalized Estimating Equation method using the assumption that any two surfaces within a participant have the same correlation, and bias-corrected sandwich estimator was used for the covariance matrix of the estimates.

** One final multivariable model include HIV infection, demographics, drinking alcohol, smoking cigarettes, brush and floss frequencies, juice/soda frequency, PI, site and region. The effect of institution was also considered as a random effect (p-value < 0.0001) in the intercept of the model.

*** Number of participants in the respective unadjusted analysis. The number of surfaces with gingival index scored for each participant ranges from 123 to 168.

aOR in PHIV cohort analyses were adjusted for all significant covariates identified in the PHIV and PHEU combined multivariable model above. The sample size of the model for the association with viral load was 173 due to two more missing in viral load.

Table 7

Surface Level Logistic Regression Models for the Risk of Interproximal Clinical Attachment Loss at least 3mm using GEE Methods *

Parameter	Level	Unadjusted Univariate Models			Adjusted Multivariable Model** (288 participants)		
		N***	OR (95% CI)	p-value	aOR (95% CI)	p-value	
HIV Infected		298	1.15 (0.69, 1.93)	0.59	1.05 (0.85, 1.31)	0.64	
Age Category (years)	19+	298	1.82 (0.83, 4.02)	0.14	0.78 (0.36, 1.72)	0.54	
	17 to <19	.	1.31 (0.60, 2.84)	0.50	0.54 (0.20, 1.44)	0.22	
	14 to <17	.	1.01 (0.52, 1.98)	0.98	0.71 (0.41, 1.25)	0.24	
	10 to <14	.	1		1		
Female Sex		298	0.87 (0.52, 1.45)	0.60	1.44 (0.93, 2.23)	0.11	
Black Race		298	0.66 (0.40, 1.11)	0.12	0.51 (0.19, 1.36)	0.18	
Hispanic Ethnicity		298	1.27 (0.77, 2.09)	0.36	0.54 (0.15, 1.95)	0.35	
Tanner Category	Stage 5	298	1.84 (0.77, 4.38)	0.17	--	--	
	Stage 4	.	1.40 (0.54, 3.67)	0.50	--	--	
	Stage 1-3	.	1	--	--	--	
Caregiver is Biological Parent		298	0.91 (0.55, 1.51)	0.72	--	--	
Caregiver has some College		296	0.47 (0.24, 0.93)	0.03	0.58 (0.34, 1.01)	0.06	
Caregiver Income <\$30,001		292	1.45 (0.77, 2.73)	0.25	--	--	
Sex Ever		292	2.33 (1.41, 3.83)	<.001	2.36 (1.50, 3.71)	<.001	
Oralsex Ever		292	2.15 (1.30, 3.55)	<.01	--	--	
Drink Alcohol: Past 3 Months		292	1.61 (0.90, 2.90)	0.11	1.11 (0.61, 2.00)	0.74	
Smoke Cigarette: Past 3 Months		290	1.50 (0.75, 2.98)	0.25	1.00 (0.42, 2.39)	1.00	
Use Marijuana: Past 3 Months		292	1.25 (0.63, 2.49)	0.53	--	--	
Brush Frequency (times/day)	<1	298	1.05 (0.38, 2.92)	0.92	0.83 (0.36, 1.93)	0.67	
	1	.	0.88 (0.51, 1.51)	0.63	0.98 (0.57, 1.69)	0.95	
	2	.	1		1		

Parameter	Level	Unadjusted Univariate Models			Adjusted Multivariable Model ^{**} (288 participants)		
		N ^{***}	OR (95% CI)	p-value	aOR (95% CI)	p-value	
Floss Frequency (times/day)	<1	298	2.08 (0.77, 5.64)	0.15	1.62 (0.69, 3.77)	0.27	
	1	.	3.60 (1.11, 11.7)	0.03	1.75 (0.67, 4.57)	0.25	
	2	.	1		1		
Have No Source of Dental Care		294	0.64 (0.32, 1.29)	0.22	--	--	
No Cleaning in Last Year		297	0.97 (0.57, 1.63)	0.90	--	--	
Meal/Snack Frequency (times/day) 5		298	0.67 (0.40, 1.13)	0.13	--	--	
Juice/Soda Frequency (times/day) 2		298	0.93 (0.52, 1.69)	0.82	--	--	
Saliva Volume (mL/min)		296	1.00 (0.61, 1.62)	0.98	--	--	
PI: 1 vs 0		298	1.95 (1.54, 2.48)	<.0001	1.74 (1.36, 2.23)	<.0001	
PI: 2 vs 0		.	3.14 (2.25, 4.39)	<.0001	2.79 (1.80, 4.32)	<.0001	
PI: 3 vs 0		.	2.76 (1.70, 4.46)	<.0001	2.38 (1.27, 4.46)	<.01	
Site		298					
Distal Buccal		.	1.85 (1.54, 2.21)	<.0001	1.74 (1.48, 2.05)	<.0001	
Mesial Buccal		.	1.73 (1.41, 2.12)	<.0001	1.61 (1.36, 1.91)	<.0001	
Distal Lingual		.	1.23 (1.08, 1.39)	<.01	1.22 (1.12, 1.32)	<.0001	
Mesial Lingual	Reference	.	1		1		
Region		298					
Upper Posterior	Teeth 2–5, 12–15		4.27 (2.81, 6.49)	<.0001	4.72 (2.43, 9.17)	<.0001	
Lower Posterior	Teeth 18–21, 28–31	.	3.80 (2.48, 5.83)	<.0001	4.15 (2.25, 7.64)	<.0001	
Upper Anterior	Teeth 6–11	.	1.44 (1.01, 2.05)	0.04	1.68 (1.32, 2.15)	<.0001	
Lower Anterior	Teeth 22–27	.	1		1		
PHIV cohort					n = 174 [#]		
CD4+ Nadir < 200 cells/mm ³		180	1.31 (0.68, 2.55)	0.42	0.97 (0.47, 2.01)	0.94	

Parameter	Level	Unadjusted Univariate Models	Adjusted Multivariable Model ^{***} (288 participants)
		N ^{***} OR (95% CI) p-value	aOR (95% CI) p-value
Current CD4+ cells/mm ³	350	180 0.59 (0.24, 1.49) 0.26	1.07 (0.65, 1.78) 0.79
HIV Viral Load copies/mL	400	178 0.43 (0.22, 0.86) 0.02	0.84 (0.42, 1.69) 0.63
History of AIDS-Defining Illness		180 1.49 (0.72, 3.10) 0.28	0.79 (0.49, 1.27) 0.33

* Generalized Estimating Equation method using the assumption that any two surfaces within a participant have the same correlation, and bias-corrected sandwich estimator was used for the covariance matrix of the estimates.

** One final multivariable model include HIV infection, demographics, drinking alcohol, smoking cigarettes, brush and floss frequencies, ever had sex, caregiver had some college education, PI, site and region. The effect of institution was also considered as a random effect (p-value < 0.0001) in the intercept of the model.

*** Number of participants in the respective unadjusted analysis. The number of surfaces with clinical attachment loss measured for each participant ranges from 58 to 112.

aOR for viral load was adjusted for all significant covariates identified in the PHIV and PHEU combined multivariable model with sample size 172. aOR for CD4+ nadir < 200 cells/mm³, for current CD4+ 350 cells/mm³ or for History of AIDS-Defining Illness was adjusted for all these covariates except female, brushing frequency and smoking in past 3 months which were selected by less significant results to avoid numerical issues.