Variation of Oral Diseases by HIV Exposure Among Kenyan Children

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Abstract

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Background: Although the prevalence of Human Immunodeficiency Virus (HIV) has significantly declined globally, largely due to increased access to antiretroviral therapy (ART) and effective prevention strategies, the disease remains a significant public health challenge, particularly in sub-Saharan Africa. While much attention has been directed towards managing the clinical manifestations of HIV and preventing its transmission, there is growing interest in how the disease and the treatment regimens impact oral health and the prevalence of dental caries.
Purpose: The aim of this study was to determine the impact of HIV exposure/treatment on 3-4-year-old Kenyan children.
Methods: This is a baseline analysis of a longitudinal study that was conducted amongst 360 children, aged 3-4-year, drawn from 31 hospitals and clinics in West Kenya. The children were divided into three cohorts of 120 children based on HIV diagnosis: HIV-infected (HIV), exposed at birth but uninfected (HEU) and unexposed uninfected (HUU). Demographics and data from a standardized oral examination were collected, besides data on ART treatment regimens, duration, viral load and adherence (HIV group). Statistical analysis was conducted using descriptive statistics, t-test and regression analysis ($P<.05$).
Results: The mean age of the 360 children was 3.4 years (SD:0.5) and 51% were female. The majority of children were enrolled in private school (47%) (public (22%); no school (31%)) and lived in rural (49%) (urban (35%), peri-urban (16%)) areas. HIV children had significantly greater prevalence (81%) of abnormal findings (submandibular lymphadenopathy parotid gland enlargement, geographic tongue, among others) compared with those in the HEU (60%) and HUU (54%) groups ($P<.001$). No significant differences in salivary pH, dmft/dmfs scores, dental caries, dental plaque or gingival bleeding upon brushing were found. Among HIV children, 93% of reported viral loads under the threshold of 1,000 copies/mL (well controlled) while ART treatment adherence threshold of above 90% was met by 78% of the patients.
Conclusions: Children living with HIV with access to ART treatment have significantly more oral diseases than the HEU or HUU. Diagnosing and treating oral diseases in HIV impacted children would improve delivery of care by HIV health providers.

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Dedication

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I. INTRODUCTION

According to the most recent global report on the HIV/AIDs epidemic completed by the World Health Organization (WHO) and UNAIDS, approximately 39 million people worldwide are infected with HIV in which 1.5 million are children or adolescents under the age of 14 years.[1] Africa accounts for the highest prevalence of cases totaling 25.6 million people living with HIV.[1] Regions within Africa are disproportionately affected as Eastern and Southern Africa have significantly more cases than Western and Central.[1] As of 2022, Kenya has reported a prevalence of 2,701,000 total individuals living with HIV in which 105,000 of the cases are children 14 years and under.[1] Although there has been a trend of decreasing incidence overall, with a 70% reduction in infection rate since 2010, there was still a reported 5,200 new cases in Kenya in 2022. The incidence rate within Kenya varies widely based on county. Kenya's AIDS Strategic Framework in 2020 identified 13 counties as priority counties based on their increasing incidence when compared to overall prevalence.[2] This data helped create prioritization for HIV resources to counties at highest risk, including Kisumu County ranking third highest incidence in Kenya.[2]

Approximately 90% of pediatric HIV cases occur through vertical transmission, which refers to mother to child transmission (MTCT), during pregnancy, labor & delivery or breastfeeding.[3] Elimination of MTCT for HIV infections is strongly supported by global commitments and the consistent promotion of preventative measures into maternal, newborn, child, and adolescent health services, as well as strengthening the health systems that are most impacted.[3] According to the UN AIDS Data Book, due to previous efforts by the Kenyan Ministry of Health and partner agencies, 91% of pregnant women living with HIV were already receiving antiretroviral therapy (ART) in 2021 yet, the rate of MTCT in Kenya remains unacceptably high at 8.9%.[4] With appropriate detection and subsequent ART, studies have shown MTCT to be as low as 1% when the mother began medication at conception and who had undetectable viral loads at delivery.[5] Although there has been increasing efforts in decreasing transmission of HIV at birth, there has been minimal research exploring the relationship between oral disease prevalence and ART in HIV

infected children (HIV) when compared to their HIV exposed, uninfected (HEU) and HIV not exposed, uninfected (HUU) peers.

It is widely accepted that transmission and subsequent HIV infection has various impacts on a child's overall health but there has been a lack of conclusive evidence in the overall prevalence and impact of oral diseases in children with HIV.[6] The literature supports that there is a wide range in reported prevalence (20-80%) of oral disease within the pediatric HIV population which is likely attributed to the varying degrees of HIV disease control.[7] The prevalence of oral manifestations tends to increase with higher viral load and/or reduced disease control.[8] A recent systematic review published in 2020 reported the most prevalent oral lesions cited included intraoral candidiasis, angular cheilitis, aphthous ulcers, HPV wart like lesions, herpetic lesions and hairy leukoplakia.[8] Contributing factors that may lead to oral manifestations include immunosuppression, decreased access or adherence to ART treatment, low socioeconomic status and difficulty accessing oral health resources. [8]The wide range in reported prevalence of oral manifestations in HIV infected children may suggest that HIV disease control through ART and modern treatment regimens may impact the oral health outcomes.[9]

The goal of our study was to explore the impact of HIV exposure and ART treatments on oral disease prevalence in 3-4-year-old Kenyan children. More specifically, our aim is to determine if HIV exposure status (HIV, HEU and HUU) has any impact on oral disease prevalence in the pediatric population. Our hypothesis predicts that children living with HIV have significantly higher prevalence of abnormal oral findings compared to the exposed uninfected and unexposed uninfected groups.

II. MATERIAL AND METHODS

Study design and population

This study was approved by the Institutional Review Board (IRB) at the University of Washington (UW) (FWA #000006878) and Jaramogi Oginga Odinga Teaching and Referral Hospital Ethics Review Committee (ISERC/JOOTRH/688/23;Kenya). The population consisted of 360 3- to 4-year-old children, recruited, and categorized by HIV

status into three cohorts: Cohort 1 (HIV-infected, HIV+, n=120), Cohort 2 (HIV-exposed uninfected, HEU, n =120), and Cohort 3 (HIV-unexposed uninfected, HUU, n=120). The children resided in west Kenya, in the county of Kisumu. Study eligibility criteria included being 3 or 4 years of age by the time of enrolment, getting a medical clearance from the primary care physician, residing in Kisumu County for the next 12 months from recruitment, child being capable of providing saliva samples and the HIV+ participants having been on antiretroviral therapy (ART) for a minimum of six 6 months. All caregivers were provided informed consent in the language of their preference (English, Swahili or Luo)

Recruitment and enrolment of participants

All participants were recruited and enrolled from April 2023 to November 2023. While HIV+ children were recruited from the HIV treatment clinics, the HEU cohort were identified through the local Prevention of Mother to Child Transmission (PMTCT) clinics, and the HUU were recruited from a pool of patients receiving wellness checkup appointments at the Mother Child Health (MCH) clinics within the same hospital and/or community health clinic. Initially, eligible participants were contacted via phone by each health site nurse and invited to participate in the study. When interested, caregivers were provided with transportation, then taken through the informed consent process. The parents who provided written informed consent for their children to participate in the study were then enrolled and a unique participant identification (PID) number was generated.

Training and calibration for oral health examinations

The oral examiner was a pediatric dentist who underwent calibration conducted by AK, a senior pediatric dentist with expertise in oral health research. This training included, but was not limited to, the diagnosis of oral manifestations of HIV, dental caries, dental trauma, dental fluorosis, dental erosion, the presence of dental plaque and gingival bleeding all using the diagnosis criteria by the World Health Organization. The Kappa score for inter- and intra-calibration achieved 0.95 for both assessments.

Data collection procedure

Saliva collection: To establish a standardized baseline, children were given water for hydration, considering the hot environmental temperatures in the study area. After a 30-minute waiting period to allow hydration and to normalize saliva composition, samples were collected. The pH of the saliva was assessed using Fisher brand plastic pH indicator strips. Subsequently, the specimen was placed in a cooler bag, a photo of the pH strip was taken, and the readings were recorded in the participant oral health assessment form.

Oral examination: The clinical examination included both extraoral and intraoral assessments which were completed in accordance with the WHO Oral Health Surveys and Record Form for Oral Manifestations of HIV/AIDS (WHO, 2018). The dental examinations were completed using a disposable mirror, overhead light and visual assessment. The extraoral and intraoral examinations assessed both soft and hard tissues. Briefly, a sequential examination of the teeth allowed for the identification of plaque accumulation, dental caries, dental trauma, dental fluorosis, missing teeth for other reasons, and other tooth-related pathologies. To evaluate gingival health, tooth brushing was performed, serving as a method for assessing gingival bleeding. All observations were recorded in the oral health assessment form.

Measured variables

Socio-demographic variables included the child's age, sex, school type (public or private), and residence (rural, urban, or peri-urban). Health-related variables were extracted from the child's medical records, and included HIV status (HIV+, HEU, HUU). For the HIV+, additional details were recorded, such as viral load, other medications, percentage adherence, duration on antiretroviral treatment, and information on initial and current ART regimen, including dosages.

Oral lesions were evaluated, considering their location, type, and size, including conditions such as candidiasis, salivary gland enlargement, and other common lesions observed in HIV-infected children. Dental hard tissues were examined for the presence or absence of dental caries, fluorosis, trauma, erosion, missing teeth for reasons other than caries, and other tooth related abnormalities. The study utilized the decayed-missing-filled surfaces

(dmfs) index for deciduous dentition, with the "m" component indicating missing due to caries. Only obvious cavitation was documented in this study. Trauma presence was categorized as 1=treated injury, 2=enamel fracture only, 3=enamel and dentine fracture, 4=pulp involvement, and 5=missing tooth due to trauma. Dental erosion scoring included 1=enamel lesion, 2=dentinal lesion, and 3=pulp involvement. Enamel fluorosis was categorized as normal=0, questionable=1, very mild=2, mild=3, moderate=4, severe=5, excluded due to crown restoration or bracket=8, and not recorded (un-erupted tooth) =9. Saliva pH was measured from the saliva specimen and appropriately documented for analysis.

Data analysis

We compared the demographics among three cohorts, HIV, HEU, and HUU, using a one-way ANOVA for continuous variables, such as age, and chi-square test for categorical variables, such as sex, school type, and living location. We reported the demographics that only applied to children with HIV infection. We compared oral diseases and saliva pH among the three cohorts, HIV, HEU, and HUU, using chi-square tests among cohorts and one-way ANOVA in the same fashion. Logistic regression models were used to estimate the association between oral diseases and cohorts, adjusted for sex, school type, and living locations. In addition, we used the same models to estimate the association of oral diseases and HIV treatment-related variables. All analyses were conducted using SAS 9.4. Statistical significance was determined at a p-value of less than 0.05.

III. RESULTS

Cohort characteristics

A total of 360 3-4-year-old Kenyan children participated in the study. The average age of the children was 3.4 years (SD = +/-0.5). Approximately half of the children were female (50.83%). The majority of the children attended private school (47.22%) compared to public school (21.67%) or no school (31.11%). Most of the children live rurally (48.60%) compared to urban (35.47%) or peri-urban (15.92%). Cohorts did not vary by age (p=0.3501), sex (p=0.7918) or location (p=0.6973). However, the type of school varied by

HIV status (p=0.0070) (Table 1). All the children within the HIV+ group (120) were receiving ART treatment. Of this group, all current treatment regimens were NRTI-based. However, previous treatment regimens varied with the majority being PI-based (65.00%) and the remaining being NRTI-based (35.00%). The overall duration of ART treatment ranged between 12 months or fewer to 49 months or greater, the majority having treatment between 25 and 48 months (61.66%). The average duration of ART treatment was 29.89 months (SD 14.38). The majority had a viral load of 50 copies/mL, deemed not detectable (65.00%) while the remaining had a viral load within 50-400 copies/mL (18.33%) or above 400 copies/mL (16.67%). The mean viral load was not able to be calculated due to incomplete reporting. Only 49 patients out of the 120 in the HIV group reported raw number for viral load. The majority of the children achieved adequate ART adherence defined as 90% or above (78.33%).

Oral disease prevalence by HIV status

Approximately half of the children had dental caries (51.11%) with the HIV group having the highest prevalence (56.67%) compared to the HEU (43.33%) and HUU (53.33%) cohorts (p = 0.0990) (Table 2). Similarly, the majority of the children had dental plaque (90.83%) with the HIV group also having the highest prevalence (93.33%) compared to the HEU (89.17%) and HUU (90.00%) (p = 0.4963). Gingival bleeding upon brushing was reported in 147 children (40.83%) with highest prevalence in the HIV group (45.00%) compared to the HEU (40.83%) and HUU (36.37%) (p = 0.4222). Children living with HIV had significant higher levels of abnormal findings (80.83%) compared to the HEU (60.00%) and HUU (54.17%) (p < 0.0001). These abnormal findings included the presence of submandibular lymphadenopathy, parotid gland enlargement, geographic tongue, general skin rash, perioral fungal infection. Distribution of enamel fluorosis, dental erosion, salivary gland swelling, angular cheilitis, herpetic lesions, HPV/wart-like lesions was not able to be calculated due to small sample size. Intervention urgency for dental and oral findings were determined based on three categories: routine/preventative needs, non-urgent treatment needs and urgent treatment needs (pain or infection). The majority of the children had routine/preventative needs (72.23%) compared to non-urgent treatment needs

(20.00%) and urgent treatment needs (7.78%) (p-value = 0.9075). Although the trends for mean dmft (3.4) and mean dmfs (5.9) scores were both higher in the HIV group, the values did not reach significance (p=0.0837, p=0.2434 respectively). There was no significant difference in salivary pH levels between the three groups with the mean reported at 6.7 (0.8) (p = 0.5086).

Association between characteristics of Kenyan children and oral findings

Multivariate logistic regression analysis indicated a 289% increased odds for abnormal findings (submandibular lymphadenopathy, parotid gland enlargement, geographic tongue, general skin rash or perioral fungal infection) and a 303% increased odds for all conditions (bleeding on brushing, abnormal findings or salivary gland swelling) in the HIV group compared to the HEU and HUU groups (Table 3, HIV $p < 0.0001$ and $p = 0.0002$, respectively). There was no significant association between HIV status and dental caries or bleeding upon brushing (Caries: HIV p=0.6687, HEU p=0.1020 and Bleeding: HIV p=0.2051, HEU p=0.5098). Prevalence of caries, bleeding, abnormal findings and all conditions did not significantly differ by sex or school. However, risk of abnormal findings and all conditions in the peri-urban location group was reduced by 70% and 65%, respectively (Table 3, p=0.0003 and p=0.0029).

Association among HIV treatment regimen characteristics and oral findings

We conducted regression analysis to identify variables related to presence of oral diseases. Among the HIV treatment group there was no association of child's sex (OR:2.08 95% CI:0.53, 8.05), duration of ART treatment (OR:1.71 95% CI:0.33, 9.01), past ART regimens (OR:0.35, 95%, CI:0.11, 21.09), viral load (OR:0.74, 95%, CI: 0.16, 3.32), adherence percentage (OR: 1.52, 95%, CI:0.11, 21.09) and use of other medications (OR: 2.63, 95% CI:0.70, 9.96) with oral findings including caries, bleeding, abnormal findings, and all conditions (Table 4).

IV. DISCUSSION

We aimed to analyze the baseline results of an ongoing longitudinal study on the impact of HIV infection and exposure on 3–4-year-old Kenyan children. The goal of this study was to determine the distribution of oral conditions by HIV exposure in young children and to identify factors associated with presence of oral diseases. Our findings confirm the hypothesis that children living with HIV have significantly higher prevalence of abnormal oral findings (80.83%) compared to the exposed uninfected (60%) and unexposed uninfected groups (54.17%) ($p < 0.0001$). These abnormal findings included the presence of submandibular lymphadenopathy, parotid gland enlargement, geographic tongue, general skin rash and perioral fungal infection. In a medically well-controlled cohort of HIV children, our results are significant at demonstrating that young children living with HIV have higher levels of oral diseases when compared to HEU and those without HIV infection.

The demographic characteristics in our study are well representative of the general Kenyan population. There are approximately equal sexes in the age bracket, with 69% attending pre-primary school (public or private) versus 31% attending no school (Table 1). According to the Kenya National Bureau of Statistics' most recent survey of 2023 it is estimated that there are 49.6% females in the 3-5 age group and 70.4% of these children in Kisumu county are attending either public or private pre-primary school.[10] According to the Society for International Development of Kenya, for children 14 years and under, approximately 36.5% live in urban setting versus 46.1% in rural areas which is adequately represented in our study with 35.5% and 48.6 % living in urban versus rural settings, respectively.[11] The characteristics of ART treatment in this study varied in duration of total treatment time and initial regimen type (NRTI vs PI-based). There have been recent concerns surrounding HIV drug resistance particularly with PI-based regimens, due to this, Kenya's first-line HIV treatment is NRTI-based remines.[12] In our study, the current regimen for 100% of HIV infected 3- to 4-year-old children is NRTI-based. The viral load (copies/mL) is a common measurement used to predict success in treatment adherence and subsequent clinical and immunological outcomes.[13] The goal of ART is to achieve adequate adherence ($\geq$95%) and maintain viral suppression (VL < 50 copies/mL or

undetectable).[13] Based on a cross-sectional study of adolescent HIV suppression rates in Sub-Saharan Africa, it was estimated that 73% of the children were virally suppressed while adequately taking ART.[14] In this study viral suppression was defined as viral load <1000 copies/mL which is stated to be a level that can still be detected and subsequently analyzed by testing.[14] This threshold was notably higher than our study's which defined successful viral load suppression <50 copies/mL and/or undetectable levels. This is important to note when considering our results as we reported 65% of our population had viral loads < 50 copies/mL and 18.3% between 50-400 copies/mL which in total represents 83.3% children in our study considered virally suppressed when comparing to thresholds used in other studies in the literature (VL <400 and VL< 1000 copies/mL).[14, 15] Adherence levels can be challenging to monitor for children. The most common and effective method of monitoring is to assess the number of missed doses which is reliant on the report from their caregiver.[15] Optimal adherence levels to achieve viral suppression are cited in the literature vary and range from ≥80% to ≥90%.[15] In our study we defined optimal adherence to be ≥95 in which 14% of our patient base reported to achieve. When using the levels in the current literature as comparison we can report that 78% of our patient based achieved optimal adherence which better reflects that 83.3% of the HIV children were able to achieve viral suppression of VL < 400mL/copies (Table 1).

The prevalence of abnormal oral findings in the HIV population varies by age. Studies from Mexico, Thailand, South Africa, Europe and North America reported that oral candidiasis is the most common finding in pediatric HIV patients.[16] Based on this literature it is unknown the extent in which these children had access to medical or dental resources nor their ART adherence levels, but it was suggested that in absence of explicit measurements of viral load and CD4+ cell counts (predictive for degree of immunosuppression), oral candidiasis and other oral lesions may be considered as strong indicators for HIV-associated immunodeficiency.[16, 17] Being that our findings differed from these prior studies in the literature in the prevalence of oral candidiasis it may suggest that our HIV study population had improved overall health outcomes due to access to HIV treatment and consistent medical care with the increasing efforts of the Kenyan HIV network of healthcare.

Although there was not a significant difference in dental caries prevalence amongst our three cohort groups, the HIV cohort had the highest prevalence (56.7% compared to the HEU (43.33%) and HUU (53.33)). Dental caries and periodontal disease are the two most common oral comorbidities among people living with HIV.[8] Current literature supports high caries prevalence in HIV-infected children when compared to the general population.[18, 19] Specifically, a meta-analysis published in 2015 reporting on dental caries rate in HIV-infected children and adolescents reported that had almost 200% increase odds of having dental caries in primary dentition when compared to non-infected children (OR: 2.98, 95% CI: 1.59,5.59, 9=0.0006).[19] From the same meta-analysis, there was insufficient data to conclude significant associations for permanent teeth.[19]

An additional factor to be considered in the increased dental caries prevalence for the HIV group is the mechanism in which they are taking daily ART medications. Successful adherence to ART medication is dependent on the child successfully consuming the oral medication which can be a barrier and challenge for their primary caregiver. It is known that the ART medications most commonly are formulated as a large pill or capsule and are bitter in taste.[20] Per the NIH guidelines for ART medications for pediatric patients, it is recommended to crush the tablet into 20mL of drinking water and swirl into suspension for the child to consume. These suspensions in water are often not palatable by children and are instead crushed with sweetened syrups to make more tolerable for consumption at this age.[20] Oral reports from our study population indicated that the crushed pill is mixed with raw sugar. Sweetened medications that are ingested frequently, as ART medications are, have been shown to contribute to increased dental caries and dental erosion in the pediatric population.[21] Longitudinal studies looking at the association between mechanism by which HIV medication is taken since birth and oral findings in the pediatric population would be beneficial in understanding this relationship.

The overall average dental caries prevalence for the 3-4-year-old children in our study was 51.1% which was higher when compared to the general Kenyan pediatric population reported by the latest Kenya Oral Health Review. The general pediatric population (5-, 12- and 15-year-olds) reported an average dental caries prevalence of 23.9% with the 5-year-old sub-population having the highest prevalence of 46.3% prevalence.[22] Of interesting

note, the prevalence of dental caries in the HEU group was markedly lower than the HIV and HUU groups. It is known that HIV-infected pregnant women in Kenya have access to various additional resources to help reduce to risk of transmission to the child.[23] Even if the child is deemed uninfected after birth, the access to health care resources continues. From a medical standpoint, follow up on the exposed and uninfected children is very important to determine if there are any adverse effects from the anti-viral medications the mothers may have been taking during pregnancy.[23] This increased access to care is most notably different when comparing to the healthy unexposed and uninfected cohort. The decrease in prevalence of dental caries within the HEU cohort could be attributed to the increasing initiatives to provide resources, maternal health education, along with increased frequency of medical exams to HIV infected mothers and subsequently their exposed and uninfected children.[4] These initiatives and programs to reduce mother to child transmission (MTCT) are notable in regions with highest rates HIV transmission which includes Kenya.[4] In direct comparison, the HIV infected group would have received similar access to these resources therefore suggesting the HIV infection itself plays a role in increased prevalence of abnormal findings regardless of access to resources and education.

Of interesting note, our study examiners interacting with the families at the clinic sites learned that the children born to mothers with HIV, that successfully prevented transmission to their child, were referred to as “miracle babies”. These children made up the HIV exposed, uninfected cohort. It was reported that these children were always well cared for and presented to each appointment in a timely manner, well-dressed and well-bathed. These observations potentially support the notion that the mothers and families of the HEU cohort utilized their access to resources to support the best possible outcomes for their children which may also translate the positive oral health outcomes discovered in this study.

We found a significant difference in the prevalence of oral diseases in the HIV cohort based on where children lived. There was a 70% decrease in abnormal findings and 65% decrease in all conditions for the HIV group living in a peri-urban location when compared to the HIV group living in an urban location. These findings suggest that living in a peri-urban location may be a protective factor against abnormal oral findings and all dental conditions.

The peri-urban region in developing countries is in the transition zone between urban and rural settings, typically located at the perimeter of an urban city.[24] Traditionally in Kenya, these areas were often home to poorer families with strained resources and markedly reduced access to healthcare leading to higher rates of infectious diseases, malnutrition and mortality.[25] Further, previous studies suggested that access to HIV treatment and subsequent adequate adherence and disease management in urban setting was significantly higher than in non-urban or rural settings. [26, 27]On the contrary, more recent evidence has suggested a shift in previously positive urban health outcomes with increasing disparities access to care and resources for families and youth living in highly population dense urban slum settlements.[28] It has been reported that HIV infection rates for the general Kenyan population is significantly higher in urban setting when compared to rural.[28] Further, there is a strong intra-urban difference in which HIV was 12% among slum residents compared with 5% and 6% among non-slum urban and rural residents, respectively.[28] More recent literature has suggested that there has been improved access to care in the peri-urban location due to efforts to provide mother-infant pairs with resources and early intervention for children born to HIV positive mothers.[29] This new evidence supports our findings that the HIV infected pediatric population living in peri-urban areas may be receiving increased healthcare resources and improved oral outcomes.

Although our study reports promising levels of viral suppression and adherence percentages within our pediatric HIV cohort, we still see increased prevalence of caries and significantly more abnormal oral findings when compared to the HEU and HUU cohorts. It is important to consider what other factors may be influencing the occurrence and progression of oral diseases among the HIV pediatric population. There is very limited data on how the oral microbiome, particularly antimicrobial peptides (AMPs) in children living with HIV may impact the presence of dental caries and other oral diseases. Historically, oral manifestations, particularly oral candidiasis, were used to early detection of treatment resistance and/or viral immunosuppression.[16] Now with increasing ART success and potential decreasing presence of pediatric HIV oral manifestations, it is important we continue to explore other screening tools that dentists and allied health professionals can use as early signs to initiate interventions when needed. In this study, we reported most abnormal findings to be lymphadenopathy (Table 2). Future studies should further analyze

if the presence of lymphadenopathy, parotid gland enlargement or other abnormal oral, head or neck findings can serve as reliable markers for immunosuppression in HIV infected pediatric patients. Future efforts may help dentists and other health care professionals more efficiently screen and subsequently intervene when explicit values like viral load and CD4 counts may not be accessible.

This study has several strengths and limitations to address. First, our study was cross-sectional. While we are only showing baseline assessments for this manuscript, this cohort of 360 children are being followed which will provide a robust understanding of the oral immune system in the context of HIV. Second, there was lack of consistency on medical data collection. In this study, we extracted medical data directly from health records rather than gathering information from caregivers, as such, we were limited by information registered such as viral loads, type and duration of ART regimen. To overcome these challenges, we decided to analyze data that was consistently present in health records. For viral load, we were able to present ranges and for medication regimens, we classified it by PI vs NRTI-based; yet, we were unable to determine the exact length of each ART medication nor how drugs were being taken (e.g. syrup, grounded pills mixed with raw sugar, etc.) and therefore we were not able to make conclusions on how formulations of ART impact oral health. Third, oral exams were completed in a non-dental clinic, thus the examining oral health providers relied on visual clinical findings without access to radiographs. Forth, we did not collect data on diet, caregiver education or socioeconomic status which all play a role in oral diseases. However, by conducting this study at the HIV clinics, we were able to merge within children's HIV medical care and therefore decrease burden of additional appointments for families and provide oral health awareness and emergency care (when needed) to our study population.

V. CONCLUSION

In conclusion, this study enriches the understanding of the complex relationship between pediatric HIV infection, ART medication and the prevalence of oral diseases in 3-4-year-old Kenyan children. We found that abnormal oral findings are significantly more

prevalent in the pediatric HIV population compared to children exposed to HIV but not infected and to children without HIV infection.

TABLES V

Table 1: Characteristics of Study Population

Variables	Total	HIV	HEU	HUU	*P Value*
	360	**120**	**120**	**120**	
Sex					
Female	183 (50.83)	58 (48.33)	63 (52.50)	62 (51.67)	0.7918
Age					
Months	3.4 (SD=0.5)	3.4 (SD=0.5)	3.4 (SD=0.5)	3.3 (SD=0.5)	0.3501
School					
Public	78 (21.67)	29 (24.17)	32 (26.67)	17 (14.17)	0.007
Private	170 (47.22)	46 (38.22)	52 (43.33)	72 (60.00)	
No school	112 (31.11)	45 (37.50)	36 (30.00)	31 (25.83)	
Location					
Urban	127 (35.47)	39 (32.50)	41 (34.17)	47 (39.83)	0.6973
Peri-urban	57 (15.92)	21 (17.50)	21 (17.50)	15 (12.71)	
Rural	174 (48.60)	60 (50.00)	58 (48.33)	56 (47.46)	
Duration of ART Treatment					

Variables	Total	HIV	HEU	HUU	*P Value*
	360	**120**	**120**	**120**	
12mo or less		20 (16.67)			
13-24mo		18 (15.00)			
25-36mo		37 (30.83)			
37-48mo		37 (30.83)			
49mo or more		8 (6.67)			
Past ART regimen					
PI-based		78 (65.00)			
NRTI-based		42 (35.00)			
Current ART regimen					
PI-based		0 (0.00)			
NRTI-based		120 (100.00)			
Viral load (copies/mL)					
VL <50, Not detectable		78 (65.00)			
VL 50-400		22 (18.33)			
VL 400+		20 (16.67)			
Adherence					

Variables	Total	HIV	HEU	HUU	*P Value*
	360	**120**	**120**	**120**	
≥95%		17 (14.17)			
90-94%		77 (64.16)			
<90%		26 (21.67)			
Other medications					
Septrin		30 (25.00)			
Anti-TB medication		3 (2.5)			
		Mean (SD)	Mean (SD)	Mean (SD)	
Duration of ART Medication			n/a		
Time in months		29.89 (14.38)			
Initial ART					
PI based regimen (only LPV/LPVR)		39 (32.5%)			
NRTI based regimen (all other meds)		81 (67.5%)			

*Mean viral load (copies/mL) unable to include due to incomplete reporting, only 49 patients out of 120 reported their raw values.

Table 2: Bivariate analysis of distribution of HIV status with oral diseases

Characteristics	Total	HIV	HEU	HUU	*P Value*
	360	**120**	**120**	**120**	
Oral Findings					
Dental caries	184 (51.11)	68 (56.67)	52 (43.33)	64 (53.33)	0.0990
Dental plaque	327 (90.83)	112 (93.33)	107 (89.17)	108 (90.00)	0.4963
Gingival bleeding at brushing	147 (40.83)	54 (45.00)	49 (40.83)	44 (36.67)	0.4222
Abnormal findings*	234 (65.00)	97 (80.83)	72 (60.00)	65 (54.17)	<0.0001
Enamel fluorosis		8	9	7	n/a**
Dental erosion		2	1	0	n/a**
Salivary gland swelling		3	2	0	n/a**
Other Oral Diseases					
Angular Cheilitis		1	0	3	n/a**
Herpetic lesions		1	0	0	n/a**
HPV/wart-like lesions		1	0	0	n/a**
Intervention Urgency					

Characteristics	**Total**	**HIV**	**HEU**	**HUU**	***P Value***
	360	**120**	**120**	**120**	
Routine/preventative needs	260 (72.23)	87 (72.50)	89 (74.17)	84 (70.00)	0.9075
Non-urgent treatment needs	72 (20.00)	25 (20.83)	21 (17.50)	26 (21.67)	
Urgent treatment needs (due to pain or infection)	28 (7.78)	8 (6.67)	10 (8.33)	10 (8.33)	
		Mean (SD)	Mean (SD)	Mean (SD)	
Salivary pH	6.7 (0.8)	6.7 (0.9)	6.8 (0.6)	6.8 (0.8)	0.5086
dmft score	2.8 (4.3)	3.4 (4.7)	2.2 (3.7)	2.9 (4.4)	0.0837
dmfs score	5 (10.5)	5.9 (11.2)	3.8 (8.6)	5.4 (11.5)	0.2534

*Abnormal findings include: submandibular lymphadenopathy, parotid gland enlargement, geographic tongue, general skin rash, perioral fungal infection

**Unable to calculate p-values due to too small of sample size

Table 3: Association among characteristics of Kenyan children and oral findings

Characteristics	Caries			Bleeding			Abnormal findings*			All conditions**		
	OR	95% CI of OR	P-value	OR	95% CI of OR	P-value	OR	95% CI of OR	P-value	OR	95% CI of OR	P-value
HIV Status												
HIV+	1.12	(0.67,1.88)	0.6687	1.4	(0.83,2.36)	0.2051	3.89	(2.13,7.09)	<.0001	4.03	(1.93,8.38)	0.0002
HEU	0.65	(0.39,1.09)	0.102	1.19	(0.71,2.01)	0.5098	1.34	(0.79,2.27)	0.2764	1.31	(0.73,2.35)	0.3651
HUU (ref)												
Sex												
Female	1.29	(0.85,1.96)	0.2403	1.13	(0.74,1.72)	0.5807	1.28	(0.81,2.03)	0.2851	1.21	(0.72,2.05)	0.4703
Male (ref)												
School												
No	1.03	(0.65,1.63)	0.8948	1.01	(0.64,1.59)	0.9825	1.04	(0.63,1.72)	0.867	1.09	(0.62,1.94)	0.759
Yes (ref)												
Location												
Rural	1.24	(0.78,1.97)	0.3582	0.75	(0.47,1.19)	0.2188	0.63	(0.38,1.04)	0.07	0.79	(0.44,1.42)	0.4281
Peri-urban	2.03	(1.09,3.79)	0.0253	0.78	(0.42,1.44)	0.4258	0.3	(0.16,0.57)	0.0003	0.35	(0.17,0.69)	0.0029
Urban (ref)												

*Abnormal findings include: submandibular lymphadenopathy, parotid gland enlargement, geographic tongue, general skin rash, perioral fungal infection
**All conditions include: bleeding on brushing, abnormal findings or salivary gland swelling

Table 4: Logistic Regression for HIV+ Cohort

Characteristics	Caries			Bleeding			Abnormal findings			All conditions		
	OR	95%	P value	OR	95%	P value	OR	95%	P value	OR	95%	P value
Sex												
Female	0.71	(0.33,1.54)	0.3887	1.08	(0.5,2.32)	0.8423	1.39	(0.53,3.63)	0.503	2.08	(0.54,8.05)	0.2901
Male (ref)												
Duration of ART Treatment												
12mo or less	5.06	(0.91,28.02	0.0633	0.22	(0.04,1.11)	0.0663	1.9	(0.26,13.97	0.528	0.2	(0.01,3.18)	0.2551
13-24mo	0.85	(0.19,3.77)	0.8302	0.72	(0.17,3.11)	0.6544	1.91	(0.25,14.92	0.5354	0.24	(0.01,5.73)	0.3794
25-36mo	0.9	(0.36,2.22)	0.813	1.05	(0.42,2.6)	0.9186	1.24	(0.41,3.75)	0.7007	1.71	(0.33,9.01)	0.5261
36+ (ref)												
Past ART regimen												
NRTI-based	2.63	(0.09,2.2)	0.3141	0.79	(0.62,13.4)	0.1795	0.76	(0.06,3.36)	0.4424	0.35	(0.11,21.09	0.7563
PI-based (ref)												
Viral load (copies/mL)												
VL <50, Not detectable	0.97	(0.36,2.59)	0.9533	1	(0.37,2.67)	0.9921	0.92	(0.28,2.96)	0.8834	0.74	(0.16,3.32)	0.6932

VL 50-400	3.45	(0.6,19.79)	0.1652	1.37	(0.27,6.9)	0.7025	5.18	(0.47,56.61	0.1779	***	***	***
VL 400+ (ref)												
Adherence												
<90%	0.44	(0.09,2.2)	0.3141	2.87	(0.62,13.4)	0.1795	0.46	(0.06,3.36)	0.4424	1.52	(0.11,21.09	0.7563
90% and up (ref)												
Other medications												
Septrin	0.87	(0.36,2.11)	0.7645	0.83	(0.34,2.04)	0.687	2.63	(0.7,9.96)	0.1534	***	***	***
No use (ref)												

*Abnormal findings include: submandibular lymphadenopathy, parotid gland enlargement, geographic tongue, general skin rash, perioral fungal infection

**All conditions include: bleeding on brushing, abnormal findings or salivary gland swelling

***Inadequate sample size for regression analysis

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