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ORIGINAL ARTICLE

Caries experience by socio-behavioural characteristics in HIV-1-infected and uninfected Ugandan mothers – a multilevel analysis

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ABSTRACT

Objectives: To assess caries experience in Ugandan mothers according to HIV status, socio-behavioural-characteristics, gingival bleeding status and to examine whether HIV status impacts the association of socio-behavioural characteristics with caries experience. Third, using multilevel analysis, this study assessed to what extent surface-specific caries experience varied between and within individuals.

Materials and methods: Caries experience was recorded using the World Health Organization's Decayed, Missed and Filled Teeth/Surfaces indices from a cohort of 164 HIV-1-infected Ugandan mothers and a cross sectional comparison group of 181 negative controls. Mixed-effects logistic regression was conducted with surface-specific caries experience as the outcome variable.

Results: The prevalence of caries in HIV-1-infected and uninfected mothers was 81% and 71%, respectively. Significant associations occurred between caries experience at surface level and women's increasing age (odds ratio [OR] = 1.8, 95% confidence interval [CI]: 1.1–2.8) and presence of gingival bleeding (OR = 2.0, 95% CI: 1.2–3.2). Intra-class correlation (ICC) coefficient amounted to 0.54 (95% CI 0.48–0.59).

Conclusions: Caries prevalence was higher in HIV-1 infected than in uninfected mothers and increased with age and gingival bleeding. ICC indicated that 54% of the variance was attributable to variation between individuals. Socio-demographic differences in dental caries did not vary by HIV-1 status.

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Introduction

Following the widespread implementation of highly active antiretroviral drug (HAART), studies have shown an increase in life expectancy as well as in the prevalence of HIV-1-infected people worldwide [1]. Sub-Saharan African countries are currently contributing 65% to the global total of 33 million people living with HIV-1 [2]. Although people with HIV-1 are particularly vulnerable to oral diseases, studies examining their dental caries experience have been rare [3]. Some studies have reported increased dental caries prevalence in children with perinatally acquired HIV-1 infection [4–6]. It is unclear, however, whether findings from those studies generalize to adult populations living with HIV-1/AIDS.

Evidence suggests that HIV-1 infection under HAART influences the oral microbiome composition, thus emphasizing the vulnerability of individuals with HIV-1 to oral microbial diseases [7]. Studies of children and adults have reported on strong associations between HIV-1 infection and oral mucosal lesions and periodontal disease [8–11].

Considering the association between HIV-1 infection and dental caries, findings have been inconsistent. No difference in dental caries was observed between uninfected and perinatally exposed HIV-1 uninfected children in Uganda [12]. A Nigerian study comparing three groups of pre-school children, reported higher caries prevalence in HIV-1 infected than in HIV-1 uninfected children, whereas no difference was found between HIV-1 uninfected and HIV-1 exposed uninfected, children [6]. A systematic review considering caries in the primary and permanent dentition of children with HIV-1 reported an increased risk of caries in the primary – but not in the permanent dentition [13]. Moscicki et al. [14] reported on higher caries prevalence in youth with HIV-1 compared with their exposed uninfected counterparts but no difference regarding periodontal disease. The Women's Interagency HIV Study (WIHS), which has the largest cohort of HIV-infected women in the United States, revealed significantly higher caries scores (number of decayed, missing filled teeth [DMFT]) in women with HIV compared to HIV negative women [15]. Moreover, reports reveal an increase in caries

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prevalence following HAART medication among people with HIV [16,17] and suggest that the prevalence of dental caries varies according to the type and length of medication taken [18]. A study in Uganda reported a caries prevalence of about 80% in HIV-infected adults, whereas the corresponding parameter in the general adult population was estimated to 67% [17].

Factors, such as xerostomia, microbial colonization, poor oral hygiene, periodontal disease and carbohydrate diet increase susceptibility to dental caries in HIV-1-infected adults in some studies [17]. Kumar et al. [11] and Soares et al. [19] reported on higher caries experience and higher prevalence of periodontal disease in HIV-1-infected patients of low – compared to higher socio-economic status. There is still uncertainty regarding the relationship between socio-economic status and oral disease prevalence and whether social inequality in oral health varies between HIV-1-infected and uninfected individuals.

There is a paucity of studies considering the prevalence and socio-behavioural covariates of dental caries among adults with HIV-1 in Sub-Saharan Africa. Most previous studies have considered individuals attending HIV care clinics and many have omitted adequate comparison groups of uninfected individuals [16–18,20]. Studies examining dental caries generate multiple outcome data. While studies examining and comparing caries data among different populations and subgroups (HIV-1 infected as an example) often report multiple outcomes, very few undertake multilevel modelling analysis for hierarchically clustered data such as in dentition where tooth surfaces are clustered within a single tooth. The teeth are also clustered within mouth quadrants and jaws in an individual.

Ignoring that tooth surfaces are clustered within teeth and that teeth are clustered within individuals by using classic statistical methods might provide biased regression estimates and underestimated standard errors [21]. A large UK survey compared the multilevel model with a simple ordinary logistic regression model, and showed that values of effect size were 4–5 times lower and standard errors of the effect size 2.3 times lower in the multilevel model compared to the ordinary logistic regression model [22]. Also, Gülcan et al. [23] demonstrated that ordinary logistic regression would have overestimated precision of estimates compared with multilevel models.

This study sought to assess caries experience in Ugandan mothers according to HIV-1 status, socio-behavioural characteristics and gingival bleeding and examine whether HIV-1 status impacts the association of socio-behavioural characteristics with caries experience. Using multilevel analysis, this study also assessed to what extent surface-specific caries experience varied between and within individuals.

Methods

This study used data from a trial cohort and a cross-sectional comparison group. The trial cohort included women with HIV-1 residing in the Ugandan site (Mbale, Eastern Uganda) of the multi-centre efficacy trial ANRS12174 PROMISE-PEP trial (ClinicalTrials.gov, number NCT00640263). The ANRS12174 PROMISE-PEP trial was described in detail previously [24]. The trial conducted between 2009 and 2013, was a multi-centre randomized trial including pregnant women with HIV-1, recruited at a gestational age of 28–40 weeks at antenatal clinics in four African sites; Ouagadougou, Burkina Faso; East London, South Africa; Mbale, Eastern Uganda; and Lusaka, Zambia. HIV-1-infected pregnant women were referred for further assessment of inclusion criteria and again with their HIV uninfected children for enrolment at day 7 postpartum. The 7-day old uninfected children were randomized to receive lopinavir–ritonavir or lamivudine in order to assess the efficacy for mother to child transmission inclusion criteria for mother were age 18 years or older, intention to continue breastfeeding, being HIV-1 infected, and not being eligible for ART (either clinically or because CD4 count >350 cells/μL at that time). All eligible mothers and infants followed the routine PMTCT with antepartum zidovudine (ZDV), intrapartum nevirapine (NVP), ZDV-lamivudine (3TC) for mothers and NVP for infants 7 d postpartum.

In 2017, 244 out of 278 mothers with HIV-1 infection and their uninfected children were eligible for re-enrolment in the follow-up study: the PROMISE-PEP Mechanism Safety study (PROMISE-PEP M&S ANRS12341). A total of 67.2% of the HIV-1-infected mothers (164/244) and their HIV-1 exposed uninfected children (HEU) were followed up leaving 32% ($n = 112$) lost to follow-up. A comparison group of 199 HIV-uninfected mothers whose uninfected children had been matched on age and sex, to the trial children were recruited from communities located in Mbale, Eastern Uganda, which was the site for the ANRS12174 PROMISE-PEP trial. Of the 199 mothers, 19 were excluded due to a positive HIV-1 test result, leaving 181 mothers for comparison.

This study is based on information from interviews and clinical oral examinations of the 164 HIV-1-infected mothers participating in the follow-up study, of the PROMISE-PEP Mechanism Safety study (PROMISE-PEP M&S ANRS12341) and 181 HIV-1-uninfected mothers recruited in 2017. The inclusion criteria for the mothers with HIV-1 was having a child that maintained an HIV-negative status since the end of the PROMISE-PEP trial. Inclusion criteria for the control mothers were having an HIV-negative result and having an unexposed uninfected child that was matched according to age and sex with the HIV-1 exposed uninfected child from the PROMISE-PEP trial.

Interviews with HIV-1-infected mothers and HIV-1 negative controls

Trained interviewers performed face-to-face interviews with mothers using semi-structured interviews in one of the local Ugandan languages, Lumasaba. The interview was constructed in English and translated into Lumasaba for use in the field. The schedule had been reviewed previously by project staff for semantic, experimental and conceptual equivalence of the source version [24,25]. Sensitivity to culture and selection of appropriate words were considered. Mothers responded to questions about themselves and their children. Information was documented on case record forms (CRFs) and electronically

with Capture software System (Clinsight) and Epidata program www.epidata.dk for the clinical oral examinations.

Socio-demographic characteristics of caretakers were assessed in terms of the level of education, type of income and marital status. Level of education was categorized into 'did not finish primary school (1), end of primary school (2) higher education' (3). Marital status was categorized: 'divorced (1), cohabiting/married (2), single (3), widowed' (4) and recoded into single/divorced/widow (0) and married/cohabiting (1). Mother's behavioural characteristics were assessed in terms of tooth brushing frequency recoded as 'once a day or less' and 'more than once a day' and frequency intake of sugared snacks recoded as 'at most occasionally and at least once a day'. Type of income was assessed in terms of (1) no regular income (2) regular income. Mothers' perceived health was assessed as very poor (1), poor (2), fair (3), good (4), very good (5).

Clinical oral examination

Two experienced and calibrated dental surgeons (NB and MM) performed oral assessments among the study participants and duplicated full-mouth oral clinical examination among HIV-1 positive and HIV negative mothers not included in the main study. The calibration exercise, comparing DMFT scores within and between examiners, revealed Cohen's Kappa values for intra- and inter-examiner reliability of 0.7 (95% CI: 0.5–0.9) and 0.6 (95% CI: 0.4–0.8), respectively.

Caries experience (outcome variable) was assessed on surface and tooth level (five surfaces per tooth) in terms of decayed (D), missing (M), and filled (F) surface/teeth (DMFS/DMFT) in accordance with the World Health Organization (WHO) guidelines for field conditions [26]. Each surface was recoded 0 for sound and 1 for caries experience and documented as decayed if it was visually cavitated with the aid of a dental mirror and periodontal probe. A surface was recorded filled when treated and a tooth was recorded missing when extracted due to caries, as confirmed by the participant. To assess gingival bleeding of the individual, the modified community periodontal index (CPI) was used [26]. Each tooth was scored according to the presence or absence of gingival bleeding, using a periodontal probe across the gingival margins of the teeth. An individual score of 'presence of gingival bleeding' was given if bleeding on probing was scored for at least one tooth in the mouth.

Maternal HIV-1 status of HIV-1 uninfected controls

Mothers in the comparison group were tested for their HIV-1 status using serial and parallel HIV-1 rapid testing with Determine, Stat-Pak and Uni-Gold, three test algorithms as recommended by the Ugandan Ministry of Health [27].

Statistical analysis

STATA SE version 16 (College Station, TX 77845 was used for data analysis. Cross tabulation with chi-square tests for categorical variables and two-sample t-tests for continuous variables were used to assess the crude associations of the outcome variables (DMFT/S) with HIV-1 status (main exposure). Surface-specific dental caries data have a clustered 3-level hierarchical structure with surfaces (level 1) clustered within the tooth (level 2) and teeth clustered within individuals (level 3). Using surface-specific measures of caries as independent observations and ignoring that observations are clustered and correlated within individuals will lead to an underestimation of the standard errors, too narrow confidence intervals (CIs) and higher type 1 error rates. In this study, the researchers first applied ordinary logistic regression with aggregated measures of DMFT as a dichotomized outcome variable (DMFT $= 0$, DMFT > 0). Then also analysed dental experience as a count variable using negative binomial regression analysis. Socio-behavioural and clinical covariates statistically significantly associated both with HIV-1 status and the outcome variable DMFT were included in the logistic regression models as potential confounding variables. Second, the researchers applied caries on all observed tooth surfaces within individuals. This was done using a random intercept model (RIM) (random intercepts for teeth and individuals) using mixed-effect logistic regression with the melogit package within the Stata program version SE 16 fitted for caries experience. Due to the high correlation of caries on a surface level, a three-level model including random intercepts for both individuals and teeth could not be fitted. Thus, we fitted a two-level model with caries at surface level correlated within individuals. Relationships between outcome and covariates were assumed with all the cluster regression lines having a fixed slope and different intercepts. The effect of dependency of caries on surface level within an individual was assessed by calculating intra-class correlation (ICC) coefficients. The ICC expresses variations between individuals as a proportion of the total variance. ICC varies from 0, which implies that caries is independent within individuals to 1 indicating no variation of caries within the individual. A likelihood-ratio test was applied to test if ICC equals 0. A statistical significance implies that the multilevel model is preferable. p Values less than .05 were considered statistically significant.

Ethics approval and consent to participate

Ethical clearance was obtained from the School of Medicine Research and Ethics committee, Makerere University (SOMREC)-REC – 030, Uganda National Council of Science and Technology (UNCST)-HS 2373 and the Regional Committee for Health and Medical Research (REK) – 2017/760/REC sør-øst C from Norway.

Results

A total of 164 HIV-1-infected (mean age [standard deviation, sd]; 35.2 [7.9]) and 181 HIV uninfected mothers (mean age [sd]; 31.6 [7.9]) were interviewed and examined for dental caries and gingival bleeding. A total of 162 participants (50%) were younger than 33 years. Prevalence of individuals with decayed teeth (i.e. the proportion of individuals with

Table 1. Socio-demographic, clinical, and behaviour characteristics of mothers by HIV-1 status in the Ugandan part of the PROMISE-PEP-M&S study.

	HIV-infected ($n = 164$)	HIV-uninfected ($n = 181$)	Total ($n = 345$)
Mothers characteristics			
Continuous variables			
Mean age (standard deviation)	31.6 (7.9)	35.2 (7.9)**	32 (8.2)
Median age (interquartile range)	35 (30–40)	31 (25–38)	33 (28–38)
Categorical variables	% (*n*)	% (*n*)	% (*n*)
Age			
18–32 years	40 (58)	58 (104)	50 (162)
33+	60 (90)**	42 (76)	50 (166)
Toothbrush			
Once a day or less	59 (97)	44 (78)	51 (175)
More than once a day	40 (66)	56 (99)**	48 (165)
Sugared snacks			
At most occasionally	92 (151)	88 (159)	90 (310)
At least once a day	8 (13)	12 (21)	10 (34)
Marital status			
Single/divorced, widow	26 (43)	18 (33)	22 (76)
Married/cohabiting	74 (121)	82 (147)	78 (268)
Type of income			
Not regular	60 (98)	72 (130)	66 (228)
Regular	49 (65)	28 (51)*	34 (116)
Educational level			
Primary school	38 (54)	40 (65)	38 (119)
End of primary school	20 (28)	22 (37)	21 (65)
Middle school/high school/college	42 (59)	38 (63)	40 (122)
DMFT			
DMFT =0	19 (31)	29 (52)	24 (83)
DMFT > 0	81 (133)	71 (129)*	3 (4.3)
DMFT count range (1–28)	5 (5.3)	3 (3.2)	76 (264)
DT > 0	76.2 (125)	46 (84)	61 (209)
DMFS			
DMFS = 0	22 (37)	54 (29.8)	26 (91)
DMFS > 0	77 (127)	70 (127)	74 (254)
DS > 0	93 (51)	120 (73.2)	62 (213)
Mothers health			
Bad/fair	35(57)	18 (33)	26 (90)
Good/very good	82 (147)	65 (107)**	74 (254)
Presence of gingival bleeding			
No	35 (58)	56 (102)	46 (160)
Yes	64 (105)	44 (79)**	54 (185)

Numbers do not add to 345 in the various cells due to missing responses.
*$p<.05$; χ^2 test, **$p<.001$; χ^2 test.

DMFT > 0) was 61.0%. The distribution of participants' socio-demographic, behaviour and clinical characteristics according to mothers' HIV-1 status are presented in Table 1. Age, type of income, mothers' perceived health, gingival bleeding and caries experience varied statistically significantly (all $p < 0.05$) according to HIV-1 status. Mothers with HIV-1 were more frequently older than 33 years of age, were less likely to brush teeth more than once a day, less likely to be married and more likely to have regular income compared to HIV negative controls. Mothers with HIV-1 were more likely to express bad perceptions of health and to present with gingival bleeding.

Table 2 depicts percentage distribution, odds ratios (ORs) with 95% CIs for dental caries experience (DMFT > 0) by HIV-1 status and socio-behaviour and clinical covariates. Significant crude associations were observed between caries experience and HIV-1 status, educational level, perceived health and gingival bleeding. Caries experience differed statistically significantly between HIV-1-infected and non-infected mothers with 81% and 71% having DMFT > 0, respectively. Moreover, 82% *versus* 69% of mothers with and without gingival bleeding presented with DMFT > 0. Adjusted ordinary logistic regression analysis revealed that HIV-1-infected mothers were more likely than their HIV-1 negative counterparts to experience DMFT > 0 (OR = 1.8, 95% CI: 1.0–3.4). Mothers with higher education (high school and college) were more likely to experience DMFT > 0 than their lower educated counterparts (OR = 1.9, 95% CI: 1.0–3.6). Moreover, mothers with gingival bleeding were more likely than mothers without gingival bleeding to present with caries experience (OR = 2.1, 95% CI: 1.1–3.8). The negative binomial regression analysis revealed findings in a similar direction as those in the logistic regression (Table 2). Two-way interaction terms between HIV-1 status and each of the socio-demographic, behaviour and clinical covariates were added to the regression model after adjustment for the main effect of the variables included in the multiplicative constructs. No significant interactions were observed.

Table 3 depicts the fixed effects on surface-specific caries of mothers' HIV-1 status, socio-demographic factors, gingival bleeding, tooth groups and type of tooth surfaces. In the multilevel logistic regression analysis, a total of 46,095 surfaces and a mean number of 158 (range 140–160) surfaces per individual were analysed. The multilevel model revealed significant positive associations between caries and women older than 33 years of age (OR = 1.8, 95% CI: 1.1–2.8), and

Table 2. Mothers' dental caries experience according to HIV status, socio-demographic and behaviour/clinical characteristics.

Mothers characteristics	Cross tabulation	Adjusted ordinary logistic regression DMFT > 0	Adjusted negative binomial regression DMFT count minimum–maximum range (1–28)
HIV-1 status	% (*n*)	OR (95% CI)[a]	IRR[b] (95% CI)
HIV-1 uninfected	71 (129)	1	1
HIV-1 infected	81 (133)*	1.8 (1.0–3.4)	1.6 (1.1–2.2)
Age			
18–32	72 (117)	1	1
33+	79 (132)	1.5 (0.8–2.7)	1.2 (0.9–1.7)
Marital status			
Single/divorced, widow	79 (60)	1	1
Married/cohabiting	75 (202)	1.0 (0.6–2.1)	1.1 (0.7–1.6)
Type of income			
Not regular	67 (175)	1	1
Regular	33 (86)	0.9 (0.5–1.8)	1.0 (0.8–1.2)
Educational level			
Primary school	74 (88)	1	1
End of primary school	71 (46)	0.8 (0.4–1.8)	0.9 (0.6–1.3)
Middle school/high school/college	82 (100)	1.9 (1.0—3.6)	1.2 (0.8–1.7)
Gingival bleeding			
Not present	69 (110)	1	1
Present	82 (152)**	2.1 (1.1–3.8)	1.4 (1.1–2.0)

Crude analysis and adjusted ordinary logistic and negative binomial regression ($n = 345$).
Numbers do not add to 345 in the various cells due to missing responses.
*$p<.05$; χ^2 test, **$p<.001$; χ^2 test, [a]odds ratio 95% confidence interval, [b]incidence rate ratio.

Table 3. Mothers' dental caries experience according to HIV-1 status, age, marital status, education, gingival bleeding, tooth groups and surfaces.

Mothers characteristics	Adjusted melogit DMFS > 0
HIV-1 status	OR (95% CI)[a]
HIV-1 uninfected	1
HIV-1 infected	1.4 (0.8 –2.2)
Age	
18-32	1
33+	1.8 (1.1–2.8)
Marital status	
Single/divorced, widow	1
Married/cohabiting	1.1 (0.6–2.0)
Type of income	
Not regular	1
Regular	0.9 (0.5–1.6)
Educational level	
Primary school	1
End of primary school	0.8 (0.4–1.4)
Middle school/high school/college	1.2 (0.7–2.1)
Gingival bleeding	
Not present	1
Present	2.0 (1.2–3.2)
Tooth group	
Premolars	1
Molars-maxilla	7.4 (6.6–8.3)
Molars-mandibular	17.0 (15.2–18.2)
Incisor	0.5 (0.4–0.7)
Surfaces	
Buccal	1
Distal	1.1 (0.9–1.2)
Mesial	1.1 (0.9–1.2)
Occlusal	0.9 (0.8–1.1)
Palatal/lingual	2.7 (2.4–3.0)
ICC within subject (adjusted for covariates)	0.54 (0.48–0.59)
Random effect	3.8 (3.0–4.8)
Model fit	4297.60; $p<.0000$
AIC	18,498.95

Multilevel analysis (melogit) allowing for clustering at individual level ($n = 46{,}095$).
Values are person-specific estimates adjusted for tooth group, surfaces and individual-level covariates calculated using a melogit multilevel regression model with a random intercept.
[a]Odds ratio (95% confidence interval).

between caries and presence of gingival bleeding (OR = 2.0, 95% CI: 1.2–3.2). Compared to premolar teeth, caries was more likely to occur in maxillary molars (OR = 7.4: 95% CI: 6.6–8.3), mandibular molars (OR = 17.0, 95% CI: 15.3–18.2) and less likely to occur in incisors (OR = 0.55, 95% CI: 0.46–0.66). Compared to buccal surfaces, caries experience was more likely (OR = 2.7, 95% CI 2.4–3.0) to occur at the buccal surface. The ICC estimate for individuals (level 3) amounted to 0.54 (95% CI 0.48–0.59), indicating that 54% and 46% of the variance in caries experience was attributable to variation between and within individuals, respectively. The likelihood ratio test confirmed that ICC was different from zero and that a two-level model is justified and an appropriate approach to the present data ($p=.001$).

Discussion

This study is among the first to report on caries experience in HIV-1-infected mothers as compared to HIV-1 negative controls living in a similar non-occidental socio-cultural setting. The prevalence of caries experience and gingival bleeding was high among both HIV-1-infected and uninfected mothers amounting to 50% or above. Regression analyses revealed marginally significant odds of caries experience at the individual level for mothers who were HIV-1 infected, having higher education, caries experience and gingival bleeding. Multilevel analyses of surface-specific caries revealed significant odds for mother's age and gingival bleeding status as well as for tooth-specific characteristics. Socio-behavioural inequalities in dental caries experience were less marked, nor did socio-behavioural inequalities in dental caries differ between HIV-1-infected and uninfected mothers. We conclude that a multilevel RIM is appropriate and efficient for analyses of dental caries data in the context of HIV-1-infected Ugandan mothers. It improves the standard logistic regression approach by the inclusion of covariates at the surface- and tooth level. A significant amount of variability was attributable to the between individual-level implying that carious surfaces and teeth were more highly correlated within than between mothers. Although we aimed to fit a 3-

level model with surfaces nested within teeth and teeth nested within individuals, there was hardly any variation of caries at tooth level.

Major strengths of this study are the use of novel statistical methods accounting for dependency in observations within individuals as well as strict characterization of HIV-1 status and use of community controls [21]. Whereas multilevel models are well established in medical research, their application is limited in dentistry [23,28,29]. Previous studies using a multilevel approach have been performed, most commonly, in the field of periodontology [30]. Yet, few studies are available utilizing multilevel analysis with hierarchically structured caries data [22]. A benefit of multilevel analysis is the possibility to separate variance estimates at different levels, allowing for estimation of ICC at the individual and tooth level. This offers the advantage of more information on caries patterns within an individual. This study utilized both ordinary- and mixed-effect logistic regression models, providing comparable results and thus confirming inequalities in mothers' caries experience at individual and surface levels. Some limitations should be considered when interpreting our findings. The lack of statistically significant association of HIV-1 status with caries experience in the multilevel analysis as depicted in Table 3 might be attributed to limited statistical power. Mixed and random effect models are computationally intensive. It is possible that caries prevalence in HIV-1-infected mothers is underestimated since only HIV-1-infected mothers passively followed-up were included in the analyses and those who might have died before follow-up examination in 2017 were not part of the group analysed in this study. Self-reported information from interviews might be biased by recall and social desirability bias. In addition, the assessment of gingival bleeding using an objective gingival inflammation index would have led to more reliable results regarding the status of gingival bleeding. Due to the particular study design, matching HEU children originating from the ANRS 121,741 PROMISE-PEP trial (ClinicalTrials.gov, number NCT00640263) with unexposed controls in 2017, their respective HIV-1 infected and HIV uninfected mothers could not be matched accordingly. Also, due to the cross-sectionally recruited control group, we had single assessments of oral health outcomes and co-variates and thus could not make causal inferences.

The prevalence of dental caries was high in this study population and matched previous estimates in the general Ugandan adult population [31]. This supports evidence that the HIV-1 epidemic in low-income countries seems to be more generalized across the socio-economic spectrum, suggesting that HIV-1 positive and negative mothers are socio-economically comparable [32]. In this study, however, HIV-1-infected mothers seemed to be at higher risk of developing dental caries compared to the uninfected controls. Although a specific measure of the duration of HAART medication was not available, in this study, HIV-1-infected mothers who were follow-up participants from the PROMISE PEP trial had been on systematic HAART medication for more than 6 years. Studies focussing caries among HIV-1-infected adults on HAART have not yet identified any specific trend [17,18]. However, a recent Ugandan study reported an increased prevalence of dental caries according to the longer duration of HAART medication [17]. Independent of mothers' HIV-1 status, findings from the multilevel analysis indicated higher odds of caries in maxillary and mandibular molar teeth and lower odds in incisor teeth as compared to premolars. This is new information among HIV-1-infected mothers. In this study, mandibular molars surfaces were even more susceptible than maxillary molar surfaces, indicating that factors commonly associated with caries, such as xerostomia, diet or type of HAART affect the mandibular caries more than maxilla. Moreover, it supports evidence in the general uninfected populations that caries varies according to different surfaces groups of teeth within individuals. Batchelor and Sheiham investigated the susceptibility of groups of teeth surfaces to caries among 5–16-year-old children and found a fixed hierarchy indicating that tooth surfaces show variation in caries susceptibility [33].

Although not statistically significant in multilevel analysis, it is important to discuss the positive association between high education and caries experience. This is contrary to previous findings among Ugandan adults living with HIV-1 showing an expected negative relationship between higher education and dental caries [17]. In support of the present findings are studies from Africa showing a higher prevalence of dental caries in people from less poor-compared to very poor households [34]. It is possible that the coding with only three categories might have failed to capture the effect of education very well. It is also possible that this association reflects a higher F component among higher than lower educated since the highly educated might be those most frequently using dental care services.

A positive association between gingival bleeding and dental caries accords with other findings reporting on a higher probability of dental caries in people with poor than with good oral hygiene [22,35]. While it appears that HAART reduces saliva flow with above 80% of the prescribed HAART medications causing xerostomia [18], HIV-1 infection might also decrease saliva irrespective of medication [18,36]. Salivary gland hypofunction, xerostomia and HAART medication are among the most important risk factors of dental caries and periodontal disease in HIV-1-infected people.

The HIV epidemic of Uganda is described as a generalized type, meaning that it cuts across all socio-economic groups in the population which is contrary to other countries where HIV infection is limited to specific groups (like sex workers or same-sex partners). For this reason, we could assume the finding to be generalizable to Uganda or a setting with the same HIV-1 distribution in the population.

In conclusion, caries prevalence was higher in HIV-1-infected than in uninfected mothers and increased with age and gingival bleeding. ICC indicated that 54% of the variance was attributable to variation between individuals. Socio-demographic differences in dental caries did not vary by HIV-1 status. We recommend that oral care and preventive strategies are included in health care programmes of HIV-1 infected as well as in uninfected Ugandan mothers. Moreover, we recommend more observational studies from

low-income settings with larger sample sizes comparing the oral health status of HIV-infected persons and community controls to further clarify oral health situation.

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Disclosure statement

The authors declare no competing interests.

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Author contributions

NB, ANÅ, IMSE JKT, LTF and SAL made contributions to conception and design of the study. NB, ANÅ and JKT contributed to data acquisition. NB, ANÅ, IMSE, JKT, LTF and SAL analyzed, interpreted, drafted, and gave final approval to this version of the manuscript.

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