ISSN: 2469-5734

Motlokwa et al. Int J Oral Dent Health 2023, 9:153
DOI: 10.23937/2469-5734/1510153
Volume 9 | Issue 2
Open Access

International Journal of
Oral and Dental Health

RESEARCH ARTICLE

# Prior Treatment for Tuberculosis is Associated with Salivary Gland Dysfunction in People with HIV

***Precious Kefilwe Motlokwa*[1,2*], *Billy M Tsima*[2,3] *and Robert Gross*[2,3]**

[1]*Princess Marina Hospital, Botswana*

[2]*University of Pennsylvania, USA*

[3]*University of Botswana, Botswana*

***Corresponding author:** *Precious Kefilwe Motlokwa, BchD, MSCE, Princess Marina Hospital, P.O Box: 71855881, Virtual post box, Squaremart, Gaborone, Botswana, Tel: 00270646426020*

## Abstract

**Background:** Since the introduction of combination antiretroviral therapy, several studies have reported an increase in salivary gland diseases and high prevalence of xerostomia and salivary gland dysfunction among people with HIV. Despite the extensive research on HIV there are few studies investigating its relation to salivary glands functionality.

**Methods:** Cross-sectional study was conducted from February 2021 to June 2021 at an HIV clinic in Botswana to determine the prevalence and risk factors of salivary gland hypo function among people with HIV. Salivary hypo function was defined as whole unstimulated saliva of < 0.1 ml/minute using the University of California School of Dentistry guidelines for saliva collection. Xerostomia was assessed using the Summated Xerostomia Inventory-Dutch Version questionnaire.

**Results:** Out of 400 enrolled participants 65% were female with a mean age of 41.94 (SD 12.26, IQR: 35-50). Prevalence of salivary gland hypo function and xerostomia were 4% and 7% respectively. In the adjusted multivariable model salivary gland hypo function was significantly associated with age and history of TB treatment.

**Conclusion:** Current study has identified history of TB treatment and younger age as a risk factors for salivary gland dysfunction in PWH. The findings prompt for further research to determine the relationship between TB treatment and salivary gland hypo function.

## Keywords

Salivary gland hypo function, HIV, Tuberculosis, Combined antiretroviral therapy (cART)

## Introduction

Since the advent of effective combination antiretroviral therapy (cART), there has been a significant decline of oral diseases in people with HIV (PWH) [1]. Yet, numerous studies have reported an increase in salivary gland diseases [2] with prevalence ranging between 2%-10% and in some studies as high as 80% [1,3]. Many studies have reported a significantly higher prevalence of xerostomia (subjective complaint of oral dryness) and salivary gland hypofunction (objective evidence of decrease in salivary flow) among PWH [3]. Decreased salivary flow increases the risk of dental caries, periodontal disease, and fungal infection, ultimately leading to tooth loss. Dry mouth also affects quality of life as it alters taste, affects chewing, swallowing and speech [3]. Systemic conditions such as tuberculosis (TB) have been documented to affect the salivary glands by granulomatous formation in the affected gland [4]. Primary TB affects the parotid most frequently whereas secondary TB is commonly seen in the submandibular and sublingual glands [5]. It has been hypothesized that TB affects the salivary glands through existing tooth or tonsillar infection, subsequently presenting as acute inflammatory or chronic tumorous lesions [5]. Despite the extensive research on HIV there are few studies investigating its relation to salivary glands functionality.

## Methods

We conducted across-sectional study to determine

**Citation:** Motlokwa PK, Tsima BM, Gross R (2023) Prior Treatment for Tuberculosis is Associated with Salivary Gland Dysfunction in People with HIV. Int J Oral Dent Health 9:153. doi.org/10.23937/2469-5734/1510153

**Accepted:** May 01, 2023: **Published:** May 03, 2023

the prevalence and risk factors associated with salivary gland hypofunction and xerostomia in patients on cART at Scottish Livingstone Hospital in Molepolole, Botswana from February 2021-June 2021.

Informed consent was sought from participants who were 18 years and older attending HIV care. Patients with known causes of salivary gland dysfunction, including Sjogren's syndrome and receiving head and neck radiation were excluded. The study was approved by the Ministry of Health, Scottish Livingstone Hospital and University of Pennsylvania Committees on Human Subjects Research.

Saliva was collected as per University of California School of Dentistry guidelines for saliva collection [6]. Saliva flow rate was calculated as: Post weight measure minus pre-weight measure divided by collection period and reported in ml/minute.

Data was abstracted in to REDcap database, analyses were performed using STATA 14 software (STATA Corp. College Station, TX). Salivary hypofunction was the primary outcome, defined as a rate of whole unstimulated saliva of < 0.1 ml/minute [6] and xerostomia was measured using the summated xerostomia inventory-Dutch Version questionnaire [7]. Salivary gland hypofunction was a dichotomous variable Yes/No. Participant's social habits including smoking and alcohol use were assessed using a questionnaire and measured as Yes/No. Medical history data including history of hepatitis C, use of anti-diabetic and anti-hypertensive, latest CD4 count, viral load, and cART regimen were collected. Data normality was assessed using skewness and kurtosis test and visualization of plots. For univariate analysis, chi square test was used to evaluate the difference in categorical variables. Student's t-test or the Wilcoxon Rank Sum test was used for continuous variables depending on data distribution. Multivariable logistic regression was used to control for confounding. Potential confounders included age, sex, CD8 count and history of TB treatment. Statistical tests were two-sided, and P-value ≤ 0.05 was considered statistically significant.

## Results

Table 1 summarizes baseline characteristics of the cohort according to salivary gland function. Out of the 400 enrolled, 17 (4%) and 27 (7%) had salivary hypo function and xerostomia, respectively 0.258 (65%) were female with a mean age of 41.94 (SD 12.26, IQR: 35-50). 379 patients were on dolutegravir based cART regimen with a median of 9 years (IQR 6-14) on ART and-the remainder were on efavirenz-based cART. A substantial proportion, 59 (15%) had a history of TB treatment. Those with salivary gland dysfunction were younger (mean age; 35.53, IQR 21-49) than those without dysfunction (mean age; 42.23, IQR 35-51), p-value 0.02.

Table 2 displays factors tested for association with salivary gland hypofunction. Those with a history of TB treatment had a greater than 6 times the likelihood of salivary gland hypofunction than those with no TB

**Table 1:** Baseline characteristics of patients under HIV care at Scottish Livingstone Hospital IDCC enrolled in the study.

| Variable | Salivary gland Hypofunction | Normal salivary Gland function | P-Value | N |
|---|---|---|---|---|
| **Sex, n (%)** | | | | |
| Male | 8 (47%) | 134 (35%) | 0.31 | 142 (35%) |
| Female | 9 (53%) | 249 (65%) | | 258 (65%) |
| Total | 17 (4.2%) | 383 (95.8) | | 400 |
| Mean age, years (SD) | 35.52 (12.14) | 42.22 (13.50) | 0.02 | 399 |
| **HAART regimen, n (%)** | | | | |
| DTG based | 15 (88) | 364 (95) | 0.22 | 379 (94.75) |
| Non DTG based | 2 (12) | 19 (5) | | 21 (5.25) |
| Total | 17 (4.25) | 383 (95.75) | | 400 |
| Median years on HAART, No (IQR) | 8 (5-9) | 9 (6-14) | 0.43 | 400 |
| Median CD4-CD8 ratio, No (IQR) | 0.87 (0.55-1.17) | 0.79 (0.57-1.11) | 0.95 | 395 |
| **Viral load category, n (%)** | | | | |
| >= 400 | 0 | 4 (1) | 0.67 | 4 (1%) |
| < 400 | 17 (100%) | 377 (99) | | 394 (99%) |
| Median CD4 count , No (IQR) | 506 (437-587) | 571 (401-787) | 0.87 | 400 |
| **History of TB Treatment, n (%)** | | | | |
| Yes | 8 (47) | 51 (13.3) | > 0.00 | 59 |
| No | 9 (53) | 332 (86.7) | | 341 |
| Median xerostomia total score, No (IQR) | 5 (5-5) | 5 (5-5) | 0.98 | 400 |
| Median CD8 count, No (IQR) | 715 (461-1129) | 724 (530-936) | 0.73 | 395 |

**Table 2:** Unadjusted and adjusted odds ratios of factors associated with salivary gland hypofunction.

| Variable | Crude OR (95% CI) | p value | C-statistic | Adjusted OR (95% CI) | p-value |
|---|---|---|---|---|---|
| Age | 0.96 (0.91, 0.99) | 0.03 | 0.63 | 0.95 (95% CI) | 0.02 |
| History of TB treatment | 5.8 (2.14-15.68) | 0.001 | 0.67 | 6.12 (2.13-17.58) | 0.001 |
| Female sex | 0.61 (0.23-1.61) | 0.31 | 0.56 | 0.56 (1.99-1.58) | 0.28 |
| Current alcohol use | 2.04 (0.69-5.98) | 0.195 | 0.56 | | |
| Current smoking | 1.91 (0.41-8.82) | 0.407 | 0.53 | | |
| Latest CD4 count with every 50 cell increase | 1 (0.91-1.10) | 0.99 | 0.51 | | |
| Number of years on cART | 0.98 (0.91-1.07) | 0.79 | 0.56 | | |
| Xerostomia score | 0.78 (0.3-2.02) | 0.61 | 0.5 | | |
| Dolutegravir-based cART regimen | 0.39 (0.08-1.84) | 0.23 | 0.5 | | |
| Antihypertensive medication use | 1.50 (0.41-5.40) | 0.539 | 0.53 | | |

treatment history. Overall, our model captured a large proportion of variability in salivary gland hypofunction with a c-statistic of 0.7842.

## Discussion

We found a low, but substantial rate of salivary gland hypofunction and xerostomia in PWH on cART in Botswana. Previous literature has reported association between salivary gland hypofunction with protease inhibitors, but there is a paucity of data on dolutegravir-based ART regimens and salivary gland hypofunction [8]. Long term use of ART has been reported to be a risk factor for salivary gland hypofunction [9], contrary to our findings. This could be due to different cART regimens under study. In our study, CD4 count did not show impact on salivary gland function, similar to results reported by Lopez, et al. and Pavithra, et al. [2,9]. This is contrary to studies done by Navesh, et al. and Tinos, et al. where low CD4 count was reported as risk factor for salivary gland hypofunction [10,11]. The conflicting results could be due to our identifying participants being seen at a clinical site who were in care and had already recovered their CD4 counts by being on cART.

From the current study, history of TB treatment had a strong association with salivary gland hypofunction in both univariable and multivariable models. Previous studies have not explored this aspect, which is worth investigating more in-depth as Botswana is one of the countries with a high HIV/TB disease burden [12] with an estimated 60% co-infection rate [13]. Due to the nature of the study design, we could not tease out if TB treatment is the cause of salivary gland hypofunction or not. Therefore, further research is warranted where salivary gland function is assessed at time of TB diagnosis and during treatment to assess effect of TB treatment on salivary glands. A case study by Dadwal has shown that TB can manifest in the salivary glands without signs or symptoms of TB, which warrants assessment as a potential screening too for TB in people living with HIV [5].

The strengths of our study were the ability to capture participants from a broad range of exposures and the fit of the model. The study was not without limitations as we did not acquire data on other medications like antidepressants and narcotic analgesics use as they might have been associated with salivary gland hypofunction as reported in a prior study on young adults [14]. There was also lack of variability in cART regimens which may have accounted for the lack of association.

## Conclusion

History of TB and younger age have shown a strong association with salivary gland hypo function in PWH. These novel findings prompt for a longitudinal study with a larger cohort of TB patients to validate them as they have not been reported elsewhere. The findings could inform policies on management of TB/HIV co-infected patients, and young adults living with HIV to improve their quality of life after TB treatment.

## Acknowledgements

Botswana Upenn Partnership for administrative support.

Scottish Livingstone Hospital, Molepolole Botswana for field work support.

## Funding

The study was funded by the HIV Clinical Epidemiology Training for Botswana, D43TW009781 grant (R.G) and supported by the Penn Center for AIDS Research, an NIH funded program (P30 AI 045008) and CFAR.

## Conflict of Interest

None.

## Author Contributions

- Conception and design: Precious K. Motlokwa, Billy M. Tsima and Robert Gross.
- Financial Support: Robert Gross.
- Administrative support: Precious k Motlokwa, Robert Gross.
- Data collection: Precious k Motlokwa.
- Data analysis and interpretation: All authors.

- Manuscript writing: All authors.
- Final approval of manuscript: All authors.

## References


1. Schiødt M, Dodd CL, Greenspan D, Daniels TE, Chernoff D, et al. (1992) Natural history of HIV-associated salivary gland disease. Oral Surg Oral Med Oral Pathol 74: 326-331.
2. Pavithra S, Ranganathan K, Rao UK, Joshua E, Rooban T, et al. (2013) Impact of highly active antiretroviral therapy on salivary flow in patients with human-immuno deficiency virus disease in Southern India. J Oral Maxillofac Pathol 17: 17-22.
3. Kumar JV, Baghirath PV, Naishadham PP, Suneetha S, Suneetha L, et al. (2015) Relationship of long-term highly active antiretroviral therapy on salivary flow rate and CD4 Count among HIV-infected patients. J Oral Maxillofac Pathol 19: 58-63.
4. Pedersen AML, Sørensen CE, Proctor GB, Carpenter GH, Ekström J (2018) Salivary secretion in health and disease. J Oral Rehabil 45: 730-746.
5. Dadwal M (2011) Primary submandibular tuberculosis: An unusual cause of submandibular salivary gland enlargement. Indian J Otolaryngol Head Neck Surg 63: 298-299.
6. Navazesh M, Kumar SKS (1939) Measuring salivary flow: Challenges and opportunities. J Am Dent Assoc 139: 35S-40S.
7. Thomson WM, van der Putten GJ, de Baat C, Ikebe K, Matsuda K ichi, et al. (2011) Shortening the xerostomia inventory. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 12: 322-337.
8. Navazesh M, Mulligan R, Karim R, Mack W, Ram S, et al. (2009) Effect of HAART on salivary gland function in the Women's Interagency HIV Study (WIHS). Oral Dis 15: 52-60.
9. López Verdín S, Andrade Villanueva J, Zamora Perez AL, Bologna Molina R, Cervantes Cabrera JJ, et al. (2013) Differences in salivary flow level, xerostomia, and flavor alteration in Mexican HIV patients who did or did not receive antiretroviral therapy. AIDS Res Treat 2013: 613278.
10. Navazesh M, Mulligan R, Barrón Y, Redford M, Greenspan D, et al. (2003) A 4-year longitudinal evaluation of xerostomia and salivary gland hypofunction in the Women's Interagency HIV Study participants. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 95: 693-698.
11. Tinós AMFG, Sales-Peres SH de C (2014) Xerostomia related to HIV infection/AIDS: A critical review. Rev Odontol UNESP 43: 214-222.
12. Mupfumi L, Moyo S, Shin SS, Wang Q, Zetola N, et al. (2019) High incidence of tuberculosis in the first year of antiretroviral therapy in the Botswana National antiretroviral therapy programme between 2011 and 2015. AIDS Lond Engl 33: 2415-2422.
13. Shipton L, Wester CW, Stock S, Ndwapi N, Gaolathe T, et al. (2009) Safety and efficacy of nevirapine- and efavirenz-based antiretroviral treatment in adults treated for TB-HIV co-infection in Botswana. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis 13: 360-366.
14. Murray Thomson W, Poulton R, Mark Broadbent J, Al-Kubaisy S (2006) Xerostomia and medications among 32-year-olds. Acta Odontol Scand 64: 249-254.