Original investigation

Prevalence and Correlates of Snuff Use, and its Association With Tuberculosis, Among Women Living With HIV in South Africa

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Abstract

Introduction: A higher proportion of people living with HIV (PLWH) smoke compared to the general population, but little information exists about the prevalence and correlates of smokeless tobacco use among PLWH. In South Africa, dry powdered tobacco is inhaled nasally as snuff.

Methods: A cross-sectional survey among PLWH attending three HIV clinics was conducted. Snuff use was assessed via self-report and urine cotinine.

Results: Given the low (3%) prevalence of snuff use among men, analysis was restricted to $n = 606$ nonsmoking women living with HIV. Half ($n = 298$, 49%) were snuff users, the majority of whom ($n = 244$, 84%) had a positive urine cotinine test. In adjusted analysis, snuff use was negatively associated with higher education (relative risk [RR] 0.55; 95% confidence interval [CI]: 0.39, 0.77) and mobile phone ownership (RR 0.83; 95% CI: 0.71, 0.98), and positively associated with ever having tuberculosis (TB) (RR 1.22; 95% CI: 1.03, 1.45). In adjusted analysis, with current TB as the outcome, snuff use was marginally statistically significantly associated with a twofold increase in odds of a current TB diagnosis (odds ratio [OR] 1.99; 95% CI: 0.98, 4.15).

Discussion: A high proportion of nonsmoking South African women living with HIV use snuff, which was a risk factor for TB. Additional research is needed to understand the relationship between snuff, TB, and other potential health risks.

Implications: PLWH have a higher prevalence of smoking than their seronegative peers, but there is a paucity of research on smokeless tobacco use in this population, especially in low-resource settings. TB is the leading cause of death among PLWH, and with improvements to HIV treatment and care, PLWH are at greater risk of tobacco-related diseases. We report an extremely high prevalence of snuff use among women living with HIV in South Africa. Further, in this population snuff use is positively associated with ever having a TB diagnosis, as well as currently having TB.

Introduction

People living with HIV (PLWH) are more likely to smoke tobacco than the general population,¹ putting them at heightened risk for smoking-related diseases including lung cancer and cardiovascular disease.² Smoking increases the risk for tuberculosis (TB), the leading cause of death for PLWH.³ Globally, nearly 37 million people are infected with HIV.³ While understanding of prevalence, health implications, and intervention strategies for smoking among PLWH is increasing, there is a paucity of data around the use of smokeless tobacco and its health effects in PLWH. Smokeless tobacco is typically taken orally or nasally and contains a range of nicotine concentrations and carcinogens.^{4,5} In the general population, smokeless tobacco is a risk factor for cancers of the head and neck,^{6,7} and pancreas,⁷⁻⁹ and for cardiovascular disease¹⁰⁻¹² and chronic bronchitis.¹³ A recent review of the available data from Demographic and Health Surveys indicated that in the Africa region, 2.6% of men and 1.9% of women were smokeless tobacco users. The difference in smokeless tobacco use between those with and without HIV infection was not statistically significant for men; however, women with HIV had a 30% increase in risk of smokeless tobacco use compared to those who were HIV-uninfected.¹

In South Africa, which has the greatest number of PLWH in the world at 7.1 million,¹⁴ the prevalence of smoking among PLWH is reported as 52% among men and 13% among women.¹⁵ Further, South Africa has the highest annual incidence of TB in the world.¹⁶ The primary smokeless tobacco product used in South Africa is dry nasal snuff—a fine powdered tobacco product either inserted between the lip and gum, or inhaled through the nose.⁵ Among South African adults in the general population, 1.4% of males and 8.4% of females use snuff, primarily inhaled through the nose.¹⁷

Given the high proportion of smoking among PLWH, smokeless tobacco use may also be disproportionately high among this population. To address this gap in knowledge, we assessed the prevalence and correlates of dry nasal snuff use among PLWH attending HIV clinics in the Matlosana District of South Africa. Given the association between smoked tobacco and TB, exploratory analysis was also conducted to assess the association between snuff use and TB in this population.

Methods

Ethics approvals were obtained from the University of the Witwatersrand Human Research Ethics Committee (Medical) and the Johns Hopkins University Institutional Review Board. Written consent was obtained from all participants prior to enrollment.

Between April 2012 and August 2013 a cross-sectional survey was conducted in three HIV clinics in Matlosana, South Africa to estimate prevalence of current tobacco use, including snuff use. Methods have been previously described.¹⁵ Briefly, every day a random seed was drawn for each clinic. Clinic staff would refer interested patients to research staff, and the random number was used to determine which of these referred patients would be eligible for inclusion (ie, the n^{th} referred adult ≥ 18 years) would be eligible for inclusion). Participants were administered a survey adapted from the Centers for Disease Control and Prevention's Global Adult Tobacco Survey (GATS). Surveys were conducted in English or alternate local languages, Setswana, Zulu or Xhosa, based on the participant's language preference.

In addition to self-reported snuff use and smoking, exhaled carbon monoxide (CO) was collected from each participant using a handheld CO monitor (coVita, Santa Barbara, CA), which measures exposure to combusted tobacco products over the previous 8 hours. A urine sample was also collected for point of care cotinine (a nicotine metabolite) testing using SmokeScreen (GFC Diagnostics,

Oxfordshire, United Kingdom). SmokeScreen, a semi-quantitative assay, indicates exposure to nicotine through colorimetric evaluation, with the urine of exposed individuals changing in color (light, medium, heavy, and very heavy exposure) after addition of the assay chemicals. The SmokeScreen urine test measures tobacco exposure over the past 48–72 hours. A positive screen was defined as values at or above 10 parts per million for exhaled CO, and at least light exposure through color evaluation for the urine test. Snuff use was defined by self-report using the question “Do you use snuff?”. We also defined participants as snuff users if they reported no snuff use but had a heavy or very heavy urine cotinine measurement and a negative CO test result. Current smoking was defined as a positive CO and urine test result in addition to self-report. Nicotine replacement therapy, including nicotine patches and gum, is not readily available in this population, and is likely prohibitively expensive given the low socioeconomic status of participants. Additionally, e-cigarettes are also not readily available in this population, although we did not ask about e-cigarette use. The use of nicotine replacement therapy and e-cigarettes were therefore not considered as contributing to the biomarker result and the definition of smoking and snuff use. Considerations to the smoking definition were made for those self-reporting snuff use and marijuana use, which would affect the urine and CO test, respectively, as well as current TB status (as isoniazid interacts with the urine test result resulting in false positives or discoloration).^{15,18} For example, if a participant self-reported as a non-smoker and had a positive urine cotinine test but also reported snuff use, they were categorized as a nonsmoker. Similarly, if a participant self-reported as a nonsmoker and had a positive CO test but also self-reported marijuana use, they were categorized as a nonsmoker.

Statistical Analysis

Prevalence of self-reported snuff use and corresponding normal approximation 95% confidence intervals (CIs) were calculated across variables of interest. Socio-demographic and clinical characteristic were compared by snuff use status using the Chi-squared (χ^2) and Wilcoxon rank-sum tests, as appropriate. Univariate log-binomial regression with snuff use as the dependent variable was conducted. Multivariate log-binomial regression models with snuff use as the outcome of interest were constructed using variables significantly associated at the univariate level ($p < .20$), or those selected for inclusion a priori. These methods were also used when building logistic regression models with TB as the outcome of interest, both with snuff use and urine cotinine concentrations as the primary exposure of interest. We have included urine cotinine concentration biomarker in the models as a proxy measure of intensity of exposure to snuff. Data were analyzed using R (Version 3.3.1).¹⁹

Results

In total, 1131 participants were included in the primary sample, of which 705 (62%) were female. As only 11 (3%) men reported snuff use, compared to 304 (43%) women, the analysis was restricted to women. Among all women, 99 (14%) were defined as current smokers, and odds of current smoking was strongly inversely associated with snuff use (odds ratio [OR] 0.12; 95% CI: 0.06, 0.22). Given this association and given that only 10 (3%) snuff users reported smoking, the final analysis was restricted to nonsmoking women.

Of the 606 nonsmoking women included in the final analysis, 294 (49%) were self-reported snuff users; only 4 (1%) women who did not report using snuff were categorized as snuff users due to their high urine cotinine test measures, for a total snuff use prevalence of 49% ($n = 298$)

(Table 1, Figure 1). Among self-reported snuff users, 48 (16%) did not have detectable levels of cotinine in their urine sample. The median (interquartile range) body mass index was 25 (21, 30), over half of the women ($n = 311$, 56%) had a CD4+ cell count greater than 350 cells/mL, and 216 (43%) had a detectable viral load. Half ($n = 298$, 49%) of participants were older than 40 years of age. Ever having TB was reported by 356 (59%) women; of those 59 (17%) reported current TB and 356 (91%) reported having TB at some point in the past.

In univariate analysis, women who were older than 40 (relative risk [RR] 1.34; 95% CI: 1.13, 1.58), on disability grants (RR 1.23; 95% CI: 1.00, 1.47), used coal or wood for cooking or heating (RR 1.40; 95% CI: 1.16, 1.65), and those who reported ever having TB (RR 1.29; 95% CI: 1.09, 2.54) or currently having TB (RR 1.27; 95% CI: 1.00, 1.56) had an increased risk of snuff use. Those who completed grade 12 or higher (RR 0.46; 95% CI: 0.32, 0.62), those who had a household income of greater than 1000 Rand (approximately US \$75) per month (RR 0.82; 95% CI: 0.70, 0.96), those with more than four rooms in their home (RR 0.72; 95% CI: 0.70, 0.96), and those with a mobile phone for themselves (RR 0.72; 95% CI: 0.61, 0.87) had lower risk of snuff use. In adjusted analysis, those with more education (RR 0.55; 95% CI: 0.39, 0.77) had lower odds of snuff use (Table 2). Ever having TB also was associated with a 22% increase in odds of snuff use in adjusted analysis (OR 1.22; 95% CI: 1.03, 1.45). The model including currently having TB did not converge.

Adjusting for sociodemographic factors, crowding, viral load, CD4+ cell count, and body mass index, the association between snuff use and an outcome of current TB approached statistical significance (OR 1.99; 95% CI: 0.98, 4.15; $p = .06$). The model for an outcome of ever having TB did not converge.

Urine cotinine was strongly associated with reported snuff use. Only four participants had to be reclassified from non-snuff to snuff users based upon urine cotinine measures. Among snuff users, 244 (84%) had detectable levels of urine cotinine, while only 19 (6%) of non-snuff users had detectable levels of urine cotinine. Additionally, concentrations of urine cotinine were strongly and positively associated with an outcome of current TB (Table 3). Those with a positive urine cotinine test had nearly six times greater odds of current TB than those without any detected urine cotinine (OR 5.68; 95% CI: 2.57, 14.02), controlling for age, education, employment, monthly household income, current living situation (house/flat vs. shack), crowding, mobile phone ownership, kerosene cooking fuel, coal or wood use for cooking or heating, body mass index, CD4+ cell count, and viral load.

Discussion

We report a high prevalence of snuff use among nonsmoking women living with HIV in South Africa. Few men in this population used snuff, but nearly half of nonsmoking women self-reported current

Table 1. Demographic Characteristics and Correlates of Snuff Use Among Nonsmoking Women ($n = 606$) Living With HIV in Matlosana, South Africa

	Total ($n = 606$)	Non-snuff user ($n = 308$)	Snuff user ($n = 298$)	p	Univariate RR (95% CI)	p
Age (y), n (%)						
<40	308 (51)	178 (58)	130 (44)		REF	
≥40	298 (49)	130 (42)	168 (56)	.0007	1.34 (1.13, 1.58)	.001
Education, n (%)						
<Grade 12	494 (82)	224 (73)	270 (91)		REF	
Grade 12 or higher	112 (18)	84 (27)	28 (9)	<.0001	0.46 (0.32, 0.62)	<.0001
Employment, n (%)						
Employed	95 (16)	55 (18)	40 (13)		REF	
Unemployed	511 (84)	253 (82)	258 (87)	.16	1.20 (0.95, 1.57)	.16
Household income, n (%)						
<1000	255 (42)	115 (37)	140 (47)		REF	
>1000	351 (58)	193 (63)	158 (53)	.02	0.82 (0.70, 0.96)	.02
Disability grants, n (%)	96 (16)	40 (13)	56 (19)	.06	1.23 (1.00, 1.47)	.04
Current living situation, n (%)						
House/flat	472 (78)	245 (79)	227 (77)		REF	
Shack	134 (22)	63 (20)	71 (24)	.37	1.10 (0.91, 1.31)	.31
Number of rooms, n (%)						
≤4	481 (79)	230 (75)	251 (84)		REF	
>4	125 (21)	78 (25)	47 (16)	.005	0.72 (0.56, 0.90)	.008
Crowding (>1 person/room)	293 (48)	146 (47)	147 (49)	.69	1.04 (0.88, 1.22)	.64
Mobile phone for self, n (%)	513 (85)	275 (89)	238 (80)	.002	0.72 (0.61, 0.87)	.0003
Kerosene (cook or heat)	104 (17)	48 (16)	56 (19)	.35	1.12 (0.90, 1.35)	.28
Coal or wood (cook or heat)	94 (16)	33 (11)	61 (20)	.001	1.40 (1.16, 1.65)	.0002
Clinical data						
Body mass index, median (IQR)	25 (21, 30)	25 (22, 30)	25 (21, 29)	.13	0.99 (0.98, 1.01)	.35
CD4 count, median (IQR) ^a	390 (236, 564)	373 (203, 527)	415 (257, 602)	.06	1.08 (0.98, 1.21)	.14
CD4 count > 350	311 (56)	151 (53)	160 (59)	.16	1.14 (0.96, 1.36)	.14
Viral load, cells/mL, median (IQR) ^a	25 (25, 2758)	25 (25, 3577)	25 (25, 1798)	.40	0.99 (0.96, 1.01)	.39
Viral load detectable	216 (43)	114 (44)	102 (42)	.80	0.97 (0.80, 1.16)	.73
Ever TB	356 (59)	163 (53)	193 (65)	.004	1.29 (1.09, 2.54)	.004
Current TB	59 (10)	23 (7)	36 (12)	.08	1.27 (1.00, 1.56)	.03

CI = confidence interval; IQR = interquartile range; RR = relative risk; TB = tuberculosis. Bolded values statistically significant at $p < .05$.

^aRR of log CD4 and viral load results for continuous measures.

Figure 1. Prevalence of snuff use among adult nonsmoking women living with HIV ($n = 606$) in Matlosana, South Africa.

snuff use. In adjusted analysis, women in higher socioeconomic categories had a lower risk of snuff use. Ever having TB was also positively associated with snuff use. Urine cotinine measurements were strongly associated with snuff use. Further, among these nonsmoking women, urine cotinine was also strongly and positively associated with current TB. Those with a positive cotinine test had nearly six times greater odds of current TB than those without detected urine cotinine. These data suggest snuff use may be an important risk factor for TB in women living with HIV.

The prevalence of snuff use among women was nearly six times higher than previously reported for women in the general population in South Africa, and three times higher than black South African women. According to Demographic and Health Surveys data, self-reported prevalence of smokeless tobacco use is 8.4% among women in the general population¹⁷ and 16.1% among black South African Women.¹³ We found the prevalence of snuff use for men to be much lower than for women, with only 3% of our male participants reporting snuff use, as compared to 1.4% of males in the general population.¹⁷ We have previously reported that 13% of women and 52% of men living with HIV attending HIV clinics in this population are current smokers.¹⁵ In a study of newly diagnosed TB patients in South Africa, among which 87% were HIV infected, 4% of the participants used smokeless tobacco, and rose to 7% among women.²⁰ The difference in the prevalence of snuff use in the present study may be due to the geographic location of the study participants. Our participants

were recruited from a smaller, peri-urban location outside of a major city, while the newly diagnosed TB patients in the referenced study were recruited from a large urban setting. Additionally, newly diagnosed TB patients may temporarily quit using tobacco products if they are feeling very sick, which may also lead to a lower prevalence of reported tobacco use. Participants recently diagnosed with TB may also under-report tobacco use to a more socially desirable response of nonuse if they feel it may be related to their current TB diagnosis. Among women with HIV infection in the African region, 1.9% of women with HIV infection reported smokeless tobacco use.¹ This number may be significantly lower than our estimate given the broad range of countries included in the African region. South Africa is not included in this study; however, Lesotho, which is geographically located within South Africa, is. The prevalence of smokeless tobacco use in Lesotho is 15.7% among women with HIV infection, significantly higher than the regional estimate. It is likely that regional estimates of prevalence do not fully capture the burden of tobacco use in vast and diverse regions like Africa.

Snuff use has potentially serious health implications. As treatment options, program implementation, and subsequent life expectancy for PLWH improves, PLWH will become increasingly susceptible to non-HIV related risks to health. Additionally, HIV-infection status may increase risk for certain cancers,²¹ pulmonary disease,²² and cardiovascular disease²³ beyond that of those who are not living with HIV. This high prevalence of snuff use, in combination with these

Table 2. Univariate and Multivariate Log-Binomial Regression for Relative Risk of Snuff Use Among Adult Nonsmoking Women Living With HIV (*n* = 606) in Matlosana, South Africa

	Non-snuff user (<i>n</i> = 312)	Snuff user (<i>n</i> = 294)	Univariate RR (95% CI)	<i>p</i>	Multivariate RR (95% CI)	<i>p</i>
Age (y), <i>n</i> (%)						
<40	178 (58)	130 (44)	REF		REF	
≥40	130 (42)	168 (56)	1.34 (1.13, 1.58)	.001	1.21 (1.03, 1.43)	.02
Education, <i>n</i> (%)						
<Grade 12	224 (73)	270 (91)	REF		REF	
Grade 12 or higher	84 (27)	28 (9)	0.46 (0.32, 0.62)	<.0001	0.55 (0.39, 0.77)	.001
Employment, <i>n</i> (%)						
Employed	55 (18)	40 (13)	REF		REF	
Unemployed	253 (82)	258 (87)	1.20 (0.95, 1.57)	.16	1.00 (0.79, 1.26)	.97
Monthly household income, <i>n</i> (%)						
<1000	115 (37)	140 (47)	REF		REF	
>1000	193 (63)	158 (53)	0.82 (0.70, 0.96)	.02	0.93 (0.79, 1.09)	.36
Disability grants	40 (13)	56 (19)	1.23 (1.00, 1.47)	.04	1.02 (0.83, 1.26)	.83
Number of rooms, <i>n</i> (%)						
≤4	230 (75)	251 (84)	REF		REF	
>4	78 (25)	47 (16)	0.72 (0.56, 0.90)	.008	0.86 (0.68, 1.08)	.20
Mobile phone for self	275 (89)	238 (80)	0.72 (0.61, 0.87)	.0003	0.83 (0.71, 0.98)	.03
Kerosene (cook or heat)	48 (16)	56 (19)	1.12 (0.90, 1.35)	.28	1.08 (0.91, 1.28)	.40
Coal or wood (cook or heat)	33 (11)	61 (20)	1.40 (1.16, 1.65)	.0002	1.17 (1.00, 1.38)	.07
Ever having TB	163 (53)	193 (65)	1.29 (1.09, 2.54)	.004	1.22 (1.03, 1.45)	.02

CI = confidence interval; RR = relative risk; TB = tuberculosis. Bolded values statistically significant at *p* < .05.

Table 3. Association of Urine Cotinine With Current TB Among Women Living With HIV (*n* = 606) in Matlosana, South Africa

Current TB								
	Total (<i>n</i> = 593)	No TB (<i>n</i> = 545)	Current TB (<i>n</i> = 48)	<i>p</i>	Univariate OR (95% CI)	<i>p</i>	Multivariate* OR (95% CI)	<i>p</i>
Urine cotinine								
No change	330 (56)	319 (59)	11 (23)	<.0001	REF		REF	
Moderate	50 (8)	71 (13)	10 (21)		4.08 (1.64, 10.06)	.002	5.39 (1.97, 15.18)	.001
Light	81 (14)	42 (8)	8 (17)		5.52 (2.04, 14.44)	<.001	8.94 (2.93, 27.71)	.0001
Heavy	52 (9)	49 (9)	3 (6)		1.77 (0.39, 5.93)	.39	2.21 (0.32, 9.82)	.34
Very heavy	80 (13)	64 (12)	16 (33)		7.25 (3.24, 16.77)	<.0001	6.24 (2.18, 18.42)	.001
Urine cotinine (continuous)	—	—	—	—	1.50 (1.25, 1.80)	<.0001	1.46 (1.17, 1.83)	<.001
Urine cotinine								
No change	330 (56)	319 (59)	11 (23)	<.0001	REF		REF	
Any change	263 (44)	226 (41)	37 (77)		4.75 (2.45, 9.95)	<.0001	5.68 (2.57, 14.02)	<.0001

CI = confidence interval; OR = odds ratio; TB = tuberculosis. Bolded values statistically significant comparing current to no TB.

*Multivariate analysis adjusted for age, education, employment, monthly household income, current living situation (house/flat vs. shack), crowding, mobile phone ownership, kerosene cooking fuel, coal or wood use for cooking or heating, body mass index, CD4+ cell count, and viral load.

underlying risk factors, may disproportionately increase the risk of certain diseases for PLWH, especially among those with uncontrolled HIV, of which TB is especially concerning.

We report a twofold increase in odds of current TB with snuff use, and strong associations between snuff use, cotinine, and current TB. A previous study among a sample of the general population in South Africa found that participants reporting previous TB used snuff at a higher proportion than those without a history of previous TB (23% vs. 16%, respectively; *p* = .06).¹³ Snuff use has been shown to decrease nasal mucociliary clearance,²⁴ which may increase susceptibility to pulmonary infections. Snuff use has also been shown to be positively associated with chronic bronchitis among black South African women.¹³ Further, snuff products have been shown to include a variety of bacterial communities,²⁵ which may alter the microbiome and lead to susceptibility to pulmonary disease. We

found that the association between snuff and an outcome of current TB approached statistical significance, while cotinine was much more strongly associated with current TB. We hypothesize this is due to the intensity of snuff use, for which cotinine is a proxy measure for. Approximately 16% of self-reported snuff users did not have detectable levels of urine cotinine, and this may contribute to the difference in effect size and statistical significance seen between association of these two measures and current TB. Further research is needed to elucidate this association.

To our knowledge, this is the first study to report prevalence and correlates of snuff use among PLWH, as well as its association with TB, and has several strengths. Our cross-sectional study randomly selected participants from HIV clinics in a high-burden setting, where information on tobacco use is understudied and extremely relevant. In addition to self-report, we used two biomarkers of tobacco use to

define smoking among participants, providing a strong definition for both smoking and nonsmoking. Our study has several limitations. Snuff use was defined as use or nonuse only, and additional information on the quantity, frequency, or duration of snuff use was not collected. We also did not collect information on whether snuff use was through oral or nasal application, although the majority of snuff use in South Africa is through nasal application as previously reported.¹⁷ Participants were recruited from only one district in South Africa, limiting generalizability. The urine cotinine and exhaled breath CO biomarkers are also limiting in their ability to differentiate between types of tobacco products. Additionally, as we consider the association between snuff use and TB, there are likely unmeasured confounders, such as exposure to a TB case, that were not included in the adjusted model. Ever or currently having TB was also obtained by self-report alone, and was not cross-validated in participant medical records.

Tobacco use in the African region has been long overlooked given serious competing public health concerns. Developing economies and increased influence of multinational tobacco companies, however, is resulting in an increasing prevalence of tobacco use.²⁶ The emerging syndemic of HIV, TB, and tobacco use is alarming, and is cause for concern. There are a variety of snuff products used in South Africa, with different constituents and properties.⁴ Additional research is needed to understand risk from different products, as well as patterns of use and subsequent health effects. Current estimates of the burden of disease from smokeless tobacco products do not include a risk for TB.²⁷ Additionally, considering the extremely high prevalence of use and the known risks to health among the general population, interventions are needed for this population.

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Declaration of Interests

None declared.

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