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Original article

Detection of *Mycobacterium tuberculosis* in tongue Swab

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ABSTRACT

Background: Sputum examination is the gold standard for the diagnosis of pulmonary tuberculosis. However, individuals particularly children, the aged, and immuno-compromised may not expectorate sputum due to some underlying conditions. Moreover, sputum produces infectious aerosols which exposes both the patients and care giver. It is also difficult to standardize sputum specimen for Mycobacterium tuberculosis. Therefore, the present study considered alternative specimen for pulmonary tuberculosis. **Aim:** To identify Mycobacterium tuberculosis in tongue swab. **Methods**: This was a cross-sectional laboratory-based study carried out in July-December 2022 on 384 tuberculosis patients attending health facilities in Karu, North central Nigeria. Using a multistage sampling technique, participants were added one at a time until the required sample size was gotten and analyzed via GeneXpert MTB/RIF. Performance of the tongue swab was compared to the combined reference standard of sputum XPERT. **Results**: The tongue swab XPERT ultra had a sensitivity of 78%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 97.4% relative to a sputum XPERT ultra reference standard. There were positive associations between the socio-demographic variables (age group, sex, family size, family type, marital status, religion, educational status, and occupation) and Mycobacterium tuberculosis infection. However, only the participant's educational status (p=0.027) and occupation (p=0.05) had statistically significant difference. **Conclusion**: Tongue swab is an alternate specimen for sputum-based molecular diagnosis for Mycobacterium tuberculosis. The procedure is less invasive, easier, and non-aerosol producing efficient alternate approach for pulmonary tuberculosis.

Introduction

According to The World Health Organization (WHO), tuberculosis is among the major causes of morbidity and mortality in the world. Every year, more than 10 million people in their prime years are infected with active tuberculosis especially in poor regions of Africa and Asia [1]. Sputum analysis is the gold standard for the diagnosis of pulmonary tuberculosis. It is a viscous substance produced by the airways of patients. However, individuals particularly children, the aged, and immuno-compromised patients may not expectorate sputum due to the underlying medical conditions [2, 3]. Moreover, sputum produces infectious aerosols which exposes both the patients and care giver. It is also difficult to standardize and prepare the sample for Mycobacterium tuberculosis DNA detection [3,4]. Therefore, modern research has looked at alternative samples such as exhaled breath concentration,

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blood, urine, and saliva [6]. Unfortunately, these samples were typically less sensitive and specific than the sputum [7].

Although, sputum samples from person's exhibiting symptoms of tuberculosis are used in the majority of contemporary diagnosis of tuberculosis, the non-sputum-based diagnosis have been identified by the World Health Organization as a high priority for diagnostic development to stop the spread of tuberculosis [2]. It is indispensable to identify and treat individuals with active tuberculosis as soon as possible. To stop the spread of tuberculosis, active case-finding demand a high-turnout sampling of a large number of persons but the use of sputum would worsen the existing problems. A simple, safe, non-invasive, and more effective alternative technique without non-aerosol such as the use of tongue swab is required to identify the instigating organism in order to support early detection and treatment of the disease.

Documented evidence abound that Mycobacterium tuberculosis can be recovered from the mouth of individuals living with pulmonary tuberculosis. Oral swabs have been shown in studies to be a suitable substitute to sputum testing. Oral swabs have the same sensitivity as a sputum sample [8,9]. Moreover, the existence of Mycobacterium tuberculosis in the bucal cavity is conceivable given that the bacteria is found in the tonsil and adenoid of patients having tonsillectomies, suggests a way to measure tuberculosis prevalence. In addition, tuberculosis testing efficiency would rise with the availability of the non-invasive oral swabs samples that are simple to collect outside the clinic while reducing the risk of exposure. In this context, addressing the underscored issues will escalate the journey towards the goal of tuberculosis elimination. Therefore, this study aimed to identify the diagnostic accuracy of Mycobacterium tuberculosis in tongue Swab.

MATERIALS AND METHODS

Study Design and Population

This is a prospective and cross-sectional laboratory-based study carried out in July/December 2022 on 384 tuberculosis patients of the age 18 years and above attending health facilities in Karu, Nasarawa State, Nigeria. Using a multistage sampling technique; stage 1 was the selection of Health Facilities, stage 2 was the selection of DOTS clinics, and stage 3 was the selection of study participants. Four (4) health facilities in Karu were selected by simple random sampling technique. The health facilities are the major hospitals located within the state providing essential, specialized, and referral medical services to the residents and neighboring states. Of the four health facilities selected, two health facilities with DOTS clinics (Mararaba Medical Center and General Hospital Uke) were selected by simple random sampling. Participants were added one at a time until the required sample size was gotten to detect the diagnostic accuracy of Mycobacterium tuberculosis using tongue swab. The study was conducted on a pool of clinical specimens- tongue swabs according to the international guidelines of Strengthening the Reporting for Observational Studies in Epidemiology (STROBE).

Ethical Approval, Recruitment, and Enrollment

This study was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human subjects. The study procedures was approved by the Ethics Committee, Bingham University Teaching Hospital Jos with Ref. No. NHREC/21/05/2005/00965. Informed consent was obtained from each study subject and confidentiality of patient information and samples was maintained at all times. Spent samples were appropriately disposed by autoclaving.

A structured questionnaire was administered to each participant to obtain socio-demographic information which was analyzed to determine the associated risk factors for Mycobacterium tuberculosis infection in the study. The study participants were given standardized questionnaires upon enrolment that inquired about their socio-demographics, clinical features, and epidemiological/laboratory data. Each participant had a sample of their sputum and tongue swab taken early in the morning. Participants were asked to refrain from eating, drinking, brushing their teeth, and using mouthwash for at least 30 minutes prior to sample collection. For the tongue swab, participants were told to stick out their tongues, and the study researcher ran a sterile, individually wrapped swab over the front 2/3 of each participant's tongue, measuring its length and width. With just the right amount of pressure, the swab shafts might be slightly bent. Samples were obtained while continually spinning the swab for 15 to 20 seconds. The sample collection bottle cap was taken off as soon as the sample was collected and the shaft

section of the swab was carefully snapped off into the bottle containing 2ml normal saline so that the cap could seal completely. Sample collection bottle was sealed tightly. For the sputum sample, the participants were instructed to perform a deep cough and generate high-quality sputum in a sputum cup as part of the recruitment process. The sample containers for each participant were suitably labeled with their initials and date of collection. At the clinic, samples were kept inside a leak-proof bio-hazard bag and then into an ice-parked box before transporting to Zankli Research Center at Bingham University for Xpert MTB/RIF test.

Expected Outcome

Performance of the tongue swab was compared to the combined reference standard of sputum XPERT, which is the WHO's suggested first line TB diagnosis. Participants who tested positive for Mycobacterium tuberculosis in their sputum were deemed to have Mycobacterium tuberculosis (TB), whereas those who tested negative were deemed to be TB negative. Swab XPERT positivity for Mycobacterium tuberculosis was used to determine the tongue swab positivity.

Statistical Analysis

Data obtained from the study were entered into Microsoft Excel 2010 and analyzed with SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). Appropriate descriptive statistic was used to summarize the socio-demographic data of the participants. Sensitivity and specificity of the tongue swab Xpert were calculated in reference to sputum Xpert for tuberculosis. Correlations between variables were determined using the Pearson Chi-square test and the statistical significance value was determined at $p \leq 0.05$.

RESULTS

Section A: Socio-demographic characteristics

Table 1: Socio-demographic Characteristics of the Study Population

Of the 384 samples analyzed for Mycobacterium tuberculosis, 57.8% (222/384) were males and 42.2% (162/384) were females, giving a gender ratio of 1:0.730 (males: females). Majority of the study participants 109 (28.4%) were of age 18–27 years while the least was the oldest age group ≥ 57 years, which included 40 (10.4%) of the individuals. It was obvious that most of the study population were literate. According to the findings of the study, 259 (67.4%) of the participants are married, 2 (0.5%) are divorced and 7 (1.8%) are widowed. Furthermore, 116(30.2%) are single and 235(61.2%) have a family size of 5 and above.

Table 2: Assessment of the Sputum for Mycobacterium tuberculosis

The positivity rate of Mycobacterium tuberculosis infection among the study population was age dependent, age group 18 – 27 years had the highest positivity rate of 13.5% (13/96) and the least was among the older age group of 57 years, 0.14% (5/35). There were positive associations between the socio-demographic variables (age group, sex, family size, family type, marital status, religion, educational status, and occupation) and Mycobacterium tuberculosis infection. However, only the educational status of the study population had a statistically significant relationship (p=0.030).

Table 3: Assessment of the throat Swab for Mycobacterium tuberculosis

The positivity rate of Mycobacterium tuberculosis infection was found among the age group 18 – 27 years, 17.2% (16/93) and the least was among the older age group 48 – 57 years, 14.3% (8/56). There were positive associations between the socio-demographic variables (age group, sex, family size, family type, marital status, religion, educational status, and occupation) and Mycobacterium tuberculosis infection. However, only the participant's educational status (p=0.027) and occupation (p=0.05) have a statistically significant difference.

SECTION B: Clinical Characteristics

Table 4: Clinical Characteristics of the Study Population

Majority 339(88.3%) of the respondents have not cough for more than two weeks. Again, 360(93%) said they don't cough with mucus. A total of 370(96.4%) respondents haven't experience weight loss over the last three months while 372(96.9%) respondents sweat at night. All the respondents have not been treated for TB nor 381(99.2%) of their immediate family has TB. About 347(90.4%) were not feeling sick.

Section C: Epidemiological and Laboratory Characteristics

Table 5: Epidemiological Characteristics of the Study Participants

All participants 384(100%) identified pulmonary tuberculosis as their site of presumptive TB and DS –TB. The overall sensitivity of

Mycobacterium tuberculosis in sputum was 10.7% (41/384) while tongue swab was 8.3% (32/384).

HIV Status of Participants

The HIV status of the study participants 7(1.8%) were positive and 256(66.7%) were negative while 119(31%) do not know their HIV status.

Overall, tongue swab XPERT detected 32(8.3%) positive and 352(91.7%) negative while the sputum XPERT detected 41(10.7%) positive and 343(89.3%) negative for pulmonary tuberculosis.

Table 6: Sensitivity Assessment of the Sputum and Tongue Swab

Table 6 shows that the validity of the swab result is 78.0% sensitive and 100% specific. The swab result is also reliable with a positive predictive value of 100% and negative predictive value of 97.4% pulmonary tuberculosis detection using tongue swab in the study population at 95% CI.

Section A: Socio-demographic Characteristics of the Participants'

Table 1. Socio-demographic Characteristics of the Study Population (n = 384).

Variable		Frequency	Percentage (%)
Age group	18 – 27 years	109	28.4
	28 – 37 years	85	22.1
	38 – 47 years	86	22.4
	48 – 57 years	64	16.7
	>57 years	40	10.4
Sex	Male	222	57.8
	Female	162	42.2
Family type	Single	186	48.4
	Joint	198	51.6
Family Size	≤5	149	38.8
	>5 members	235	61.2
Marital Status	Single	116	30.2
	Married	259	67.4
	Separated	2	0.5
	Widow	7	1.8
Religion	Christianity	334	87.0
	Islam	50	13.0
Occupation	Farming	45	11.7
	Business	170	44.3
	Student	91	23.7
	Unemployed	52	13.5
	Others	26	6.8
Educational Status	None	19	4.9
	Primary	80	20.8
	Secondary	200	52.1
	Tertiary	85	22.1

Table 2. Assessment of the Sputum for *Mycobacterium tuberculosis*.

		Sputum/XPERT Result (%)		X^2	P-value
Variables		**Positive (n)**	**Negative (n)**		
Age group	18 – 27 years	13 (3.39%)	96 (25%)	6.758	0.149
	28 – 37 years	2 (0.52%)	83 (21.61%)		
	38 – 47 years	7 (1.82%)	79 (20.57%)		
	48 – 57 years	5 (1.30%)	59 (15.36%)		
	>57 years	5 (1.30%)	35 (9.11%)		
Sex	Male	20 (5.21%)	202 (52.60%)	0.314	0.575
	Female	12 (3.13%)	150 (39.06%)		
Family type	Single	14 (3.65%)	172 (44.79%)	0.307	0.579
	Joint	18 (4.69%)	180 (46.88%)		
Family Size	<= 5	14 (3.65%)	135 (35.16%)	0.360	0.549
	>5 members	18 (4.69%)	217 (56.51%)		
Marital Status	Single	11 (2.86%)	105 (27.34%)	1.036	0.793
	Married	21 (5.47%)	238 (61.98%)		
	Separated	0 (0.00%)	2 (0.52%)		
	Widow	0 (0.00%)	7 (1.82%)		
Religion	Christianity	30 (7.81%)	304 (79.17%)	1.413	0.235
	Islam	2 (0.52%)	48 (12.50%)		
Occupation	Farming	3 (0.78%)	42 (10.94%)	9.071	0.059
	Business	11 (2.86%)	159 (41.4%)		
	Student	9 (2.34%)	82 (21.35%)		
	Unemployed	3 (0.78%)	49 (12.76%)		
	Others	6 (1.56%)	20 (5.20%)		
Educational Status	None	5 (1.30%)	14 (3.65%)	8.942	0.030
	Primary	7 (1.82%)	73 (19.01%)		
	Secondary	13 (3.39%)	187 (48.70%)		
	Tertiary	7 (1.82%)	78 (20.31%)		

*** Statistically significant values are determined at $p \leq 0.05$.**

Table 3. Assessment of the tongue swab for *Mycobacterium tuberculosis*.

		Swab Result (%)		X^2	P-value
Variables		**Positive**	**Negative**		
Age group	18 – 27 years	16 (4.12%)	93 (24.22%)	7.561	0.109
	28 – 37 years	3 (0.78%)	82 (21.35%)		
	38 – 47 years	8 (2.08%)	78 (20.31%)		
	48 – 57 years	8 (2.08%)	56 (14.58%)		
	>57 years	6 (1.56%)	34 (8.85%)		
Sex	Male	24 (6.25%)	198 (51.56%)	0.010	0.921
	Female	17 (4.43%)	145 (37.76%)		
Family type	Single	19 (4.95%)	167 (43.49%)	0.081	0.776
	Joint	22 (5.73%)	176 (45.83%)		
Family Size	<= 5	18 (4.69%)	131 (34.11%)	0.503	0.473
	>5 members	23 (5.99%)	212 (55.20%)		
Marital Status	Single	15 (3.91%)	101 (26.30%)	1.804	0.614
	Married	26 (6.77%)	233 (60.68%)		
	Separated	0 (0.00%)	2 (0.52%)		
	Widow	0 (0.00%)	7 (1.82%)		
Religion	Christianity	39 (10.16%)	295 (76.8%)	2.687	0.101
	Islam	2 (0.52%)	48 (12.50%)		

Occupation	Farming	4 (1.04%)	41 (10.68%)	9.496	0.050
	Business	14 (3.65%)	156 (40.63%)		
	Student	12 (3.13%)	79 (20.57%)		
	Unemployed	4 (1.04%)	48 (12.50%)		
	Others	7 (1.82%)	19 (4.95%)		
Educational Status	None	6 (1.56%)	13 (3.89%)	9.175	0.027
	Primary	8 (2.08%)	72 (18.75%)		
	Secondary	19 (4.95%)	181(47.14%)		
	Tertiary	8 (2.08%)	77 (20.05%)		

* Statistically significant values are determined at $p \leq 0.05$.

SECTION B: Clinical Characteristics

Table 4. Clinical characteristics of the study population.

Variables		Frequency	Percentage (%)
Cough for two (2) weeks	Yes	45	11.7
	No	339	88.3
Cough with mucus	Yes	24	6.3
	No	360	93.8
Weight loss within three (3) months	Yes	14	3.6
	No	370	96.4
Night sweating	Yes	12	3.1
	No	372	96.9
Previous TB treatment	Yes	0	0.0
	No	384	100.0
Immediate family members with TB	Yes	3	0.8
	No	381	99.2
Currently feeling sick	Yes	37	9.6
	No	347	90.4
History of smoking	Yes	0	0.0
	No	384	100.0

Section C: Epidemiological and Laboratory Characteristics of the Study Participants

Table 5. Epidemiological characteristics of the study participants.

Variables		Frequency	Percentage (%)
Site of Presumptive TB	Pulmonary TB	384	100.0
Type of Presumptive Tuberculosis	DS-TB	384	100.0
HIV Status	Positive	7	1.8
	Negative	256	66.7
	Unknown	119	31.0
Reason for Examination	Diagnosis	384	100.0
Test Requested	Xpert/MTB/RIF	384	100.0
Swab/XPERT Result	Positive	32	8.3
	Negative	352	91.7
Sputum/ XPERT Result	Positive	41	10.7
	Negative	343	89.3

Table 6. Cross tabulation on sputum Xpert and swab Xpert.

		Sputum Xpert		
		Positive	**Negative**	**Total**
Swab Xpert	**Positive**	32= TP (%)	0= FP (%)	32= (TP+FP)
	Negative	9= FN (%)	343= TN (%)	352= (FN+TN)
	Total	41= (TP+FN)	343= (FP+TN)	384= N

Where TP is True Positive; FN is False Negative; FP is False Positive, TN is True Negative and N is total number of samples

Sensitivity= [TP/(TP+FN)] ×100% = **78.0%**

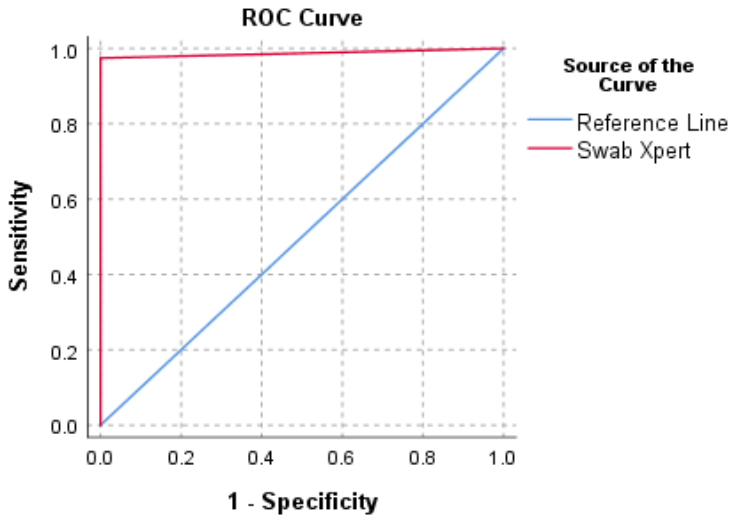
Specificity= [TN/(TN+FP)] ×100% = **100%**

PPV= [TP/(TP+FP)] ×100% = **100%**

NPV= [TN/(TN+FN)] ×100% = **97.4%**

Accuracy= (TP+TN)/N ×100% = **97.7%**

Figure 1. Receiver's operating characteristic curve of sputum Xpert and swab Xpert
From the ROC graph, the area under the curve is c = 0.974 which indicates good predictive power of the tongue swab.



Younden index = Sensitivity (%)+Specificity (%)-100 = 78%, The cut-off point for having an acceptable Younden index is 50% hence, 78% is above 50% which denotes that the tongue swab meets empirical benchmarks for being administered for diagnostic purposes of tuberculosis.

Discussion

Some patients, children, the aged, and immuno-compromised may not expectorate quality sputum for testing Mycobacterium tuberculi due to underlying medical conditions [10, 11, 12]. Oral swabs provide several potential diagnostic benefits for the most part in community settings where sputum collection for TB is unfeasible . This study aimed to identify the diagnostic accuracy of Mycobacterium tuberculosis in tongue Swab. Our data showed that participants between the ages of 18 - 27 years had the highest positivity rate for Mycobacterium tuberculosis. This finding is tandem with previous reports [13, 15, 16].

In this cross-sectional laboratory-base study, we found that tongue swab has similar sensitivity for Mycobacterium tuberculi in comparison to the sputum sample. Similar studies were reported by Luabeya et al. [11] in South Africa and [12]. Tongue swab could be used to diagnose Mycobacterium tuberculosis. A sensitivity rate of 45% was obtained in a study on cheek swab in Peru [4]. In another study of mass TB screening among prisoners in Brazil indicated a sensitivity rate of 51% on tongue swabs. Besides, another study showed a single swab sensitivity of 88%(44/50) on day 1 and 94.4%(17/18) on day 2 with a specificity of 79.2%(42/53) [14, 17, 18]. Erroneous TB

diagnoses especially in high-burden countries with limited access to healthcare resources could widen the case-detection gap and promotes transmission rate of tuberculosis [19]. In the present study, the tongue swab GeneXpert performance in the detection of Mycobacterium tuberculosis was higher than the sputum GeneXpert in the early morning sample collection before engagement in any oral activity. Moreover, tongue swab has the advantage of lowering biosafety concerns regardless of the bacterial viability. Consequently, this study adds to the growing body of knowledge regarding the use of tongue swabs in the diagnosis of tuberculosis. Even though the morning oral swab had the maximum sensitivity, it only detected 78.0% of individuals with laboratory-confirmed pulmonary TB.

According to our results, one oral swab's sensitivity was 78% valid. The significant absence of overlap in MTB detection across the samples collected from the participants was another intriguing finding. Pulmonary TB is the site of presumptive TB for all participants with DS-TB as the type of presumptive TB. A good number of the participants 119(31.0%) said they don't know their HIV status while the majority of the participants (66.7%) knew their status as HIV negative and 7(1.8%) as HIV positive. All the participants' reason for examination is the diagnosis for XPERT/MTB/RIF in which 91.7% tested negative on sputum XPERT/MTB/RIF and 89.3% tested negative on swab XPERT/MTB/RIF respectively.

From the correlation table above the value of 87.2% shows a positive relationship between the Swab result and the sputum gene Xpert result. The relationship, however, has a significant effect ($0.001<0.01$) which means that there are sufficient reasons to uphold the alternate hypothesis. This shows that swab kits are valid and reliable in line with previous reports [20, 21, 22, 23].

CONCLUSION

Our finding demonstrated that Mycobacterium tuberculosis could be found in tongue swab especially for individuals who had difficulty producing sputum. The potential for non-sputum base diagnostics could be enhanced by the use of tongue swab. The procedure is less invasive, easier, and non-aerosol producing efficient alternate approach for pulmonary tuberculosis and should be further investigated.

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Conflict of Interest

Nothing to declare.

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