Determining the prevalence of tuberculosis in emergency departments in the Eastern Cape region of South Africa and the utility of the World Health Organization tuberculosis screening tool

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Background. South Africa (SA) faces a significant tuberculosis (TB) burden complicated by high rates of HIV-TB co-infection. In SA, emergency departments (EDs) play an important role in screening for TB.
Objectives. To determine the prevalence of TB in the ED and the effectiveness of the World Health Organization (WHO) TB screening tool.
Methods. This was a cross-sectional observational study, conducted in the ED at Livingstone Hospital, Port Elizabeth, from 4 June to 15 July 2018. All patients aged >18 years and able to consent were administered the WHO TB screening questions and underwent a point-of-care HIV test and demographic data collection. Patients were followed up for 1 year and tracked in the National Health Laboratory Service database to determine TB status using laboratory testing.
Results. Over the study period, 790 patients were enrolled. Overall, 121 patients (15.3%) were TB-positive, with 46 (38.0%) diagnosed after presenting to the ED and 75 (62.0%) with a previous TB history determined by self-report or confirmed laboratory testing. A greater proportion of the TB-positive patients were HIV-positive (49.6%) compared with the TB-negative population (24.8%). TB-positive individuals were more likely to present to the ED with a chief complaint of shortness of breath (SoB) (18.2%) compared with the TB-negative population (10.5%). Overall, the WHO TB screening tool had poor sensitivity (46.5%) and specificity (62.5%) for identifying TB-positive patients in the ED. A multiple logistic regression analysis, controlled for age and sex, showed HIV status (odds ratio (OR) 2.81; $p<0.001$) and SoB (OR 2.19; $p<0.05$) to be significant predictors of TB positivity. Adding positive HIV status and a presenting complaint of SoB increased sensitivity to 78.3%.
Conclusions. EDs in SA face a high burden of TB. While WHO screening guidelines identify some of these patients, including routine HIV testing in the ED could significantly affect the number of TB diagnoses made.

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Tuberculosis (TB) remains one of the top 10 causes of death worldwide and is the leading cause of death from a single infectious agent.[1] Globally, an estimated 10 million people become infected with TB each year, with six countries accounting for 60% of the global TB burden.[1] Among these countries, South Africa (SA) has the highest burden of HIV co-infected cases.[1,2] In 2018, there were an estimated 301 000 incident cases of TB in SA, compounded by 177 000 new HIV-positive TB cases.[3] While TB mortality rates in SA have declined as a result of the expansion of antiretroviral therapy (ART) programmes to treat HIV, TB remains the leading cause of death in the country.[4,5] Despite estimates that TB incidence rates and mortality are decreasing, the current rate of decline is unlikely to meet the World Health Organization (WHO) End TB Strategy targets to reduce TB deaths by 95% and TB cases by 90% before the year 2035.[2,6,7] In SA, reaching these targets requires a significant response from the National Tuberculosis Control Programme. While the programme has largely focused on treatment success rates, this focus fails to address upstream losses due to individuals not accessing TB-specific health services and those who remain undiagnosed with TB.[2] A better understanding of the TB care cascade and the utility of diagnostic screening services is therefore needed in order to improve TB detection processes and connect infected individuals with care.[8]

While effective asymptomatic testing is available for HIV diagnosis, point-of-care (PoC) screening tools for asymptomatic TB infection are not currently in use.[9,10] As a result, many individuals with TB are diagnosed late in the disease course despite opportunities for earlier detection.[1,11] Delay in the diagnosis of TB results in excess morbidity and mortality, particularly among HIV-infected individuals.[11,12] One of the reasons for the increasing difficulties in early detection of TB involves the changing demographics of and comorbidities with the disease. Although TB incidence rates are strongly associated with increasing age, the highest TB burden has

shifted from older to younger populations in SA.[13,14] Among all patients infected with TB, 65% are co-infected with HIV, and HIV-TB co-infection age rates are associated with the peak ages of HIV incidence.[1,14] Although TB incidence rates have historically been higher in males, recent data suggest that the incidence among HIV-infected females has increased significantly and that the peak TB prevalence occurs at an earlier age in women compared with men.[15] As a result of these changing demographics and TB incidence profiles with high rates of HIV co-infection, screening for TB has become increasingly complicated.

In SA, the emergency department (ED) remains a safety net of the public healthcare system and manages a significant proportion of the acute healthcare burden. Much of the care provided by EDs is related to trauma and HIV, with the patients utilising EDs largely representing populations that cannot otherwise access or seek primary services.[16,17] The EDs in Eastern Cape Province are typically staffed by junior doctors or medical officers with little training in emergency medicine, and these departments continue to suffer from a lack of resources, staff and equipment.[16] Given the endemic burden of TB and high rates of ED use in SA, EDs have an important role in providing healthcare services to individuals with TB and can contribute to earlier detection of TB. As a result, low-cost options requiring little advanced training are necessary to screen for TB. However, significant gaps remain in terms of screening patients for TB throughout SA.[18]

In order to connect TB-positive patients with earlier care, EDs in SA must be better equipped to identify patients with TB and TB-associated comorbidities. The WHO has developed a screening questionnaire to identify patients with TB based on the patient's answers to four symptom-related questions.[19] Although this tool can be applied easily in the ED setting and can screen asymptomatic individuals quickly in high-volume care facilities, its utility and effectiveness have yet to be evaluated.

Objectives

To assess the utility of the WHO screening tool in the ED setting and determine the prevalence of TB in the ED. We sought to determine the sensitivity of the WHO screening tool in detecting TB-positive cases and to develop a model to increase the utility of this tool.

Methods

This cross-sectional observational study was conducted from 4 June to 15 July 2018. During the study period, PoC HIV testing was implemented in accordance with the SA national testing guidelines and data were collected on patient demographics, chief complaint, severity of illness, medical history, ED course of care, and responses to the WHO TB screening tool. A detailed description of the Walter Sisulu Infection Screening in the Emergency Department (WISE) study methodology is available elsewhere.[10]

Study setting

The study was conducted in the ED of Livingstone Hospital in Port Elizabeth, Eastern Cape Province, SA. Livingstone Hospital is a tertiary-care centre providing 24-hour service 7 days a week and receives patients from up to 200 km away. The ED receives 100 - 150 patients per day, has <50 beds, and during the study period was staffed by medical officers and nurses with limited formal training in emergency medicine. Patient medical records are kept in paper files, and handwritten logbooks are used as patient tracking systems. Laboratory tests are tracked and reported using an electronic-based system through the National Health Laboratory Service (NHLS).

Study procedures

All patients presenting for care in the ED during the study period who were aged >18 years, fully conscious and clinically stable were eligible for enrolment. Study staff were instructed to approach patients immediately after the triage process was completed, and patients were requested to provide consent to a PoC HIV test, collection of information using the WHO TB screening tool (Fig. 1), collection of demographic data, and follow-up using the NHLS LabTrak system.

Data on demographics and PoC HIV test status and from the WHO TB screening tool were collected by study staff using case report forms, which were then scanned and entered using intelligent character recognition DataFax software (Clinical DataFax Systems Inc., Canada) and centrally double-verified by independent data technicians. Patients were then traced in the NHLS LabTrak system for 1 year after their initial ED presentation, where data were collected at the end of the year on TB testing as well as other serological and microbiology testing.

ADULT TB SYMPTOM SCREENING				
Symptoms				
Temperature	BP	Pulse	Weight	Height
Cough ≥2 weeks OR of any duration if HIV-positive			Yes	No
Persistent fever >2 weeks			Yes	No
Unexplained weight loss >1.5 kg in a month			Yes	No
Drenching night sweats >2 weeks			Yes	No
MEDICAL HISTORY				
Close contact of a person with infectious TB		Yes	No	Unknown
Type of index patient		DS TB	MDR/XDR TB	
Diabetes		Yes	No	Unknown
HIV status		Positive	Negative	Unknown

Fig. 1. The World Health Organization TB screening tool. (TB = tuberculosis; BP = blood pressure; DS = drug-sensitive; MDR = multidrug-resistant; XDR = extensively drug-resistant.)

The primary outcome measure sought to determine the prevalence of undiagnosed TB among HIV-positive individuals. Data analysis was approached using a descriptive statistical method using Stata version 15 (StataCorp, USA). The overall prevalence of TB was determined using NHLS testing data and patients' self-reported history of TB diagnosis. The odds of positive TB status based on screening tools and clinical indicators was calculated using simple and multiple logistic regression analysis. Crude (unadjusted) and adjusted odds ratios (ORs) were used to examine the odds of TB infection and clinical factors.

The Johns Hopkins University School of Medicine Institutional Review Board (ref. no. IRB00105801), the Walter Sisulu University Human Research Ethics Committee (ref. no. 002/2016) and the University of Cape Town Human Research Ethics Committee (ref. no. 401/2013) approved this study. All participants enrolled in the study provided written consent to receive a PoC HIV test and have detailed demographic data collected on both their reason for presentation and their ED course.

Results

A total of 790 patients were enrolled throughout the study period, of whom 121 (15.3%) were confirmed TB-positive. Of these, 46 patients (38.0%) were diagnosed with TB within 12 months after presenting to the ED (i.e. had asymptomatic TB during their ED stay) and 75 (62.0%) had a known diagnosis of TB with a previous history of TB determined by self-report or confirmed laboratory testing up to 12 months before the study period. As shown in Table 1, significant differences in TB status by age category (p=0.023) and sex (p=0.001) were seen. A significant burden of patients aged <35 years

Table 1. Characteristics of the study population by TB status

	Positive (*N*=121), *n* (%)	Negative (*N*=258), *n* (%)	Not tested (*N*=411), *n* (%)	Total (*N*=790), *n* (%)	*p*-value (χ^2 test)
Age (years)					0.023*
<20	1 (0.8)	6 (2.3)	16 (3.9)	23 (2.9)	
20 - 34	49 (40.5)	86 (33.3)	172 (41.8)	307 (38.9)	
35 - 49	47 (38.8)	94 (36.4)	113 (27.5)	254 (32.1)	
≥50	24 (19.8)	72 (27.9)	110 (26.8)	206 (26.1)	
Sex					0.001*
Male	64 (52.9)	135 (52.3)	160 (38.9)	359 (45.4)	
Female	57 (47.1)	123 (47.7)	251 (61.1)	431 (54.6)	
Reason for ED visit					0.096
Medical	70 (57.8)	129 (50.0)	192 (46.7)	391 (49.5)	
Trauma	51 (42.1)	129 (50.0)	219 (53.3)	399 (50.5)	
Time of presentation†					0.592
In hours	47 (38.8)	104 (40.3)	178 (43.3)	329 (41.6)	
After hours	74 (61.2)	154 (59.7)	233 (56.7)	461 (58.3)	
Transport					0.234
Ambulance	50 (41.3)	87 (33.7)	120 (29.2)	257 (32.5)	
Police	2 (1.7)	3 (1.2)	10 (2.4)	15 (1.9)	
Self-transport	69 (57.0)	167 (64.7)	280 (68.1)	516 (65.3)	
Unknown	0	1 (0.4)	1 (0.2)	2 (0.2)	
SATS					0.156
Emergency	3 (2.5)	5 (1.9)	8 (2.0)	16 (2.0)	
Very urgent	14 (11.6)	17 (6.6)	21 (5.1)	52 (6.6)	
Urgent	67 (55.4)	141 (54.7)	213 (51.8)	421 (53.3)	
Routine	37 (30.6)	95 (36.8)	169 (41.1)	301 (38.1)	
HIV status					<0.001*
Known positive	33 (36.4)	51 (19.8)	40 (9.7)	135 (17.1)	
New positive	16 (13.2)	13 (5.0)	18 (4.4)	47 (5.9)	
Negative	48 (39.7)	138 (53.5)	234 (56.9)	420 (53.2)	
Unknown	13 (10.7)	56 (21.7)	119 (29.0)	188 (23.8)	
Disposition					0.184
Death	0	0	1 (0.2)	1 (0.1)	
Admission	23 (19.0)	24 (9.3)	32 (7.8)	79 (10.0)	
ICU admission	0	0	1 (0.2)	1 (0.1)	
Emergency surgery	0	0	1 (0.2)	1 (0.1)	
Transfer	25 (20.7)	55 (21.3)	77 (18.7)	157 (19.9)	
Discharge	70 (57.8)	170 (65.9)	285 (69.3)	525 (66.5)	
Absconded	3 (2.5)	6 (2.3)	10 (2.4)	19 (2.4)	
Unknown	0	3 (1.2)	4 (1.0)	7 (0.9)	

TB = tuberculosis; ED = emergency department; SATS = South African Triage Scale; ICU = intensive care unit.
*Statistically significant at the p<0.05 level.
†In hours designated as 08h00 - 16h00 and after hours as 16h01 - 07h59.

(41.3%; *n*=50/121) were TB-positive compared with those who were TB-negative (35.6%; *n*=92/258). A large number of patients in the ED did not receive any TB testing (i.e. no TB testing during the ED visit or up to 1 year subsequently). Higher proportions of individuals aged <20 years (69.6%; *n*=16/23) and of females (58.2%; *n*=251/431) were not tested for TB compared with older populations (51.3%; *n*=395/767) and males (44.6%; *n*=160/359), despite a higher proportion of younger patients and males testing positive for TB.

There was no significant difference in TB prevalence by medical v. trauma complaints, although as expected more trauma patients (53.3%; *n*=219/411) were not tested for TB compared with medical patients (46.7%; *n*=192/411). A higher proportion of the TB-positive population was HIV-positive (40.5%; *n*=49/121) compared with the TB-negative population (24.8%; *n*=64/258).

In Table 2, we compare the characteristics of patients who were TB-positive (*n*=121). Of the 46 recent positives, 41 (89.1%) received testing in Port Elizabeth and 5 (10.9%) received testing outside Port Elizabeth. One recent positive was determined by biopsy and was the only case in which biopsy was used to determine TB status. No significant differences were found in age categories, sex, HIV status, or prevalence of comorbidities/co-infections when comparing patients recently diagnosed as TB-positive with those with a history of TB diagnosis.

There was limited completion of testing for additional pathogens or infections in the recent TB diagnosis population (Fig. 2). GeneXpert (82.6%; *n*=38/42) and Auramine O (87.0%; *n*=40/46) were used to diagnose TB more frequently than solid or liquid TB cultures (50.0%; *n*=23/46) or biopsy (2.2%; *n*=1/46). Resistance testing

Table 2. Demographic characteristics of TB-positive populations

	Previously positive (*N*=75), *n* (%)	Recent positive (*N*=46), *n* (%)	Total (*N*=121), *n* (%)	*p*-value (χ^2 test)
Age (years)				0.544
<20	1 (1.3)	0	1 (0.8)	
20 - 34	29 (38.7)	20 (43.5)	49 (40.5)	
35 - 49	32 (42.7)	15 (32.6)	47 (38.8)	
≥50	13 (17.3)	11 (23.9)	24 (19.8)	
Sex				0.211
Male	43 (57.3)	21 (45.7)	64 (52.9)	
Female	32 (42.7)	25 (54.3)	57 (47.1)	
HIV status				0.232
Positive	33 (44.0)	27 (58.7)	60 (49.6)	
Negative	32 (42.7)	16 (34.8)	48 (39.7)	
Unknown	10 (13.3)	3 (6.5)	13 (10.7)	
Comorbidities/co-infection				
Heart disease	1 (1.3)	1 (2.2)	2 (1.7)	0.725
Diabetes	4 (5.3)	1 (2.2)	5 (4.1)	0.397
Respiratory condition	12 (16.0)	5 (10.9)	17 (14.1)	0.430

TB = tuberculosis.

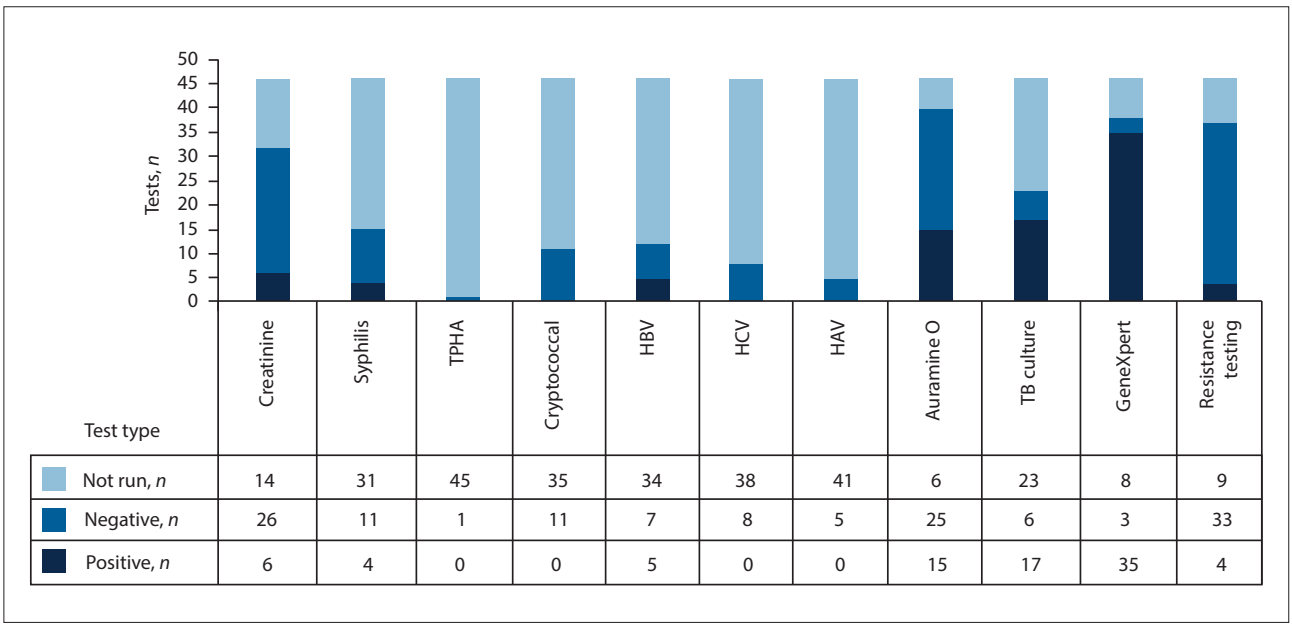

Fig. 2. Testing patterns in the recent TB-positive population (N=46). *(TB = tuberculosis; TPHA =* Treponema pallidum *haemagglutination; HBV = hepatitis B virus; HCV = hepatitis C virus; HAV = hepatitis A virus.)*

was completed on 37 patients (80.4%) with a recent TB diagnosis. Additionally, creatinine tests (69.6%; *n*=32/46) were the tests most frequently ordered in conjunction with TB testing, while *Treponema pallidum* hemagglutination (TPHA) tests (2.2%; *n*=1/46) were the least frequently ordered. Tests for IgM and IgG antibodies against cytomegalovirus and tests for toxoplasmosis were never completed in the recent TB diagnosis population.

Of the 790 individuals who presented to the ED in Port Elizabeth, 135 (17.1%) screened positive for TB using the WHO TB screening questions, while only 45 (5.7%) had testing-confirmed TB (Auramine O, TB culture, GeneXpert, pathology) (Table 3). As expected, TB-positive individuals presented to the ED with a chief complaint of shortness of breath (SoB) (18.2%; *n*=22/121) more often than the TB-negative population (10.5%; *n*=27/258). The WHO tool was effective in identifying some positive TB patients, but had poor sensitivity (46.5%; *n*=20/43) and specificity (62.5%; *n*=45/72).

The WHO TB screening tool with a positive response to any of the tool's individual questions (cough >2 weeks, fever >2 weeks, weight loss >1.5 kg, drenching night sweats >2 weeks) and a positive HIV status were all statistically significant ($p<0.001$) predictors of a positive TB diagnosis, as reflected in Table 3. Outside of the WHO TB screening tool, a chief complaint of SoB was determined to be a significant predictor of a positive TB history ($p=0.037$). Interestingly, individual chief complaints similar to the WHO TB screening tool questions (i.e. cough/bloody cough, weight loss/wasting, fever/chills) were not significant predictors of a positive TB history.

A multiple logistic regression analysis, controlled for age and sex, showed HIV status (OR 2.81; $p<0.001$) and SoB (OR 2.19; $p<0.05$) to be independently significant predictors of TB positivity (Table 4). The single most significant predictor of positive TB status when adjusting for age and sex was found to be drenching night sweats for >2 weeks (OR 4.08). However, the odds of positive TB status was 3.57 times higher when combining positive WHO TB screening and positive HIV status, and was only 3.13 times higher when combining positive WHO TB screening, positive HIV status and a complaint of SoB. The addition of positive HIV status and a presenting complaint of SoB increased sensitivity to 78.3%, although it decreased specificity to 36.5%.

Discussion

A high burden of TB was found in this SA ED, with a TB prevalence of 15.3% based on previous history determined by self-report and confirmed laboratory testing 1 year from the index visit. The most recent WHO estimate of TB prevalence in SA estimated 696 cases per 100 000 population (0.696%), which is significantly lower than the prevalence in our study population.[20] Additionally, the 2016 South Africa Demographic and Health Survey reported the proportion of self-reported TB in women and men to be 5% and 6%, respectively.[21] These proportions are again much lower than those found in our study. SA has made notable progress in reducing TB prevalence and deaths and improving treatment outcomes for new smear-positive TB cases, but the burden of TB remains enormous. Strengthening case finding and the use of Xpert MTB/RIF as a replacement for sputum smear microscopy are necessary to further accelerate progress towards improved TB control in SA and beyond.[22] The ED remains an untapped opportunity where both of these strategies could be applied.

Similar to other studies, a lower proportion of females were tested for TB compared with males.[14] Additionally, peak ages for TB positivity were in the 20 - 34- and 35 - 49-year age groups, which has also been observed elsewhere.[13,14] Although the burden of TB in EDs throughout SA varies by centre, the high prevalence of TB found in this setting can probably be applied to other ED settings given the endemic burden of TB and the role of these departments in managing the

Table 3. Predictors of TB status as binary variables

	TB-positive (*N*=121), *n* (%)	TB-negative (*N*=258), *n* (%)	Total (*N*=379), *n*	*p*-value (χ^2 test)
Age (years)				
<20	1 (14.3)	6 (85.7)	7	0.312
20 - 34	49 (36.3)	86 (63.7)	135	0.175
35 - 49	47 (33.3)	94 (66.7)	141	0.651
≥50	24 (25.0)	72 (75.0)	96	0.092
Female	57 (31.7)	123 (68.3)	180	0.918
HIV-positive	60 (48.4)	64 (51.6)	124	<0.001*
History of respiratory condition	17 (34.7)	32 (65.3)	49	0.656
Regular tobacco use	42 (38.9)	66 (61.1)	108	0.066
+ Cough >2 weeks	33 (50.0)	33 (50.0)	66	<0.001*
+ Fever >2 weeks	27 (54.0)	23 (46.0)	50	<0.001*
+ Weight loss >1.5 kg	33 (55.9)	26 (44.1)	59	<0.001*
+ Drenching night sweats >2 weeks	32 (60.4)	21 (39.6)	53	<0.001*
+ WHO TB screening	**47 (51.7)**	**44 (48.3)**	**91**	**<0.001***
Chief complaint: SoB	22 (44.9)	27 (55.1)	49	0.037*
Chief complaint: cough/bloody cough	2 (50.0)	2 (50.0)	4	0.436
Chief complaint: fever/chills	1 (100.0)	0 (0.0)	1	0.144
Chief complaint: weight loss/wasting	0 (0.0)	0 (0.0)	0	-
Triage RR >16/min	93 (30.7)	210 (69.3)	303	0.461
Triage temperature >37.8°C	3 (42.9)	4 (57.1)	7	0.549
Triage systolic BP <90 mmHg	2 (50.0)	2 (50.0)	4	0.432

TB = tuberculosis; WHO = World Health Organization; SoB = shortness of breath; RR = respiratory rate; BP = blood pressure; No tint (white) = WHO screening tool.
*Statistically significant at the $p<0.05$ level.

Table 4. Odds of a positive TB diagnosis by WHO screening criteria, HIV status and SoB

	Unadjusted			Adjusted†		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
HIV status	2.69	1.66 - 4.36	<0.001*	2.81	1.72 - 4.59	<0.001*
WHO cough >2 weeks	2.58	1.50 - 4.46	0.001*	2.65	1.53 - 4.60	0.001*
WHO fever >2 weeks	2.96	1.61 - 5.44	<0.001*	2.94	1.60 - 5.41	0.001*
WHO weight loss >1.5 kg	3.37	1.90 - 5.99	<0.001*	3.39	1.91 - 6.04	<0.001*
WHO drenching night sweats >2 weeks	4.12	2.25 - 7.56	<0.001*	4.08	2.22 - 7.49	<0.001*
WHO screen positive	3.13	1.91 - 5.13	<0.001*	3.21	1.95 - 5.29	<0.001*
WHO + HIV status	3.51	2.21 - 5.58	<0.001*	3.57	2.24 - 5.71	<0.001*
WHO + HIV status + SoB	2.97	1.87 - 4.71	<0.001*	3.13	1.96 - 5.01	<0.001*
Chief complaint: SoB	1.90	1.03 - 3.50	0.039*	2.19	1.16 - 4.11	0.015*

TB = tuberculosis; WHO = World Health Organization; SoB = shortness of breath; OR = odds ratio; CI = confidence interval; No tint (white) = variables increasing WHO screening tool sensitivity with multiple regression analysis.
*Statistically significant at the $p<0.05$ level.
†Adjusted for age and sex.

acute care of patients who may present later in the disease course.[23,16] The present study found a high number of patients with previously undetected TB, with 38% of the patients determined to be TB-positive having never received a previous TB diagnosis. Almost half (49.6%) of the TB-positive patients were co-infected with HIV, further supporting the high rates of co-infection determined elsewhere.[1,11,24]

A high percentage of HIV-infected patients presented with subclinical TB that was diagnosed only by screening and further laboratory testing, indicating a need for simultaneous screening for both HIV and TB on presentation to the ED.[24,25] Given this evidence, a positive HIV test should prompt further TB screening if not completed simultaneously in high-HIV/TB endemic settings. Evidence from this and other studies suggests that the most effective TB screening should be done in conjunction with HIV testing, especially given the development of affordable PoC HIV tests that can be conducted in resource-limited settings.[10,24-26] Furthermore, since WHO guidelines recommend that TB should be diagnosed and treated together with the initiation of ART, screening for TB should be conducted in all cases of known and incident HIV.[27] However, obstacles to PoC testing for HIV in EDs have been well documented, warranting the need to assess these barriers and their effect on PoC TB screening and testing.[28] The WHO has previously recommended a cough duration of 2 - 3 weeks as a symptom screen for TB, but this is now recognised as inadequate for HIV-associated TB, with the sensitivity frequently found to be <50% in HIV-positive patients.[29] Similar results were found in this study, with the four-question WHO screening tool providing an overall sensitivity of just 46.5%. These data and the high rates of HIV co-infection in the study population suggest that the WHO TB screening tool is largely inadequate in the setting of endemic HIV co-infection.

Although the WHO screening questions have been developed as a low-cost screening option requiring minimal advanced training to administer, the present study demonstrates that this tool has limited efficacy in its current form. The assessment of the WHO screening questionnaire in this study reveals the inadequacy of non-serological tools in detecting subclinical cases of TB, particularly in the setting of endemic HIV co-infection. With the modifications of the tool applied in our model, adding HIV status and a chief complaint of SoB to the four questions already included in the screening questionnaire substantially increased the sensitivity of the screening tool to 78.3%. Given the availability of low-cost PoC HIV testing in SA, this should be conducted together with TB screening in order to increase the efficacy of these efforts. Modifying the WHO screening tool in this way not only improves its ability to detect TB-positive patients, but also provides a low-cost option to detect TB more reliably in EDs that face a high burden of the disease. However, more importantly, this study provides a use case for PoC TB testing in the ED. While the WHO screening strategy may allow health facilities to more appropriately identify candidates for PoC Xpert MTB/RIF testing, without PoC testing many ED patients are unlikely to receive the follow-up care they require. The 2011 FIND study was a multicentre feasibility and accuracy study evaluating the implementation of Xpert MTB/RIF testing, and included a Ugandan ED as one of the clinical sites.[30] A recent multicountry southern African study demonstrated that not only did this PoC strategy increase treatment initiation, but it was also cost-effective when compared with current standard-of-care testing strategies.[31] Our study provides further evidence that given the high prevalence of TB and HIV, the ED is a viable and necessary venue to implement PoC TB testing if we are to achieve epidemiological control.

Study limitations

Owing to its design as a secondary data analysis, several factors limited this study in terms of data collection. Many patients were excluded from analysis because they could not be matched to hospital records or were not found in the NHLS database. Furthermore, because no confirmatory laboratory testing was completed in a large number of patients, the comparison groups were greatly reduced for assessing the effectiveness of the WHO TB screening tool. Some patients may have been diagnosed using chest radiographs, PoC focused assessment with ultrasonography for HIV, or PoC urinary lipoarabinomannan assay, and these data would not be reflected in the NHLS database. Further assessment is also needed to determine barriers to PoC TB testing in the ED setting.

Conclusions

Emergency centres in SA continue to face a high burden of TB. While WHO screening guidelines identify some of these patients, modifying these guidelines and including routine HIV testing in the ED could significantly affect the number of TB diagnoses made by increasing the sensitivity of this tool.

Declaration. None.

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Conflicts of interest. None.

1. World Health Organization. Global Tuberculosis Report 2019. 15 October 2019. https://www.who.int/publications/i/item/global-tuberculosis-report-2019 (accessed 1 December 2020).
2. Naidoo P, Theron G, Rangaka MX, et al. The South African tuberculosis care cascade: Estimated losses and methodological challenges. J Infect Dis 2017;216(S7):S702-S713. https://doi.org/10.1093/infdis/jix335
3. World Health Organization. Tuberculosis country profiles. 2019. https://www.who.int/tb/publications/global_report/tb19_Report_country_profiles_15October2019.pdf (accessed 1 December 2020).
4. Loveday M, Mzobe YN, Pillay Y, Barron P. Figures of the dead: A decade of tuberculosis mortality registrations in South Africa. S Afr Med J 2019;109(10):728-732. https://doi.org/10.7196/SAMJ.2019.v109i10.14073
5. Reniers G, Blom S, Lieber J, et al. Tuberculosis mortality and the male survival deficit in rural South Africa: An observational community cohort study. PLoS ONE 2017;12(10):e0185692. https://doi.org/10.1371/journal.pone.0185692
6. World Health Organization. The End TB Strategy. Geneva: WHO, 2015. https://www.who.int/tb/strategy/End_TB_Strategy.pdf (accessed 1 December 2020).
7. Statistics South Africa. Mortality and causes of death in South Africa, 2016: Findings from death notification. Statistical release P0309. Pretoria: Stats SA, 2018. https://www.statssa.gov.za/publications/P03093/P030932016.pdf (accessed 1 December 2020).
8. Cazabon D, Alsdurf H, Satyanarayana S, et al. Quality of tuberculosis care in high burden countries: The urgent need to address gaps in the care cascade. Int J Infect Dis 2016;56:111-116. https://doi.org/10.1016/j.ijid.2016.10.016
9. Johnson LF, van Rensburg C, Govathson C, Meyer-Rath G. Optimal HIV testing strategies for South Africa: A model-based evaluation of population-level impact and cost-effectiveness. Sci Rep 2019;9(1):12621. https://doi.org/10.1038/s41598-019-49109-w
10. Hansoti B, Stead D, Parrish A, et al. HIV testing in a South African emergency department: A missed opportunity. PLoS ONE 2018;13(3):e0193858. https://doi.org/10.1371/journal.pone.0193858
11. Meintjes G, Schoeman H, Morroni C, Wilson D, Maartens G. Patient and provider delay in tuberculosis suspects from communities with a high HIV prevalence in South Africa: A cross-sectional study. BMC Infect Dis 2008;8(1):72. https://doi.org/10.1186/1471-2334-8-72
12. Heunis JC, Kigozi NG, Chikobvu P, Botha S, van Rensburg HD. Risk factors for mortality in TB patients: A 10-year electronic record review in a South African province. BMC Public Health 2017;17(1):38. https://doi.org/10.1186/s12889-016-3972-2
13. Blaser N, Zahnd C, Hermans S, et al. Tuberculosis in Cape Town: An age-structured transmission model. Epidemics 2016;14:54-61. https://doi.org/10.1016/j.epidem.2015.10.001
14. Wood R, Lawn SD, Caldwell J, Kaplan R, Middelkoop K, Bekker L-G. Burden of new and recurrent tuberculosis in a major South African city stratified by age and HIV-status. PLoS ONE 2011;6(10):e25098. https://doi.org/10.1371/journal.pone.0025098
15. McLaren ZM, Brouwer E, Ederer D, Fischer K, Branson N. Gender patterns of tuberculosis testing and disease in South Africa. Int J Tuberc Lung Dis 2015;19(1):104-110. https://doi.org/10.5588/ijtld.14.0212
16. Wallis LA, Garach SR, Kropman A. State of emergency medicine in South Africa. Int J Emerg Med 2008;1(2):69-71. https://doi.org/10.1007/s12245-008-0033-3
17. Hsia RY, Thind A, Zakariah A, Hicks ER, Mock C. Prehospital and emergency care: Updates from the disease control priorities, version 3. World J Surg 2015;39(9):2161-2167. https://doi.org/10.1007/s00268-015-2997-5
18. Christian CS, Gerdtham UG, Hompashe D, et al. Measuring quality gaps in TB screening in South Africa using standardised patient analysis. Int J Environ Res Public Health 2018;15(4):E729. https://doi.org/10.3390/ijerph15040729
19. World Health Organization. Systematic screening for active tuberculosis: Principles and recommendations. Geneva: WHO, 2013. https://www.who.int/tb/publications/Final_TB_Screening_guidelines.pdf (accessed 1 December 2020).
20. World Health Organization. Global Tuberculosis Report 2015. Geneva: WHO, 2015. https://www.who.int/tb/publications/global_report/gtbr15_main_text.pdf (accessed 1 December 2020).
21. National Department of Health, South Africa, Statistics South Africa, South African Medical Research Council, and ICF. South Africa Demographic and Health Survey 2016. Pretoria, South Africa, and Rockville, Md, USA: NDoH, Stats SA, SAMRC, and ICF, 2019. https://dhsprogram.com/pubs/pdf/FR337/FR337.pdf (accessed 1 December 2020).
22. Churchyard GJ, Mametja LD, Mvusi L, et al. Tuberculosis control in South Africa: Successes, challenges and recommendations. S Afr Med J 2014;104(3):244-248. https://doi.org/10.7196/SAMJ.7689
23. Cox H, Dickson-Hall L, Ndjeka N, Hoog A, et al. Delays and loss to follow-up before treatment of drug-resistant tuberculosis following implementation of Xpert MTB/RIF in South Africa: A retrospective cohort study. PLoS Med 2017;14(2):e1002238. https://doi.org/10.1371/journal.pmed.1002238
24. Oni T, Burke R, Tsekela R, et al. High prevalence of subclinical tuberculosis in HIV-1-infected persons without advanced immunodeficiency: Implications for TB screening. Thorax 2011;66(8):669-673. https://doi.org/10.1136/thx.2011.160168
25. Bassett IV, Wang B, Chetty S, et al. Intensive tuberculosis screening for HIV-infected patients starting antiretroviral therapy in Durban, South Africa. Clin Infect Dis 2010;51(7):823-829. https://doi.org/10.1086/656282
26. Lawn SD, Wood R. Tuberculosis in antiretroviral treatment services in resource-limited settings: Addressing the challenges of screening and diagnosis. J Infect Dis 2011;204(S4):S1159-S1167. https://doi.org/10.1093/infdis/jir411
27. World Health Organization. Improving the diagnosis and treatment of smear-negative pulmonary and extra-pulmonary tuberculosis among adults and adolescents. Recommendations for HIV-prevalent and resource-constrained settings. Geneva: WHO, 2007. https://apps.who.int/iris/bitstream/handle/10665/69463/WHO_HTM_TB_2007.379_eng.pdf?sequence=1&isAllowed=y (accessed 1 December 2020).
28. Hansoti B, Mwinnyaa G, Hahn E, et al. Targeting the HIV epidemic in South Africa: The need for testing and linkage to care in emergency departments. E Clin Med 2019;15:14-22. https://doi.org/10.1016/j.eclinm.2019.08.007
29. Reid MJA, Shah NS. Approaches to tuberculosis screening and diagnosis in people with HIV in resource-limited settings. Lancet Infect Dis 2009;9(3):173-184. https://doi.org/10.1016/S1473-3099(09)70043-X
30. Boehme CC, Nicol MP, Nabeta P, et al. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: A multicentre implementation study. Lancet 2011;377(9776):1495-1505. https://doi.org/10.1016/S0140-6736(11)60438-8
31. Pooran A, Theron G, Zijenah L, et al. Point of care Xpert MTB/RIF versus smear microscopy for tuberculosis diagnosis in southern African primary care clinics: A multicentre economic evaluation. Lancet Glob Health 2019;7(6):e798-807. https://doi.org/10.1016/S2214-109X(19)30164-0

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