Latent Tuberculosis Infection (LTBI) Knowledge and Practice of Physicians in Lagos

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ABSTRACT

Background: Nigeria has the highest incidence of both drug-susceptible and MDR-TB in Africa and is among the 30 high TB burden countries in the world. While TB remains an important public health issue with a programmatic approach to its treatment, this appears to be towards the active form of the disease while those with LTBI, who are likely to progress remain within the community without much attention. This group is frequently seen by doctors in the community for other ailments. It is therefore of immense importance to assess the knowledge and practices of these doctors regarding the management of patients with LTBI. This will be shifting focus to utilizing one of the core components of the WHO End TB strategy, which is prevention of TB disease by treatment of LTBI.

Methods: This is a descriptive cross-sectional study of 206 doctors practicing in Lagos State between March and July 2021.This was an online survey.

Results: Majority of the participants, 162 (78.9%) had good overall knowledge of LTBI and general TB epidemiology. Only 26 (12.6%) of the participants routinely screen at-risk patient groups for LTBI in their routine practice.

Conclusion: This study showed a defect in the screening of at-risk individuals with propensity for TB reactivation by their attending physicians. This gap will lead to reduction in detection and treatment of LTBI by doctors in Lagos State. There is need for more capacity building and engagement of doctors on LTBI detection and treatment to key into the WHO strategy to end TB.

Keywords: Latent Tuberculosis Infection (LTBI), Knowledge, Treatment, End TB Strategy.

INTRODUCTION

Latent tuberculosis infection (LTBI) is defined as a state of persistent bacterial viability, immune control, and no evidence of clinically manifested active tuberculosis(TB).[1] In LTBI, there is a persisting subclinical infection with small numbers of bacilli, insufficient to produce

symptomatic disease unless there is occurrence of immune dysfunction, allowing the bacilli to multiply rapidly and metabolize at a higher rate resulting in active TB disease.[2] Currently there is no "gold standard" test for LTBI, therefore global burden is not known with certainty; however it is estimated that up to one third of the world's population is infected with M. tuberculosis and the vast majority have no signs or symptoms of TB disease and are not infectious, however they are at risk for active TB disease and for becoming infectious due to some risk factors, the most important being immunological status.[3,4] Suppression of cellular immunity by human immunodeficiency virus (HIV) infection, tumor necrosis factor α inhibitors, glucocorticoids, and solid organ or hematologic transplantation increases the risk of progression of latent infection substantially. End-stage renal disease confers an increased likelihood of progression to active tuberculosis. Silicosis and exposure to silica dust are also associated with increased rates of progression.[1]

Active TB is of global public health concern with an estimated 10 million incident cases and 1.2 million deaths reported world-wide in 2019.[5] Nigeria has the highest incidence of TB in Africa (4.4%) and is one of the thirty countries with high TB burden with an incidence of 219 per 100,000 population.[5]

Currently, it is not possible to directly diagnose M. tuberculosis infection in humans; therefore, latent tuberculosis infection is diagnosed by response to in vivo or in vitro stimulation by M. tuberculosis antigens with the use of the tuberculin skin test or interferon-γ release assays (IGRAs).[1] It is also essential that active TB disease is ruled out by evaluating for symptoms and signs of active disease such as fever, weight loss, drenching night sweats, cough, hemoptysis or other organ-specific symptoms of extra-pulmonary TB, and carrying out a chest X-ray to evaluate for lesions that may suggest active disease such as cavitations or infiltrations in characteristic lung zone distribution.[1] This is necessary to prevent development and propagation of resistant mycobacterial strains in individuals who have active TB disease and are exposed to LTBI therapy.

The World Health Organization (WHO) End TB Strategy has set the goal to reduce TB incidence worldwide by 80% and TB deaths by 90% by 2030,[6] and a key pillar to the realization of this goal involves the detection and treatment of LTBI in individuals at risk of reactivation.[7,8] Practicing physicians in their everyday interaction with different categories of patients, are well positioned to identify those individuals who are at high risk of reactivation of LTBI due to underlying factors. They are major stakeholders in carrying out appropriate screening for and treatment of LTBI in these patients.

It is therefore essential that all practicing physicians in the country are equipped with appropriate level of knowledge to optimally implement this strategy. In a comparative cross-sectional study on awareness and knowledge of health care workers at DOTS facilities on management of TB disease, 60% of those in the private sector were found to have good knowledge.[9] There is paucity of local studies in our environment assessing current gaps in knowledge, attitude and practice of Doctors on the subject of LTBI. This study was designed to determine the magnitude of knowledge gap and assess

current practices amongst physicians practicing in Lagos, Nigeria, regarding this concept.

METHODOLOGY

Study Design: This cross-sectional study was conducted with the use of a standardized online questionnaire designed using the Microsoft office form. This was developed using the WHO guide to developing KAP surveys and other existing data.[10,11]

Study Population

Inclusion criteria: All practicing medical doctors registered with the Lagos State chapter of the Nigerian Medical association, working in both the public and private sector and captured in the Telegram/ WhatsApp of the association. This consisted of House-officers, Medical officers, Residents doctors and Consultants involved in seeing patients in general out-patient settings.

Exclusion criteria: Doctors who declined participation

Sample size: The sample size was calculated based on the formula, $nf= n/[1+(n/N)]$

Where nf is the desirable sample size when study population is less than 10,000; at present 8000 doctors are on the Lagos NMA register (Nigerian Medical Association), this figure is cumulative over the past decade and includes an unspecified number of those no longer practicing within Lagos. However, 499 members who are currently practicing within Lagos, were identified cumulatively in the Telegram and WhatsApp groups of the association as at the time of circulation of this survey.

$n=Z2 (p*q)/d2$

$n=1.962 (0.6*0.4)/ 0.0025$

$n=189$

Z= standard estimate (1.96) , p= prevalence, given as 0.6, based on the knowledge of health workers on TB management in a descriptive comparative cross-sectional study of health workers at TB DOTS facilities in Lagos state.[9]

q= 1-p, d= precision (0.05), N= is the estimate of population size (499)

$nf= n/[1+(n/N)]$

$nf= 189/[1+(189/499)]=189/1.4$, nf=135

Desired sample size = 135

Convenience sampling method was used. The questionnaire was circulated via a link posted in the Lagos NMA WhatsApp and telegram groups over the period of five months, March-July 2021. Responses were anonymous and automatically recorded. More participants were enrolled above the desired sample size and this data was included in the analysis to increase the power of the study.

Data was analyzed using SPSS version 27.0. Categorical variables were expressed as frequencies and percentages. Chi square was used to analyze association between categorical variables.

Ethical approval was obtained from the Lagos State University Teaching Hospital (LASUTH) health research and ethics Committee (LREC/06/10/1701)

Informed consent was obtained from each of the participants.

Study questionnaire: It was designed using the WHO guide to developing KAP surveys and other existing data.[10-12] It comprised of four sections A-D. Section A was used to obtain sociodemographic information from participants as shown in table 1. Section B assessed knowledge of participants regarding TB disease and LTBI epidemiology, symptoms of active pulmonary TB disease, risk factors for

reactivation of LTBI infection and categories of individuals who should be routinely screened for LTBI in daily practice. Section C assessed knowledge of participants regarding appropriate tools for LTBI screening and available treatment options. It also assessed participants' practices regarding routine screening of at risk individuals for LTBI. Section D assessed attitude of the participants regarding setting of treatment of patients diagnosed with LTBI; recognition of risk of acquisition of LTBI and willingness to undergo screening for LTBI as a practicing physician.

The questionnaire was pre-tested among 600 level medical students.

A total of 40 questions was used to assess overall knowledge of participants on LTBI. Correct response for each question was scored as 1 while incorrect responses were scored as 0. Maximum score was 40 and minimum score was 0. Score of above 20, being the average, was graded as good and score of 0-20 was graded as poor.

RESULTS

Sociodemographic Characteristics

A total of 206 doctors participated in the study and response rate was 41% (n=499). Mean age of participants was 33.01±8.0 years, majority of respondents were medical officers, 110 (53.4%), 151 (73.3%) worked in government owned facilities, and 123 (59.7%) had been practicing for ≤ five years,. In the past twelve months only 24 (11.7%) of the participants had attended a lecture/ seminar/ workshop on latent TB infection. Other demographic characteristics are as shown in Table 1.

General Knowledge of TB and LTBI Acquisition and Reactivation

Knowledge of TB epidemiology assessed through questions regarding the burden of disease, routes of transmission and symptoms of active pulmonary TB disease was found to be optimal as 163(78.9%) of the participants demonstrated good knowledge. 147 (71.4%) correctly identified Nigeria as a high TB- burden country. However, only 51(24.8%) of the participants correctly answered the question on world-wide burden of LTBI and 82(39.8%) of the participants had no idea.

Concerning knowledge of participants on group of patients at risk of LTBI acquisition and reactivation and hence should be routinely screened for LTBI; 205(99.5%), 156(75.7%) and 130(63.1%) of the participants correctly identified HIV infected individuals, organ transplant patients and individuals with diabetes mellitus respectively. However, only 49 (23.8%) and 90 (43.7%) of the participants correctly identified, patients receiving hemodialysis and individuals with silicosis, respectively. Other specific questions and participants responses regarding LTBI are as seen in tables 2 and 3.

Only 58 (28.2%) of the participants were aware that LTBI had available treatment options, among which 33 (16%) indicated the correct drug regimens for LTBI treatment.

163(78.9%) of participants had good overall knowledge of LTBI. Factors associated with good knowledge were: designation or cadre of the doctor (p-value 0.003): those of higher cadre such as consultants, had better knowledge compared to those of lower cadre; duration of practice (p-value 0.009), where those who had practiced for more than 10 years had better knowledge than those

who had practiced for less than 5 years, and level of healthcare service rendered (p-value 0.043), where those working in tertiary settings had better knowledge than those working in primary setting. Details of associations are as seen on table 4 with positive associations highlighted in bold print.

Attitudes and Practices of participants on LTBI

Only 26 (12.6%) of the participants routinely screen for LTBI in their everyday practice. The most commonly employed mode of screening used by the participants was tuberculin skin testing by 16(61.5%). Worthy of note, of the 26 doctors who routinely screen for LTBI 22(84.6%)

erroneously employ sputum MTB/RIF nucleic acid amplification test (GeneXpert) as a tool for screening. 12 (46.2%) and 13 (50%) out of those who routinely screen also employed chest X-ray and Sputum GeneXpert respectively. Only 8 (30.8%) out of those who screen employed interferon gamma release assays.

Majority of our participants, 145 (70.4%) are aware that treating LTBI has a role in the "end TB strategy". Even though 180 (84.7%) of participants think that health care workers are at higher risk of acquiring LTBI and 183 (88.8%) expressed willingness to be screened for LTBI, only 44 (21.4%) of the participants had ever taken a test to screen for LTBI.

Table 1: Socio-demographic characteristics of participants

Variable	Frequency (n=206)	Percentage
Age group (Years)		
<30	80	38.8
30-39	88	42.7
≥40	38	18.4
Mean±SD	33.01±8.0	
Gender		
Male	89	43.2
Female	117	56.8
Designation		
House officer	26	12.6
Medical officer	110	53.4
Residents	57	27.7
Consultant	13	6.3
Type of facilities		
Government owned	151	73.3
Military owned	5	2.4
NGO/faith based	6	2.9
Private	44	21.4
Level of healthcare service render in facilities		
Primary		
Secondary	36	17.5
Tertiary	76	36.9
	94	45.6
Duration of practice (Years)		
≤5	123	59.7
6-10	38	18.4

>10	45	21.8
Specialist qualification		
Yes	34	16.5
No	172	83.5
Average patients seen per week		
≤50	129	62.6
51-100	60	29.1
>100	17	8.3
Average TB patients seen per week		
None (Rarely)	138	67.0
1-5 (Often)	42	20.4
>5 (Frequently)	26	12.6
Attended lecture/seminar/workshop on latent TB infection		
Yes	24	11.7
No	182	88.3

Table 2: General knowledge of LTBI

Question	Don't know	No	Yes
A person with latent infection do not differ significantly from someone with active TB	12(5.8)	176(85.4)	18(8.7)
A person with latent TB is infected with mycobacterium tuberculosis germ but do not have TB disease	8(3.9)	31(15.0)	167(81.1)
A person who is infected with TB can go through life without getting sick	11(5.3)	38(18.4)	157(76.2)
A person with latent TB infection usually have a skin test or blood test indication TB infection	32(15.5)	40(19.40	134(65.0)
A person with latent TB infection has a normal chest X ray and a negative sputum test	25(12.1)	54(26.2)	127(61.7)
A person with latent TB infection has TB bacteria in his/her body hat are alive nut inactive	15(7.3)	3(1.5)	188(91.3)
A person with latent TB infection is usually sick and can spread disease to others	11(5.3)	185(89.8)	10(4.9)

Table 3. Knowledge of LTBI Acquisition and Reactivation

| Variable	Frequency (n=206)	Percentage
Risk factors for progression from LTBI to active TB disease		
HIV infection	203	98.5
Organ transplant recipient	185	89.8
Individual on high dose steroid	194	94.2
Individual on immunosuppressive medication such as TNF therapy	198	96.1
Diabetes mellitus	188	91.3
Silicosis	124	60.2
End stage renal disease	177	85.9
Group of people who should have routine screening for LTBI		
HIV infected individual	205	99.5
HIV negative household contacts with pulmonary TB	173	84.0
Organ transplant recipient	156	75.7
Injection drug users	130	63.1
Resident or employees of high risk congregate setting	172	83.5
Silicosis	90	43.7
Diabetes mellitus	130	63.1
Patients receiving dialysis	49	23.8
Patients preparing for solid organ or hematological transplant	69	33.5
Smokers	53	25.7
Underweight individual	35	17.0
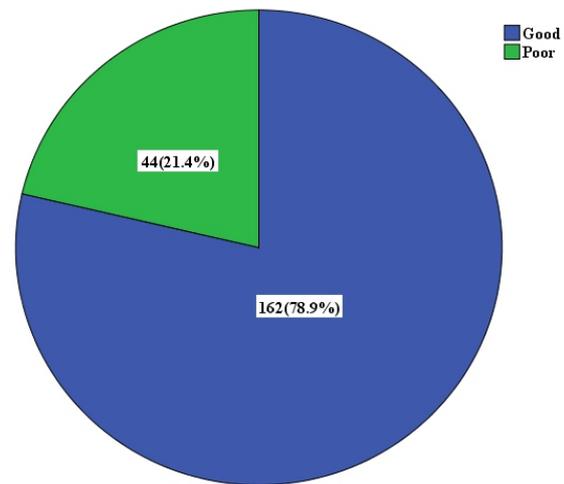
Figure 1: overall general knowledge of LTBI

Table 4: Association between knowledge of LTBI and socio-demographic characteristics

Total= 206	Good (%)	Poor (%)	X²	p-value
Age group (Years)				
<30 (n=80)	60(75.0)	20(25.0)	1.376	0.503
30-39 (n=88)	70(79.5)	18(20.5)		
≥40 (n=38)	32(84.2)	6(15.8)		
Gender				
Male (n=89)	71(79.8)	18(20.2)	0.120	0.729
Female (n=117)	91(77.8)	26(22.2)		
Designation				
House officer (n=26)	20(76.9)	6(23.1)	13.843	**0.003***
Medical officer (n=103)	70(70.0)	33(30.0)		
Residents (n=57)	52(91.2)	5(8.8)		
Consultant (n=13)	**13(100.0)**	0(0.0)		
Type of facilities				
Government owned (n=151)	122(80.0)	29(19.2)	2.311	0.510
Military owned (n=5)	3(60.0)	2(40.0)		
NGO/faith based (n=6)	4(66.7)	2(33.3)		
Private (n=44)	33(75.0)	11(25.0)		
Level of healthcare service render in facilities				**0.043***
Primary (n=36)	23(63.9)	13(36.1)	6.301	
Secondary (n=76)	60(78.9)	16(21.1)		
Tertiary (n=94)	**79(84.0)**	15(16.0)		
Duration of practice (Years)				
≤5 (n=123)	88(71.5)	35(28.5)	9.375	**0.009***
6-10 (n=38)	33(86.8)	5(13.2)		
>10 (n=45)	**41(91.1)**	4(8.9)		
Specialist qualification				
Yes (n=34)	29(85.3)	5(14.7)	1.073	0.300
No (n=172)	133(77.3)	39(22.7)		
Average patients seen per week				
≤50 (n=129)	99(76.7)	30(23.3)	1.110	0.574
51-100 (n=60)	50(83.3)	10(16.7)		
>100 (n=17)	13(76.5)	4(23.5)		
Average TB patients seen per week				
	106(76.8)	32(23.2)	0.896	0.639
None (n=138)	35(83.3)	7(16.7)		
1-5 (n=42)	21(80.8)	5(19.2)		
>5 (n=26)				
Attended lecture/seminar/workshop on latent TB infection				0.365	0.551
	20(83.3)	4(16.7)		
Yes (n=24)	142(78.0)	40(22.0)		
No (n=182				

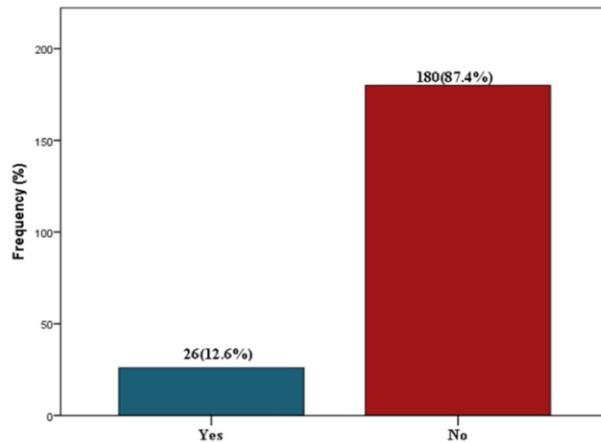*Positive associations shown in bold print.

Figure 2: Participants who routinely screen for LTBI in everyday practice.

DISCUSSION

Nigeria is a high-burden TB incidence country despite strides in detection and treatment of active TB cases. As recommended by WHO, LTBI detection and treatment plays an important role in achieving the 2030 goals for reduction in TB incidence and deaths globally.

This study showed a major defect in the practice of screening at-risk individuals for LTBI, suboptimal knowledge of most appropriate screening tools and specific drug treatment for LTBI despite good overall general knowledge of LTBI demonstrated by the participants. This will likely lead to a low detection rate among individuals with LTBI, increasing rates of reactivation TB disease in at-risk individuals and further impact negatively on the burden of TB disease in the state and nation at large.

Our finding compares favorably with a study done by Lobue et al, who carried out a KAP survey on TB among 384 physicians in San Diego, California (USA) and found an overall median knowledge of 83%.[14] In this study, majority of the respondents (69%) were doctors working in a tertiary setting comprising infectious disease and internal medicine and had been practicing for over 10 years (72%). These demographic factors likely accounted for the good knowledge of TB, despite USA being a low TB-burden country, and was demonstrated with associations found between good knowledge and the characteristics of location of medical education, medical specialty, and the number of TB patients treated.[14] However, even though our study population was quite different from that of Lobue et al, where more than half of our study participants worked in a primary or secondary setting 112(54.4%), majority had been practicing for less than 10 years 161 (78.3%) and lacked specialist training 172 (83.5%), overall knowledge of LTBI was just slightly lower at 78.9%. This is likely because unlike in the USA, Nigeria is classified by WHO as a high-TB burden country, so irrespective of the medical specialty of the physician, baseline knowledge of TB remains good. Be that as it may, our study found associations between good knowledge; duration of practice and level of healthcare service rendered, similar to the findings by Lobue et al.[14]

Our findings are also comparable to what was obtained by Ngo et al, in their KAP survey and screening for LTBI among health care workers in Vietnam, which included 140 physicians; with good general knowledge of TB and LTBI demonstrated in 84.6% of participants who were physicians.[15] Vietnam is also a high TB- burden country and the study population was similar to ours with the most common age group between 30-39

years and median duration of practice less than 10 years.[15] This population however slightly differed from ours as more than half of the participants (58.4%) had attended a TB seminar prior to the survey, unlike our own population where only 24 (11.7%) had attended a TB seminar. Also, the questions asked in this survey centered mostly on TB disease, rather than TB infection. These could be the reasons for the slightly higher overall knowledge obtained in this survey compared to our own findings.[15]

Treatment options available for LTBI are recommended based on disease burden and incidence in the region. In high burden regions, options include six months of Isoniazid monotherapy (300mg daily), Rifampicin (600mg) plus isoniazid (300mg) daily for 3 months or Rifapentine and isoniazid weekly for 3 months.[16-18] Anti-TB drugs are available in DOTS centers, but it is however not readily accessible to patients because management of LTBI is not currently captured under the national TB treatment programme, therefore, patients are forced to buy the medications from pharmacy outlets.

Our findings differ remarkably from what was obtained by Ramos et al, who evaluated knowledge and perceptions of TB transmission and prevention among physicians (55) and nurses (46) in three Brazilian cities with high TB incidence. He found overall knowledge of LTBI was less than 50% despite 57% of the participants having previously received formal training on LTBI.[19] The lower LTBI knowledge reported in this study is probably because responses were from both physicians and nurses, and the physicians all worked in primary care. Also majority of the survey assessed

knowledge on details of treatment of LTBI with very few questions on category of patients at-risk of LTBI reactivation and no question on TB disease epidemiology. However in this study, 56% of the participants had good knowledge of optimal LTBI therapy which is much better compared to the 16% (33) we obtained from our study. This is likely because very few of our study participants, 24 (11.7%) had received formal training on LTBI.[19]

Despite adequate overall knowledge demonstrated by participants in this study, this failed to translate to clinical practice, as 180 (87.4%) of participants admittedly do not routinely screen at risk individuals for LTBI in their everyday practice. Amongst the 26 (12.6%) who routinely screen for LTBI, a significant number of them 22 (84.6%) erroneously considered sputum gene Xpert a tool for screening, in addition to use of tuberculin skin testing (manteoux test). Less than a third of those who routinely screen employed use of interferon gamma release assays.

This is an important knowledge gap in the practice of LTBI screening as evidence states that either a tuberculin skin test (TST) or interferon-gamma release assay (IGRA) can be used to test for LTBI.[4] The low uptake of use of IGRA among the participants may be as a result of the prohibitive cost of running the test. Even though sputum GeneXpert is not a recommended tool for LTBI screening, our study participants may have chosen this method due to the test being provided free of charge at easily accessible TB treatment centres across the city. Overall, this suggests that very few physicians in Lagos actively screen for LTBI which will result

in poor detection rate of LTBI among at risk individuals.

A systematic review and meta-analysis on the prevalence of LTBI among healthcare workers in high burden countries obtained a pooled prevalence of 47%, indicating a high burden of LTBI among HCWs.[20] The study by Ngo et al in Vietnam also screened physicians for LTBI using tuberculin skin testing and found a prevalence of 56.3%.[15] 180 (84.7%) of our participants acknowledge that being a health care worker (HCW) leads to increased risk of acquisition of LTBI and 183 (88.8%) were willing to undergo testing for LTBI; this demonstrates better attitude compared to a study done in Georgia, which is also a high-burden TB country, where only 52% of the physician participants were willing to undergo screening for LTBI.[21]

This is likely to be the first study in the country to assess the knowledge and practice of physicians to LTBI, as other previous studies have centered on active TB disease and sequelae. Similarly, there is paucity of data on KAP studies among physicians focusing on only LTBI globally. We anticipate that this study will contribute to stimulating further discussion and research locally and globally on this very important pillar of the end TB strategy.

A limitation of this study is the study design in which the participants were enlisted from a social media chat group, coupled with the suboptimal response rate (41%) and small sample size, as it would be difficult to determine if the findings are truly representative, keeping in mind that the non-responders may have had different practice or better knowledge. Also, responses were obtained from participants who were mostly practicing in government owned facilities, considering the large number of private-owned health care facilities in the state, this may not be a true representation of the overall knowledge and practice of physicians to LTBI in the state.

CONCLUSION

Physicians practicing across the country are key stakeholders, who will be directly involved in actively screening for and treating cases of LTBI. Knowledge of physicians concerning LTBI is modest but the practice is poor.

Implementation of the WHO end TB strategy, involving detection and treatment of LTBI is low among physicians in Lagos state. Knowledge gaps identified include appropriate screening tools for LTBI and specific drug treatments. There is need for stakeholders to provide further education on LTBI, in the form of continuing medical education (CMEs), also to put in place measures to ensure that knowledge obtained translates to routine daily practice for example, using public-private partnerships. There is need for development of national guidelines to address implementation of the LTBI strategy in routine practice.

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