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Prevalence and risk factors of active tuberculosis disease in contacts of tuberculosis cases treated in a teaching hospital in southeast Nigeria: a cross-sectional study

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Abstract: **Background: Contacts of index cases of active tuberculosis (TB) disease were at a higher risk of developing active TB disease than the general population who were not so exposed. This research was aimed at determining the prevalence and risk factors of active TB disease among contacts of patients with active TB disease.**

Methods: This is a cross-sectional study involving the contacts of index TB cases at Chukwuemeka Odumegwu Ojukwu University Teaching Hospital Awka. Patients diagnosed of active TB disease were recruited and their contacts identified through in-depth interview. The contacts underwent clinical screening, and relevant samples were also collected for Xpert MTB/RIF Ultra assay.

Results: A total 121 index cases of active TB disease were enrolled for this study and they generated 474 contacts. Active TB disease was detected in 2.9% of the entire contacts investigated and in 3.3% of the under-five contacts. Occurrence of active TB disease in the contacts was significantly associated with presence of symptoms of TB ($p < 0.05$) but not significantly associated with some other identified risk factors including age, gender, type of contacts, and smear positivity of index case ($p > 0.05$).

Conclusion: Contacts of patients with active tuberculosis disease, by virtue of their characteristic of sharing the same enclosed space for living, working and other social gathering points, were at a higher risk of developing active TB disease than the general population. An effective and wholistic investigation of contacts of persons with active TB disease is essential for finding previously undiagnosed TB cases especially in high TB burden settings like Nigeria.

Keywords: **tuberculosis, contacts, prevalence, risk factors.**

I. INTRODUCTION

Tuberculosis (TB), a global public health concern, is a chronic communicable disease which is a major cause of illness as well as a leading cause of death worldwide, especially in low- and middle-income countries (LMIC) of the world [1], [2]. [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16]. The causative organism for TB is the bacillus *Mycobacterium tuberculosis* (TB bacilli) [1], [7], [8], [16], [17], [18]. An estimated 1.7 billion individuals worldwide are affected by TB, with 8 to 10 million new cases and over 1.6 million deaths each year [7], [18], [19]. Over a third of the population of the world has been infected with TB bacilli, hence at risk of developing active TB disease later in life [20].

Tuberculosis thrives wherever there is poverty, overcrowding, chronic debilitating illness, diabetes mellitus, chronic lung disease, chronic renal failure, alcoholism, immunosuppression, HIV infection, undernourishment, cancer, old age, smoking, use of immunosuppressive drugs etc. [1], [7], [16], [17], [18], [21], [22]. Most infections are acquired by person-to-person transmission of airborne organisms from an active case to a susceptible host, with the bacilli released into the air through coughing, talking, spitting, sneezing, shouting, singing etc. [1], [7], [8], [17], [18].

Tuberculosis presents a wide spectrum of clinical forms, but pulmonary involvement is the most common presentation as well as the most important epidemiologically as it is primarily responsible for the transmission of the infection [1], [7], [17]. Transmission of tuberculosis is majorly airborne by droplets, droplet nuclei and dust thus, inadequately ventilated and crowded places favor transmission of tuberculosis [1], [7], [18]. Prior to the coronavirus pandemic, TB was designated as a leading cause of mortality from a single etiological agent ahead of human immunodeficiency virus (HIV) [1], [2], [5], [23].

Patients with smear-positive pulmonary TB may infect their contacts, some of whom will progress to active TB disease and transmit the infection further, to other persons [17], [24]. An individual with active pulmonary TB (PTB), who is not treated, will infect between 10 and 15 persons annually [17], [24]. Previous studies have shown that contacts of TB patients were 10 – 60 times more likely to have the disease than the general population [8]. An estimated 10 – 14% of all TB patients were accounted for by previous contacts of TB cases [8]. The natural history of TB is marked by a multiple stage period of latency during which recently infected persons were deemed to be at the highest risk of progressing to active TB disease [25]. These individuals may also enter a long latency period ultimately progressing to active TB disease years after initial infection, although approximately 80% of them never develop active TB disease [25]. The above statistics show that the contacts of active TB cases were at a higher risk of developing active TB disease than the general population who were not so exposed [26], [27], [28].

Contact investigation in TB management refers to the systematic identification and evaluation of contacts of TB patients to identify those with active disease or LTBI and, if necessary, provision of appropriate TB treatment or TB preventive treatment or therapy (TPT) before the occurrence of serious illness [4], [8], [10], [11], [17], [24], [25], [29], [30], [31], [32], [33], [34]. The aim of contact investigation is to reduce the ability of infectious patients to transmit the disease to other people by effectively reducing the time needed to detect and treat a case [5], [35], [36]. Contact investigation is a very important activity required to find persons with previously undetected TB [17]. A household contact of a TB patient is a person who shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with the index case during the three months before commencement of the current treatment episode [17], [37]. A close contact on the other hand is a person who is not in the household but shared an enclosed space, such as a social gathering place, work place or facility, for extended periods during the day with the index case during the three months before commencement of the current treatment episode [17], [37]. All household and close contacts of diagnosed TB patients should be evaluated for TB. In addition, contacts of children diagnosed with TB should also be evaluated, a process known as Reverse contact tracing [17].

Contact investigation involves some of the following processes; clinical screening, Xpert MTB/Rif Ultra assay of relevant specimen, smear microscopy for acid fast bacilli (AFB), chest X-ray, Mantoux test, and Quantiferon TB-Gold-Plus Assay (QFT-Plus). Clinical Screening for TB is conducted using History taking and Physical Examination of subjects to determine the cardinal symptoms and signs of presumptive TB. These include: Cough of two weeks or more duration or current cough in people living with Human immunodeficiency virus (HIV); unexplained fever; unexplained weight loss; drenching night sweats; and in addition, in children, failure to thrive [38], [39]. Xpert MTB/Rif Ultra assay is a molecular test and the primary diagnostic tool for TB. It is a highly sensitive and specific test for TB diagnosis that detects DNA sequences specific for *Mycobacterium tuberculosis* and rifampicin resistance [15], [40], [41]. Xpert MTB/RIF Ultra assay has revolutionized the diagnosis of TB by reason of its speed, sensitivity and specificity [15], [42], [43]. It is a cartridge-based automated diagnostic test that makes use of sealed and disposable cartridges thereby circumventing the problem of cross contamination [42], [44]. This assay is a nucleic acid amplification test (NAAT) based on the principle of polymerase chain reaction (PCR) requiring minimal technical capabilities [40], [42], [44]. This test requires only one clinical specimen (sputum for adults, faecal matter for children who cannot produce sputum and other body fluids) and can detect both *Mycobacterium tuberculosis* and rifampicin-resistance in less than 2 hours, specifically 1 hour 52 minutes. It is more sensitive than smear microscopy [15], [17]. This research assessed the prevalence of active TB disease in contacts of index TB patients and the associated risk factors.

II. METHODS

This study was conducted in the Chest/TB clinic of Chukwuemeka Odumegwu Ojukwu University teaching hospital (COOUTH) Awka, southeastern Nigeria. This was cross-sectional research involving index TB cases and their identified contacts. All patients diagnosed of active TB disease were consecutively enrolled into the study, as well as their contacts. In-depth interview of the index cases led to identification of their contacts who were invited to the TB clinic.

An interviewer administered questionnaire was used to obtain information from the study participants. In addition, the contacts went through the process of clinical screening involving history taking and physical examination to ascertain the presence of the cardinal symptoms and signs of presumptive TB. These include: Cough of two weeks or more duration or cough of any duration in people living with Human immunodeficiency virus (HIV); fever; unexplained weight loss; drenching night sweats; and additionally in children, failure to thrive. Appropriate samples (sputum sample in adults and stool sample in children who cannot produce sputum) were also collected from the contacts for the Xpert MTB/Rif Ultra assay.

Quantitative data collected were analyzed with the aid of the computer software: SPSS version 20. Frequency distribution of all relevant variables was presented in tables and charts for easy appreciation. Relevant percentages, means and standard deviations were calculated and tests of statistically significant differences of proportions and associations were carried out using the chi square test for proportions, with level of significance(α) at 0.05.

III. RESULTS

The modal age group for the index TB patients was 36 – 45 years with a mean age of 40.49 years, and they were mostly males (Table 1). The contacts had a modal age group of ≤ 15 years with a mean age of 24.01 years, and they were mostly females. Majority of the contacts were household contacts (Table 2). Almost all (99.2%) the index TB cases had pulmonary TB, 82.6% of them were smear positive while 28.1% were HIV positive (Table 3). At least one symptom of TB was present in 17.5% of the contacts, while active TB disease was detected in 2.7% of them (Table 4). The presence of symptoms of TB was significantly associated with active TB disease in contacts, p-value = 0.000 (Table 5).

Table 1: Distribution of index TB patients by some of their socio-demographic characteristics

Variables	Frequency (N = 121)	Percentage
Age group (years)		
≤ 15	4	3.3
16 – 25	18	14.9
26 – 35	25	20.7
36 – 45	32	26.4
46 – 55	21	17.4
56 – 65	12	9.9
≥ 66	9	7.4
Mean age ± SD (40.49 ± 16.258)		
Sex		
Male	69	57
Female	52	43
Place of residence		
Urban	55	45.5
Rural	66	54.5

Table 2: Distribution of contacts of index TB patients by some of their socio-demographic characteristics

Variables	Frequency (N = 474)	Percentage
Age group (years)		
≤ 15	198	41.8
16 – 25	90	19
26 – 35	70	14.8
36 – 45	54	11.4

46 – 55	24	5.1
56 – 65	23	4.9
≥ 66	15	3.2
Mean age ± SD (24.01 ± 18.979)		
Sex		
Male	194	40.9
Female	280	59.1
Place of residence		
Urban	228	48.1
Rural	246	51.9
Type of contacts		
Household contact	451	95.1
Close contact	23	4.9

Table 3: Distribution of index TB patients by some disease characteristics and treatment outcomes

Variables	Frequency (N = 121)	Percentage
Site of Disease		
Pulmonary TB	120	99.2
Extra-pulmonary TB	1	0.8
Type of TB		
Drug sensitive TB	112	92.6
Drug resistant TB	9	7.4
HIV status		
HIV positive	34	28.1
HIV negative	87	71.9
Bacteriologic diagnosis		
Smear positive	100	82.6
Smear negative	21	17.4
Treatment outcomes		
Treatment success	82	67.8
Died	8	6.6
Lost to follow up	31	25.6

Table 4: Distribution of contacts of index TB patients by some disease characteristics and treatment outcomes

Variables	Frequency (N = 474)	Percentage
Presence of symptoms of TB		
Yes	83	17.5
No	391	82.5
Xpert MTB/RIF ultra result		
MTB detected	13	2.7
MTB not detected	461	97.3
HIV status		
HIV negative	13	2.7
Not determined	461	97.3
Treatment outcomes	**(N = 13)**	
Treatment success	9	69.2
Lost to follow up	4	30.8

Table 5: Relationship of some characteristics of contacts of TB patients with Xpert MTB/RIF ultra result

Variables	MTB detected n (%)	MTB not detected n (%)	X^2	p-value
Age of contacts				
≤15 years	5 (2.7)	183 (97.3)		
>15 years	8 (3.1)	254 (96.9)	0.061	0.806
Sex				
Male	8 (4.4)	174 (95.6)		
Female	5 (1.9)	263 (98.1)	2.473	0.116
Symptoms of TB				
Present	13 (16.5)	66 (83.5)		
Absent	0 (0.0)	371 (100.0)	57.138	0.000
Type of contact				
Household contact	12 (2.8)	415 (97.2)		
Close contact	1 (4.3)	22 (95.7)	0.184	0.668
Site of disease in Index case				
PTB	13 (2.9)	433 (97.1)		
EPTB	0 (0.0)	4 (100.0)	0.120	0.729
Bacteriologic diagnosis of Index case				
Smear positive	12 (3.6)	324 (96.4)		
Smear negative	1 (0.9)	113 (99.1)	1.347	0.246

PTB – Pulmonary TB, EPTB – Extra pulmonary TB

IV. DISCUSSION

A total of 121 patients with active TB disease were recruited for this study and they generated 474 contacts. The modal age group for the index TB patients was 36 – 45 years with a mean age of 40.49 years, and mostly males in contrast to the contacts which had a modal age group of ≤ 15 years with a mean age of 24.01 years, and mostly females. Majority of both index TB patients and the contacts reside in rural areas. An overwhelming majority of the index TB patients had pulmonary TB (PTB) which is similar to findings in previous studies across the world [5], [11], [24], [31], [36], [39], [45], [46], [47]. A great proportion of the contacts were household contacts, similar to findings in various studies across Europe [37], [48], [49]. This implies that not all eligible contacts, especially those from the schools, work places, places of worship, and other social gathering points, were identified or screened. This could be attributed to the phobia of stigma, lack of willingness to identify all contacts by the index patients, poorly motivated contacts who are unwilling to visit health facilities for screening among other reasons. At least one of four symptoms of cough, fever, drenching night sweats and unexplained weight loss was present in 17.5% of the contacts.

This presence of symptoms was significantly associated with a smear positive index case. This is similar to a study conducted in Kyrgyz republic [37], lower than findings in Ethiopia [31] and South Africa [28], [50], [51] but higher than findings in Uganda [39], Malawi [45], Botswana [52], Kenya [34], and South Africa [53], [54]. These differences in the presence of symptoms among contacts of active TB cases could be due to sample size effect, study areas (rural or urban), and type of contacts etc. Active TB was detected in 2.9% of the contacts of the index cases using Xpert MTB/RIF Ultra assay. This compares to findings in other studies across the world, with a range of 2.5 – 4% [24], [48], [50], [53], [54]. Most studies carried out in developed parts of the world had a range of 0.2 – 2.3% [11], [19], [26], [49], [55], [56], [57], [58]. The highest percentage (6.6%) was detected among contacts of active TB cases in a study in Pakistan [3]. These varied prevalences of active TB among contacts of index cases could be attributed to the type of TB disease in the index case (pulmonary or extrapulmonary), type of contacts, social factors (poverty, undernutrition, poor housing conditions, poor

ventilation) etc. Patients with pulmonary TB have a higher likelihood of spreading or releasing the TB bacteria through the air when they speak, sneeze, shout, or cough. These droplets are then inhaled by their contacts. This, however, may not be the case with those with extrapulmonary TB. Household contacts and other close contacts usually live with or spend a large amount of time with the index cases, hence their chances of increased exposure to the TB bacteria leading to possible active disease. A lot of social factors including but not limited to poverty, poor nutrition, poor ventilation, poor housing conditions are contributory to the development of active TB disease among contacts. Nigeria, as well as other developing countries of the world, is bedeviled by these social factors hence the increased prevalence of active TB among the contacts from developing countries.

There was no statistically significant relationship between occurrence of active TB disease in contacts and some identified risk factors including age of contacts, gender of contacts, type of contacts, and smear positivity of index case. This finding contrasts sharply with findings in other studies around the world which identified smear positivity of index cases, household contacts/type of contacts, males and older contacts as risk factors for active TB disease in contacts, with risk of active TB being two times higher in under-fives [37], [48], [49], [55], [56], [59]. This contrast was unexpected and surprising. This is because occurrence of active TB is linked with poor or weakened immune system of contacts, so extreme of ages (under-fives and old age) with associated lowered immunity is expected to be a risk factor for active TB. Household and very close contacts of active TB cases are expected to be more at risk of developing active TB due to the fact that they usually have a prolonged period of contact with the index cases. Smear positive index cases release TB bacteria – laden droplets into the air which are then inhaled by their contacts predisposing them to active TB disease. This contrast in finding could be attributed to the composition of the contacts, sample size effect etc.

There was, however, a statistically significant relationship between presence of symptoms in contacts and occurrence of active TB disease which is similar to findings in previous studies [37], [48], [49], [55], [56], [59].

V. CONCLUSION

Tuberculosis remains an infectious disease of global public health concern as well a leading cause of mortality especially in low- and middle-income countries of the world. Contacts of patients with active tuberculosis disease, by virtue of their characteristic of sharing the same enclosed space for living, working and other social gathering points, were at a higher risk of developing active TB disease than the general population who were not so exposed. An effective and wholistic investigation of contacts of persons with active TB disease is essential for finding previously undiagnosed TB cases especially in high TB burden settings like Nigeria. Contact investigation and initiation of appropriate treatment will ultimately lead to the significant reduction of the incidence of active TB disease. An effective TB contact investigation is a very important TB control strategy.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the COOUTH Health Research Ethics Committee (HREC), with HREC assigned number: COOUTH/ETH.C/VOL.1/ FN:04/302 and all the study participants signed an informed consent form. Those who declined signing were excluded from the study.

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

Competing interests

The authors declare that there are no competing interests.

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Authors' contributions

Ifeoma Anne Njelita: conception, design, data analysis and interpretation, write up of manuscript, literature search. Chinyerem Cynthia Nwachukwu: original draft review and literature search. Ifeanyi Gabriel Eyisi, Chijioke Amara Ezenyeaku and Hilary Nkem Okeke: data acquisition and manuscript review. All authors read and agreed to the final version of the manuscript.

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