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ORIGINAL ARTICLE

PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AMONG PATIENTS SUCCESSFULLY TREATED FOR PULMONARY TUBERCULOSIS

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ABSTRACT

Introduction: *Chronic Obstructive Pulmonary Disease is currently the fourth leading cause of death in the world. In 2012, more than 3 million people died of Chronic Obstructive Pulmonary Disease, accounting for 6% of all deaths globally. Several epidemiologic studies have shown that pulmonary tuberculosis is emerging as a potential risk factor in the pathogenesis and severity of Chronic Obstructive Pulmonary Disease. This finding is especially concerning given the high prevalence of pulmonary tuberculosis in low resource countries.*

Objective: *This study was conducted to evaluate the prevalence of Chronic Obstructive Pulmonary Disease in patients successfully treated (cured plus treatment completed) for pulmonary tuberculosis seen at Tikur Anbessa Specialized Hospital, the largest public tertiary hospital in Ethiopia.*

Methodology: *We conducted a cross-sectional study of patients > 15 years of age who were successfully treated for pulmonary tuberculosis and followed in the Chest Unit at Tikur Anbessa Specialized Hospital between August 2016 to September 2017. Patients with signs and symptoms of active pulmonary tuberculosis were excluded. All patients had lung function measured using a Diagnostic EasyOne Plus model 2001 SN spirometer. Spirometric acceptability and reproducibility were determined using the published criteria of the European Respiratory Society/American Thoracic Society. A diagnosis of Chronic Obstructive Pulmonary Disease was based on a post-bronchodilator FEV1/FVC<70% as recommended by the Chronic Obstructive Pulmonary Disease guidelines.*

Results: *A total of 99 patients were included in the analysis. Of these 55(55.6%) were male; the mean age of the group was 42.7 years. Forty-one of 99 (41.4%) study participants had post-bronchodilator FEV1/FVC<70%, meeting the study criteria for Chronic Obstructive Pulmonary Disease. This percent was approximately 8 times higher than the 5% previously determined for Chronic Obstructive Pulmonary Disease in the general population for sub Saharan Africa. In addition, a majority of those diagnosed with Chronic Obstructive Pulmonary Disease in our study had moderate to severe Chronic Obstructive Pulmonary Disease stage disease.*

Conclusions: *The prevalence of Chronic Obstructive Pulmonary Disease is high in our Ethiopian patients who were successfully treated for pulmonary tuberculosis , and higher than expected from previously published population based studies. Although selection bias may have contributed to our results, we believe that patients successfully treated for pulmonary tuberculosis are at significant risk for developing Chronic Obstructive Pulmonary Disease, and should be strongly considered for screening and possible treatment.*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive life-threatening lung disease that causes breathlessness (initially with exertion) and predisposes to exacerbations and serious illness (1). In 2016, the Global Burden of Disease Study reported a global COPD prevalence of 251 million cases.

Furthermore, in 2012, there were an estimated 3.17 million deaths from COPD, accounting for 5% of all deaths globally that year. More than 90% of COPD deaths occur in low- and middle- income countries (2).

COPD is characterized by chronic airway inflammation with progressive lung function deterioration and is a major cause of not only mortality but also morbidity and disability (3). There is growing evidence of co-morbidity between COPD and tuberculosis (TB), the leading global cause of death due to respiratory infection (3). Tuberculosis poses a global public health threat and remains the leading cause of death among infectious diseases, especially in low- and middle-income countries(4). While TB can occur in any organ or tissue, the respiratory system is the most common site of active disease. Without treatment, PTB has a mortality rate of 50% within five years (5).

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Although standard anti-TB treatment is highly effective, with a rapid resolution of symptoms and low rate of relapse, non-adherence remains a great obstacle to successful treatment (6). Even after completing treatment for PTB, approximately two-thirds of patients have pulmonary function abnormalities, with an obstructive defect being the main abnormality detected (7-10).Those previously treated PTB patients have a greater risk of death from respiratory causes (11-14) and are thought to be significant contributors to the growing worldwide burden of COPD (15-18).

In Ethiopia, a low resource country with a high burden of TB, the prevalence of COPD among those previously treated for PTB is unknown. The main objective of this study was to determine the prevalence of COPD among patients previously treated for PTB who had regular follow up in the Chest Unit of Tikur Anbessa Specialized Hospital (TASH).

PATIENTS AND METHODS

Study design and population

We conducted a hospital-based descriptive cross-sectional study in the Chest Unit of TASH from August 2016 to September 2017. TASH is tertiary level hospital in Addis Ababa, Ethiopia, offering diagnosis and treatment for approximately 370,000–400,000 patients per year. There are 16 outpatient clinics located within the hospital; the Chest Unit itself has over 500 visits/month for patients with various respiratory symptoms and pulmonary diseases including previously treated PTB. It was an optimal site for the study because of the large volume of patients, the well-organized longitudinal database, and the availability of diagnostic expertise with spirometry, bronchoscopy, Gene Xpert, and chest imaging.

The study population included all consecutive Chest Unit patients who were aged $\geq$15 years who had previously been successfully treated (cured or treatment completed) for PTB. Patients with active TB were excluded from the study using WHO systematic screening criteria. Data were collected from clinical records and patient interviews using a structured questionnaire. Information obtained included socio-demographics, PTB diagnosis and treatment history, smoking history, and exposure to biomass fuel from domestic cooking.

All participants provided written informed consent. Ethical approval for the study was obtained from the College of Health Sciences, Addis Ababa University Institutional Review Board.

Pulmonary function measurements

Lung function was measured for all patients using a Diagnostic EasyOne Plus model 2001 SN spirometer by an appropriately-trained technician. Spirometric acceptability and reproducibility were determined using the published criteria of the European Respiratory Society and the American Thoracic Society (19).

Based on the spirometric findings, patients were first classified as normal or abnormal (i.e., obstructive, restrictive, mixed) according to the algorithm from the National Lung Health Education Program (NLHEP) (20).Airflow obstruction was defined as an FEV_1/FVC ratio below the lower limit of normal (LLN) and FVC above LLN. Restriction was defined as an FEV_1/FVC ratio$\geq$ LLN and an FVC < LLN. A mixed pattern was defined as a FEV_1/FVC ratio, FEV_1, and FVC all < LLN. For those with airflow obstruction, a diagnosis of COPD was based on a post-bronchodilator FEV1/FVC<70% as recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines (21). Severity of obstruction (mild, moderate, and severe) was classified according to the GOLD guidelines (21) and the American Thoracic Society/European Respiratory Society (ATS/ ERS) task force recommendations (19), respectively.

Subjects whose spirometric tests did not meet ATS/ ERS acceptability and reproducibility criteria and those with significant post-bronchodilator reversibility of more than 12% were excluded (19).

Data analysis

Data were analyzed using SPSS (version 20.0) statistical software. Means ± standard deviation (SD) and proportions were calculated for continuous and categorical data respectively. Median and interquartile range (IQR) was used for non-normally distributed numerical data. We assumed that the FEV_1, FVC, FEV_1/FVC ratio data were normally distributed.

Linear regression was used for continuous variables (FEV_1, FVC, FEV_1/FVC,) and logistic regression was employed to determine predictors of COPD; the dependent variable was COPD (present or absent), and the independent variables included age, gender, level of education, smoking status, TB episode number (first episode or recurrent), HIV sero-status (positive or negative) and biomass exposure. Findings were considered statistically significant if $p<0.05$.

RESULTS

A total of 99 patients were included in the analysis. There was a male–female ratio of 55:44 (56%:44%) and a mean age for the group of 42.7 years. Thirty-five (35.4%) of the subjects were in the 31–45 years age group. Forty-six (46.5 %) had exposure to biomass, of which 31(31.3%) had ≥10-years exposure.

A history of active smoking and second hand smoke exposure were noted in 16(16.2%) and 7 (7.1%) patients, respectively. The median smoking pack year was 5.5 with IQR (3-17.5). Most of the patients, 68 (68.7%), had a history of one episode of PTB, while 31(31.3 %) had two or more episodes of PTB. Approximately 7.1 % of the group was HIV co-infected, 28.3% were HIV negative, and 64.6 % had an unknown HIV sero-status. (Table 1)

Table 1: Socio-demographic characteristics of pulmonary tuberculosis patients at the Chest Clinic, Tikur Anbessa Specialized Hospital, August 2016-September 2017 (N=99)

Characteristics	Frequency	Percent (%)
Age groups (years)		
15-30	24	24.2
31-45	35	35.4
46-60	32	32.3
≥65	8	8.1
Sex		
Male	55	55.6
Female	44	44.4
Level of education		
Illiterate	37	37.4
Literate	62	62.6
Occupation		
Unemployed	16	16.2
Employed	55	55.6
Farming	12	12.1
Housewife	16	16.2
Smoking history		
Never smoked	83	83.8
Smoker (in the past or still smoking)	16	16.2
Passive smoker		
Yes	7	7.1
No	92	92.9
TB episode		
1X	68	68.7
≥2X	31	31.3
HIV Status		
Positive	7	7.1
Negative	28	28.3
Unknown	64	64.6
History of Asthma		
Yes	16	16.2
No	83	83.8
Cooking History ≥10years (Biomass fuel)		
Yes	46	46.5
No	53	53.5

The group's mean spirometric values were: FEV_1 53.9 % predicted, FVC 63.1% predicted, and FEV_1/ FVC 59.2%. Of the participants 14(14.1%) had normal spirometry, 41(41.1%) had obstructive spirometry, 42(42.4%) had restrictive spirometry, and 2(2.0%) had a mixed pattern. (Table 2)

Table 2: Types of lung function abnormalities in pulmonary tuberculosis patients, Chest Clinic, Tikur Anbessa Specialized Hospital, August 2016- September 2017 (N=99)

No	Type of Impairment	Number (%)
1	Normal	14 (14.1)
2	Obstructive pattern (FEV1/FVC ratio < LLN	41(41.4)
3	Restrictive pattern (FEV1/FVC ratio >LLN	42(42.2)
4	Mixed pattern (FEV1/FVC ratio <LLN	2(2.0)

In our study 14(14.1%) were normal, 41(41.4%) had an obstructive pattern, 42(42.4%) had a restrictive pattern and 2(2%) had a mixed pattern (Table 2). Forty-one of 99(41.4%) study participants met the criteria for COPD with a post-bronchodilator FEV_1/ FVC<70%. In addition, most of those participants diagnosed with COPD had GOLD stage II (moderate disease) which was detected in 18(43.9%) patients. Fourteen (34.1%) and 7(17.1%) of patients were diagnosed with stage III (severe) or stage IV (very severe) disease stage respectively (Figure 1). No additional risk factors were identified for those post-PTB subjects with spirometric findings of COPD.

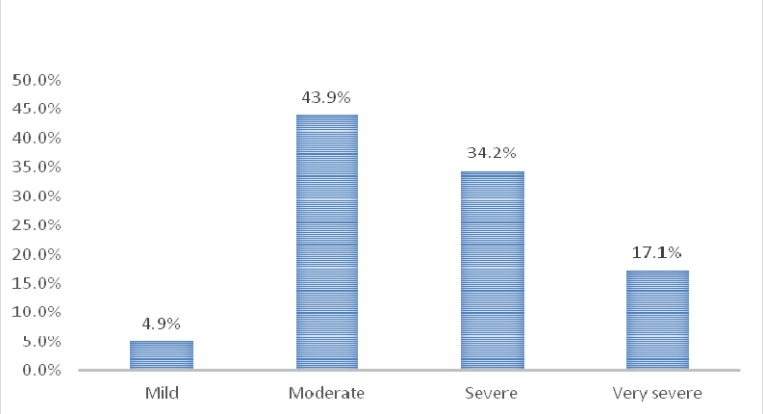

Figure 1: Severity of Chronic Obstructive Lung Disease in pulmonary tuberculosis patients, Chest Clinic, Tikur Anbessa Specialized Hospital (N=41)

DISCUSSION

In our study, 41 (41.2%) successfully treated PTB patients followed in the Chest Unit of TASH fulfilled the spirometric criteria of COPD. Furthermore, most of these patients had moderate and severe stage disease.

These findings suggest that successfully treated PTB can be a significant risk factor for reduced lung function, and may be a cause of chronic lung disease, especially in countries where the tuberculosis burden is high, and diagnosis and treatment may be delayed.

Our results are similar to other previously published research. A large multicenter population-based study (N=5,571 participants) performed in 5 Latin American countries, PLATINO, found that FEV_1 was reduced compared to FVC in most of those with physician diagnosed PTB (17). Another study done in Pakistan reported 26(55.3%) post-PTB subjects had an obstructive ventilatory defect, of which 18(69.2%) had severe COPD impairment (22). In their study, Wilcox and Ferguson determined that 65% of those patients previously treated for PTB more than 10 years earlier showed an obstructive ventilatory defect (23). Additionally, the obstructive changes correlated with the degree of residual scarring on chest radiograph.

A study conducted in Egypt on chronic obstructive pulmonary disease in treated pulmonary tuberculous patients demonstrated irreversible obstructive pattern in 22(44%) patients who underwent pulmonary function testing, denoting chronic obstructive pulmonary disease (COPD). Seven patients had a restrictive ventilatory defect, and three patients had a mixed obstructive and restrictive pattern.

In the same study, 11(50%) patients had mild obstruction, 9(40.9%) patients had moderate obstruction, and two (9.1%) patients had severe obstruction (24). Our results may have differed slightly from those of others as our patients were younger, had their PTB successfully treated, and were followed in an outpatient setting of a large tertiary referral center.

Although in high income countries, tobacco smoking is recognized as an important risk factor of COPD, the prevalence of COPD among non-smokers in those countries is estimated to be 6.6% of the population with an estimated 25-45% of COPD patients having never smoked (25,26). Indoor air pollution from biomass fuel, occupational dusts, and exposure to toxic gases, a history of pulmonary tuberculosis (PTB), chronic asthma, poor socio-economic status, and genetic factors are also recognized as potential factors contributing to the diagnosis of COPD (25,27).

A nationwide survey conducted in South Africa suggests that in a TB endemic area, pulmonary TB may be the strongest risk factor of COPD (28). We were unable to determine additional risk factors for COPD in our post-TB patients, possibly reflecting the data collected and the relatively small number of participants.

Limitations

There were several study limitations. Our sample size was relatively small, lowering the likelihood of finding all the significant associations. This was especially evident in determining risk factors for COPD other than previous PTB. The study was conducted at a tertiary referral center raising the possibility of selection bias. Finally, the study was conducted at a single center, whereas a multicenter study could have produced results that would have been more robust.

Conclusion

The prevalence of COPD was high in our Ethiopian patients who were successfully treated for PTB, and higher than expected from previously published population based studies.

Although selection bias may have contributed to our results, we believe that patients successfully treated for PTB are at significant risk for developing COPD, and should be strongly considered for screening and possible treatment.

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Competing interest

The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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