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## **Prevalence, risk factors and clinical correlates of COPD in a rural setting in Tanzania.**

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### **ABSTRACT**

Chronic obstructive pulmonary disease (COPD) causes substantial burden of disease in developed countries, but there are limited data from Africa. We aimed to estimate the prevalence of COPD in Tanzania and identify the risk factors associated with it.

This was a cross-sectional descriptive survey involving adults aged  $\geq 35$  years. We collected data on symptoms and risk factors using the Burden of Obstructive Lung Diseases questionnaire. Spirometry was performed and COPD diagnosed based on post-bronchodilator forced expiratory volume in 1 s/forced vital capacity  $< 70\%$ . We also measured indoor and outdoor carbon monoxide (CO) levels.

A total of 869 participants (49.1% females) completed the questionnaires. Of these, 57.1%

completed post-bronchodilator spirometry. Of the 25.2% ever-smokers, only 5.4% were current smokers. COPD prevalence was estimated at 17.5% (21.7% in males and 12.9% in females). COPD was associated with a history of cough, phlegm production and wheezing. 51.7% of COPD patients reported cough and 85% had mild to moderate airway limitation. Females had a higher rate of exacerbation. Pulmonary tuberculosis (TB) was reported in 10% of patients. Only 1.7% of patients who were diagnosed as COPD had ever received any medication, with only one female COPD patient having received an inhaler. 99.5% of the population used biomass fuels for cooking. The majority of households had CO levels up to 20 ppm.

The prevalence of COPD in Tanzania is high, with a peak at a relatively young age and a preponderance in males. A history of TB, cigarette smoking and male sex are important risk factors. Indoor air pollution coupled with use of biomass fuel for cooking and heating may be an important risk factor for developing COPD in rural Tanzania. However, these factors need to be studied further.

**KEYWORDS:** chronic obstructive pulmonary disease, risk factors, mining, air pollution, cigarette smoking, spirometry.

## BACKGROUND

Chronic obstructive pulmonary disease (COPD) is an important cause of morbidity and mortality in developed countries, albeit with scarce data in Africa [1-3]. Cigarette smoking and occupational exposure to air pollution are well known risk factors for developing COPD worldwide [4, 5]. However, recently, exposure to biomass smoke and traffic pollution are increasingly recognized as major risk factors for developing COPD in developing countries [6]. In parallel, the current social and economic transitions in Africa characterized by increased urbanization, industrialization and extensive mineral explorations in the context of lack of work safety standards is likely to contribute to air pollution and increased exposure to occupational diseases.

COPD is characterized by the presence of progressive and irreversible airway limitation resulting from chronic airway inflammatory response due to prolonged exposure to air pollutants [7]. COPD is a recent phenomenon in Africa as many patients with the disease are often misdiagnosed and managed as cases of adult-onset asthma using long-term inappropriate treatment options. The ageing populations together with increased cigarette smoking habits and

the rising trends in air pollution are potential drivers for the continued rise in COPD in developing countries. Prolonged exposure to inhalational pollutants in specific occupational groups, who often don't use proper protective gear, exposes individuals to an increased risk of developing COPD. The absence of a policy and legal protection framework as well as weak law enforcement agencies and authorities regarding acceptable safety standards and environmental protection are bottlenecks in the prevention of chronic respiratory diseases in Tanzania.

Patients with COPD present with chronic cough and sputum production with or without dyspnoea. This clinical presentation tends to be ignored by patients until they present late at advanced stages of disease often after developing intolerable dyspnoea. Regrettably, due to lack of expertise and diagnostic facilities such as spirometry, patients with COPD are often misdiagnosed as cases of pulmonary tuberculosis or heart failure and offered inappropriate treatment [8]. The current management of COPD requires stepwise administration of bronchodilators and steroids preferably via the inhalational route during stable states and exacerbation. However, due to shortages of expertise and resources the guidelines based on the Global Initiative on Chronic Obstructive Lung Diseases (GOLD) are often not adhered to in routine clinical practice in Tanzania [8].

Currently, there are widespread, unregulated artisanal mining sites in Tanzania. The mining activities are characterized by lack of proper protective gear and weak regulatory authorities with a greater risk of exposure to excessive level of inhalational pollutants. In the current study we set to determine the burden of COPD in this high risk population and assess the air quality within the underground microenvironment where mining activities were undertaken.

## METHODOLOGY

**Study area and study design:** We conducted a case – control study in the Mererani small-scale hard-rock mining site in Northern Tanzania. The mining site consists of large-scale and small-scale sites operated respectively by the large-scale investors and small-scale local miners. The small-scale mining site is organized into 100 mining pits across the site. Besides other minerals, tanzanite is a major mineral ore extracted from the area. The miners come from throughout Tanzania and nearby countries. In the current study we recruited three groups of participants namely; active miners, ex-miners and non-miners. The cases (active and ex-miners) were defined based on their exposure status. The latter served as controls recruited

from the same, or nearby, areas. The study was preceded by conducting community sensitization meetings at the selected study sites.

**Sampling and sample size estimation:** We recruited 577 active miners and 211 ex-miners and 63 non-miners. We randomly selected 20 mining pits from the available 100 mining pits, from which we recruited a sample size of 577 active miners. The number of workers in each mining pit was pre-determined and all eligible participants were selected. 211 ex-miners and 63 non-miners aged  $\geq$  to 30 years were randomly selected and recruited from the local area. .

**Fieldwork and data collection:** We collected information about respiratory symptoms, occupation, respiratory diagnoses, co-morbidities, health care utilization, medication use, activity limitation, and health status together with basic demographic data and personal particulars. We also performed anthropometry measurements, and measured blood pressures and pulse. We assessed the burden and determinants of COPD using the BOLD protocol ([www.boldstudy.org](http://www.boldstudy.org)) with slight modification. The interviewers administered a set of BOLD validated questionnaires.

Participants underwent spirometry using 3L-syringe daily calibrated NDD EasyOne™ spirometer ([www.nddmed.com](http://www.nddmed.com)) which was repeated 15 to 20 minutes after inhalation of 200µg of salbutamol via a spacer. The diagnosis of COPD was made based on a history of exposure to risk factors and the presence of airflow limitation that is not fully reversible, with or without the presence of symptoms. A post-bronchodilator FEV<sub>1</sub>/FVC <70% and a post-bronchodilator (BD) FEV<sub>1</sub> <80% predicted confirmed the presence of airflow limitation that is not fully reversible.

**Pollution monitoring:** Mining pits were monitored for air pollution in the underground mining tunnels based on particulate matter with an aerodyne mic diameter <10 µm (PM<sub>10</sub>) using TSI Side Pak™ AM510 personal aerosol monitors ([www.tsi.com](http://www.tsi.com)) with a sampling rate of one minute. Two pre-programmed air sampler units were taken into the underground pits by the volunteer mining workers and positioned at two specific positions; the blasting point and at the exit point of the tunnel, a few meters from the blasting point, where the rest of the miners hide during active blasting. The monitors were left at these positions for the up to 12 hours until the mining shift was over and then carried back to the fieldworkers.

## RESULTS

The current COPD survey recruited 851 male participants (577 active miners; 211 ex-miners and 63 non-miners). Over 53% of participants were in 31-40 age-group and the mean age was  $40.95 \pm 9.21$ . Two-thirds of all participants were either former or current cigarette smokers (Table 1). About 83% (702 of 851) of all respondents who completed the questionnaires underwent post-bronchodilator (BD) spirometry. Of these, 75.30% had received primary education and 72.80% had good nutritional status. About 68%, 25% and 7% of active miners, ex-miners and non-miners respectively reported either current or former cigarette smoking status (Table 2). Notably, over 40% of active miners were current smokers while about 48% of ex-miners were former cigarette smokers (Table 2).

The prevalence of COPD based on the criteria of post-BD  $FEV_1/FVC < 70\%$ , was estimated at 15.20%, 17.10% and 15.40% for active miners, ex-miners and non-miners respectively (Table 3). The prevalence of COPD generally increased with age both in cases and controls (Table 4). Over 18% of all current cigarette smokers had significant nicotine dependence on the Fagerstrom scale. This dependence was significantly associated with the duration of cigarette smoking and the number of pack years (Tables 4 and 5).

As shown in Table 6, cough was the most common respiratory symptom presented by patients with COPD. Moreover, 56.5% of ex-miners with COPD presented with shortness of breath compared to about 25% of both active miners and non-miners. The majority of COPD patients had increased frequency of 3 or more exacerbations within the preceding 12 months. It is further observed that ex-miners had the worst mean  $FEV_1$ , FVC and  $FEV_1/FVC$  values. Notwithstanding the exposure status, the majority of COPD patients had mild to moderate airway limitation as assessed by GOLD classification. In all respondents including patients with COPD, oral aminophylline, often taken intermittently, was the most commonly prescribed medication for respiratory symptoms as shown in Table 7. Very few took regular medication.

The 24-hour measurements of air quality in underground mining tunnels and blasting sections revealed up to  $5000\mu g/m^3$  levels of  $PM_{10}$  well beyond the acceptable  $50\mu g/m^3$  WHO limits (Fig. 1, 2, and 3).

Table 1: Demographic characteristics of responders who completed BOLD questionnaire

Study variable		Responders (N = 851)	
		Number	Percentage
Gender	Male	851	100.00%
Age-group in years	20 - 30	20	2.40%
	31 - 40	453	53.20%
	41 - 50	249	29.30%
	51 - 60	90	10.60%
	60+	39	4.60%
Mean age (in years)		40.95 ± 9.21	
Smoking Status	Never smokers	288	33.80%
	Smokers	563	66.20%
Exposure Status	Non-miners	63	7.40%
	Ex-miners	211	24.79%
	Active miners	577	67.80%

Table 2: Demographic characteristics of responders who completed post-bronchodilator spirometry

Variable		Exposure status			
		Active miners	Ex miners	Non-miners	Total
Gender	Male	480 (68.40%)	170 (24.20%)	52 (7.40%)	702 (100.00%)
Education	Primary Education	358 (74.70%)	137 (80.60%)	33(63.50%)	528 (75.30%)
	Secondary Education	53(11.10%)	17 (10.00%)	8 (15.40%)	78 (11.10%)
	Others	14 (1.30%)	2 (0.60%)	6 (1.90%)	22 (1.10%)
	No education	52 (10.90%)	14 (8.20%)	5 (9.60%)	71 (10.10%)
	Unknown	2 (0.40%)	0 (0.00%)	0 (0.00%)	2 (0.30%)
Body mass index	Underweight	27 (5.70%)	13 (7.70%)	5 (9.60%)	45 (6.50%)
	Normal weight	369 (77.70%)	112 (66.30%)	26 (50.00%)	507 (72.80%)
	Overweight	65 (13.70%)	37 (21.90%)	16 (30.80)	118 (17.00%)
	Obesity	14 (2.90%)	7 (4.10%)	5 (9.60%)	26 (3.70%)
Smoking status	Non-smokers	163 (34.00%)	45 (26.50%)	28 (53.80%)	236 (33.60%)
	Former smokers	123 (25.60%)	81 (47.60%)	10 (19.20%)	214 (30.50%)
	Current smokers	194 (40.40%)	44 (25.90%)	14 (26.90%)	252 (35.90%)

Table 3: Prevalence estimates of COPD for active miners, ex-miners and non-miners

Variable	COPD Status	Miner's status			
		Active miners	Ex miners	Non-miners	Total
<b>COPD<sup>1</sup> Post Test Result</b>	Yes	73 (15.20%)	29 (17.10%)	8 (15.40%)	110 <b>(15.70%)</b>
	No	407	141	44	592
<b>COPD<sup>2</sup> LLN PB Post Test Result</b>	Yes	56 (11.70%)	17 (10.00%)	4 (7.70%)	77 <b>(11.00%)</b>
	No	424	153	48	625
<b>COPD<sup>3</sup> Age Post Test Result</b>	Yes	104 (21.70%)	35 (20.60%)	7 (13.50%)	146 <b>(20.80%)</b>
	No	376	135	45	556

1: Post-BD FEV1/FVC<70%; 2: Post-BD FEV1/FVC<LLN; and 3: Age <40 years; Post-BD FEV1/FVC<75%; Age (40-60) years; Post-BD FEV1/FVC<70% and Age <60 years Post-BD FEV1/FVC<65%.

Table 4: Prevalence of COPD by exposure group and age-categories among respondents

Exposure categories	COPD ±	Age-categories					Total
		30.01 to 40	40.01 to 40	40.01 to 50	50.01 to 60	Above 60	
<b>Active miners</b>	Yes	0	26	30	9	8	73
		0.00%	8.70%	22.70%	32.10%	66.70%	<b>15.20%</b>
	No	9	272	102	19	4	406
<b>Ex-miners</b>	Yes	0	3	12	8	5	28
		0.00%	5.30%	21.40%	21.60%	33.30%	<b>16.60%</b>
	No	4	54	44	29	10	141
<b>Non-miners</b>	Yes	0	0	3	2	3	8
		0.00%	0.00%	20.00%	15.40%	42.90%	<b>15.40%</b>
	No	5	12	12	11	4	44

1 Post-BD FEV1/FVC<70%



Table 5: Association between nicotine dependence and current cigarette smoking status

Variable	Nicotine Addiction Scale	N	Mean	SD	Mean Difference	95% Lower CI	95% Upper CI	p-Value
Age	Low to Moderate Dependence	152	39.96	8.21	-2.929	-6.109	0.251	0.071
	Significant Dependence	34	42.89	9.71				
No. of smoking years	Low to Moderate Dependence	152	19.28	9.58	-4.113	-7.778	-0.449	<b>0.028</b>
	Significant Dependence	34	23.39	10.72				
No. of pack years	Low to Moderate Dependence	152	8.33	7.86	-30.742	-72.536	11.052	<b>0.002</b>
	Significant Dependence	34	39.08	119.73				

Table 6: Respiratory symptoms and disease severity based on GOLD classification

Clinical characteristics	Exposure categories		
	Active miners (N= 480)	Ex-miners (N=170)	Non-miners (N=52)
<b>Respiratory symptoms</b>			
Cough	38 (52.1)	18 (62.1)	7 (87.5)
Phlegm	34 (46.6)	15 (51.7)	5 (62.5)
Wheeze	29 (39.7)	15 (51.7)	3 (37.5)
Shortness of breath	17 (25.8*)	13 (56.5^)	2 (25.0)
<b>Exacerbation in the past 12 months</b>			
0	3(12.0)	3(23.1)	0(0.0)
1	4(16.0)	1(7.7)	1(33.3)
2	4(16.0)	5(38.5)	1(33.3)
3 or more	14(56.0)	4(30.7)	1(33.3)
<b>Post-Test spirometry</b>			
FVC (L)	3.75 ± 0.90	3.33 ± 0.85	3.53 ± 1.00
FVC (% predicted)	4.12 ± 0.49	3.85 ± 0.56	3.37 ± 0.88
FEV1 (L)	2.43 ± 0.66	1.87 ± 0.61	2.31 ± 0.93
FEV1 (% predicted)	3.38 ± 0.43	3.12 ± 0.50	2.71 ± 0.78
FEV1/FVC pre	64.75 ± 8.91	57.34 ± 15.24	63.25 ± 13.74
FEV1/FVC post	61.67 ± 7.8	58.9 ± 12.48	60.69 ± 11.89
<b>Severity of airway limitation in GOLD classification</b>			
1 (Mild Obstruction)	22(30.1)	6(20.7)	4(50.0)
2 (Moderate Obstruction)	40(54.8)	17(58.6)	3(37.5)
3 (Severe Obstruction)	10(13.7)	4(13.8)	1(12.5)
4 (Very Severe Obstruction)	1(1.4)	2(6.9)	0(0.0)

Table 7: Type and frequency of medication use for respiratory problems among responders

Variable	Medications	Active miners	Ex-miners	Non-miners
Use of medications for respiratory problems	Yes	9(1.6)	6(2.8)	6(9.5)
	No	570(98.4)	205(97.2)	57(90.5)
Type of medication	Aminophylline	5 (55.6)	3 (50.0)	0 (0.0)
	Decongestants	0 (0.0)	0 (0.0)	2 (33.3)
	Chlorphenyllamine maleate	0 (0.0)	1 (16.7)	3 (50.0)
	Salbutamol	2 (22.2)	2 (33.3)	1 (16.7)
	Don't remember	1 (11.1)	0 (0.0)	0 (0.0)
	Unknown	3 (33.3)	0 (0.0)	0 (0.0)
	Inhaler	1 (11.1)	0 (0.0)	0 (0.0)
	Prednisolone	0 (0.0)	1 (16.7)	0 (0.0)
Formulation	Pills	8 (88.9)	7 (71.4.0)	5 (83.3)
	Inhaler	3 (33.3)	2 (28.6)	1 (16.7)
	Injection	1 (11.1)	0 (0.0)	0 (0.0)
Frequency	Most days	0 (0.0)	0 (0.0)	0 (0.0)
	Symptoms	2 (20.0)	1 (12.5)	1 (16.7)
	Other	10 (80.0)	8 (88.0)	5 (83.3)
Duration	Days/Week	1 (10.0)	0 (0.0)	0 (0.0)
	0-3 months	5.33 ± 2.89	3.75 ± 2.22	3.40 ± 1.14
	4-6 months	4 (40.0)	6 (75.0)	4 (80.0)
	7-9 months	1 (11.1)	0 (0.0)	0 (0.0)
	10-12 months	2 (22.2)	0 (0.0)	2 (33.3)

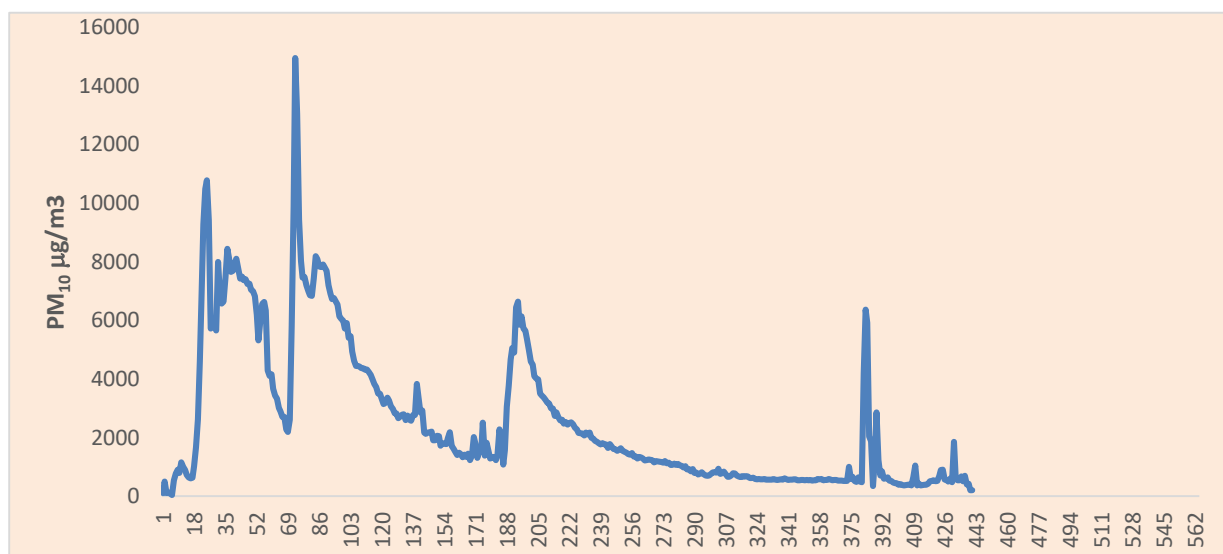


Figure 1: Variation of PM<sub>10</sub> in a typical monitoring session in underground mining tunnel. The spikes indicate points of blasting.

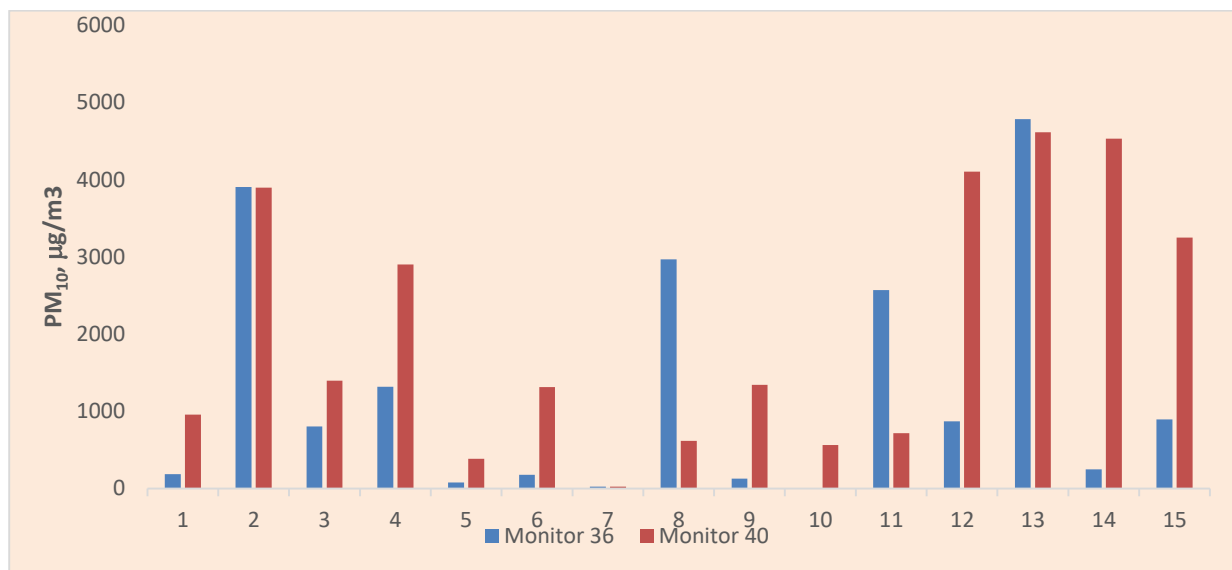


Figure 2: Variation in daily average PM<sub>10</sub> concentrations for two monitors situated at blasting section (monitor 40) and tunnel exit point (monitor 36) in a typical underground microenvironment.

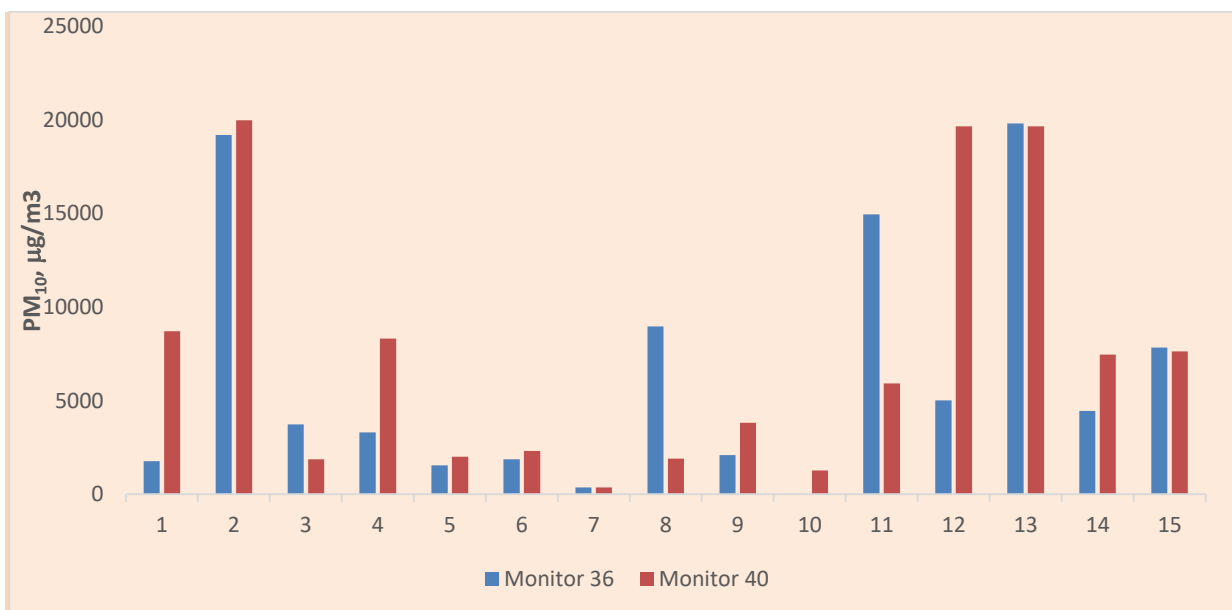


Figure 3: Variation in maximum PM<sub>10</sub> concentrations for two monitors in underground microenvironment.

## DISCUSSION

The prevalence of occupational-related COPD ranged from 15 to 17% in the studied mining population in Tanzania in-line with previous studies conducted elsewhere [9, 10]. Intriguingly, the prevalence did not appear to differ significantly in relation to exposure status in our study. This observation could be explained by either the presence of confounding factors in the population or individuals who responded as non-miners might have worked intermittently in

the mining activities and were thus misclassified as non-exposed [11]. The current study reported 40% and 48% of active and ex-miners respectively as current and former cigarette smokers. A study by Adepoju E.G. *et al* reported the prevalence of cigarette smoking in a community based study in Nigeria to range from 8.7% (current smokers) to 22% (in ever smokers) [12]. These figures suggest that the prevalence of cigarette smoking is typically much higher among miners compared to the general population. Notably, a substantial proportion of all current cigarette smokers had nicotine dependence on the Fagerstrom scale. These individuals are unlikely to quit smoking, thus constituting an at-risk population for developing COPD in the absence of purposeful therapeutic intervention for smoking cessation [12]. The interplay between cigarette smoking and occupational exposure to pollutants among miners accelerates the deterioration in lung function, particularly FEV<sub>1</sub>, and subsequent development of COPD [13, 14]. This observation highlights the importance of integrating smoking cessation in the overall strategy for prevention of COPD [15, 16]. Smoking cessation programs comprises the combination of psychotherapy together with pharmacotherapy, the latter constituting varenicline, nicotine replacement therapy (NRT) or bupropion slow release (SR) formulation [16, 17].

Besides cigarette smoking, ex-miners were more likely to be older than the active miners, thus age, as a determinant for cumulative risk exposure, could be contributing to the increased risk of developing COPD in susceptible individuals [18]. Further explanation would be the fact that in an unregulated mining industry, people tend to retire from the mining activities when they develop intolerable dyspnea. It is thus prudent to suspect that some ex-miners retired from working after developing COPD, thus, contributing to a higher burden of disease in among the ex-miners compared to the active miners.

Similar to other studies conducted elsewhere, patients with COPD commonly presented with cough as a predictor of progression while breathlessness or dyspnoea signifies severity [19]. In the current study, it was revealed that the majority of ex-miners with COPD presented with dyspnoea which could indicate disease severity probably also associated with inadequate treatment. This observation is in line with other previous studies which reported dyspnoea as a predictor of disease severity [20, 21]. The majority of COPD patients had increased frequency of exacerbations regardless of their exposure status which could indicate inadequate or inappropriate disease management. It was further observed that ex-miners had the worst mean spirometry parameters including FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC, However, these poor spirometry

results were not reflected in the clinical manifestation and disease severity. Notwithstanding the exposure status, the majority of COPD patients had mild to moderate airway limitation as assessed by GOLD classification. It remains elusive whether the small proportion of patients with severe COPD might be explained by increased mortality in this group.

Accurate diagnosis and proper administration of appropriate drugs through appropriate routes and duration are keys to the reduction of patients' suffering and mortality. The shortage of expertise in respiratory medicine and lack of diagnostic facilities including spirometry are major hurdles in the management of patients with COPD in Africa [1]. In the absence of proper diagnosis, patients with COPD may be misdiagnosed for other conditions including pulmonary tuberculosis. For instance, in our study 10% of patients were reported to have a history of pulmonary tuberculosis (TB). However, it is well known that miners constitute a population group at increased risk for developing pulmonary TB thus highlighting the possibility of co-morbidity [22-24]. In particular, several studies indicate the presence of latent TB among hard-rock miners in the absence of predetermined exposure [24]. Standard guidelines for management of COPD are often not adhered to resulting in increased adverse effects and poor health-related quality of life. The current study revealed the inappropriate use of drugs, which are often administered through inappropriate routes and intermittently rather than regularly [25]. For instance, aminophylline was the most commonly prescribed medication for respiratory symptoms in all respondents including patients with COPD. The current, 2017 GOLD guidelines recommends limited use of methylxanthines due to their limited clinical efficacy and narrow therapeutic index [26].

The 24-hour measurements of air quality in underground mining tunnels and blasting sections revealed extremely high levels of PM<sub>10</sub> well beyond the WHO acceptable safety limits [27]. The survey revealed up to 5000µg/m<sup>3</sup> of PM<sub>10</sub>; 100-fold higher than the acceptable WHO limits of 50µg/m<sup>3</sup>. The miners, who are invariably without protective gear are constantly exposed to these extreme levels of air pollution.

## CONCLUSION

The current study reported a substantial burden of COPD among young miners in Tanzania. Our study affirms that cigarette smoking and air pollution are important risk factors for developing COPD. The small-scale mining companies do not have appropriate technology and facilities to ensure protection of workers. Furthermore, patients identified with COPD are not aware of their diagnoses and the majority are frequently misdiagnosed and mismanaged.

Patients with COPD do not receive standard treatment as recommended by GOLD guidelines. This inadequate treatment often results in frequent exacerbations, hospitalizations and poor health-related quality of life.

These research findings suggest the need for the urgent development of a national social protection and legal framework for occupational health in Tanzania. The strategies may include development of better approaches for enforcement of policy and regulations for promotion of workers health and prevention of occupational diseases; and empowerment of health facilities with skills and capacity for improving practice and uptake of existing management guidelines for COPD in Tanzania.

## **ROLE OF INVESTIGATORS**

NFM and RWW conceived and designed the study. The study was reviewed by MDS, JDM, AKN and SSS. NFM, MDS, JDM, AKN and AAS developed training materials and offered training to the fieldworkers. ASS coordinated and supervised the field activities, performed spirometry and supervised data entry. SSS, KKA and SJM performed statistical analysis. NFM prepared the results and wrote the first draft of the manuscript. All investigators reviewed the final version of the manuscript.

## **DECLARATION OF CONFLICT OF INTEREST**

All authors declare no competing interests.

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