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The role of infectious pathogens in exacerbation of chronic obstructive pulmonary disease in Dakahlia Governorate

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Abstract

Background: Exacerbations of chronic obstructive pulmonary disease (COPD) represent important events in the management of COPD because of its negative impact on health status and disease progression. The etiology of acute exacerbations of chronic obstructive pulmonary disease (COPDAE) is heterogeneous and still under discussion. So, this study was planned to investigate the role of infectious pathogens (fungi and atypical mycobacteria in addition to the well-known bacteria) in patients with COPD exacerbation in our locality.

Results: This observational cross-sectional study was conducted on 100 patients with acute exacerbation of COPD. Sputum specimens were collected for mycobacterial and fungal examination in addition to routine sputum bacteriology. All sputum samples were negative for typical and atypical mycobacteria whereas sputum samples of 18 patients (18%) were negative for fungi. Mixed fungal growth was found in 19 patients (19%). *Candida* was isolated from 67 patients (67%), *Aspergillus* was isolated from 27 patients (27%), *Alternaria* was isolated from 3 patients (3%), and other fungi were isolated from 4 patients (4%). As regards sputum bacteriology, sputum samples of 49 patients (49%) have bacterial growth. *Streptococcus pneumoniae* was isolated from 16 samples (16%) and represents the most frequent bacterial isolate in this study.

Conclusion: The present study indicates that typical and atypical mycobacteria have no role in COPD exacerbations in our locality. However, fungi and bacteria may have a role in COPD exacerbations.

Keywords: COPD, COPD exacerbations, Atypical mycobacteria, Fungal infection

Criteria of inclusion (target population)

The target population

This study included 100 COPD patients diagnosed according to GOLD 2017 with acute exacerbation. Informed written consents were taken from all patients enrolled in the study after approval of our institutional research board under code (MD/17.02.88).

Patients who refused participation, or patients presented with other associated diseases such as bronchiectasis, history of tuberculosis, and bronchial carcinoma were excluded from the study.

Location of the study

This study was conducted at the Chest Medicine Department, Mansoura University Hospital, and Mansoura Chest Hospital over 24 months from May 2017 to May 2019 in collaboration with the Microbiology and Immunology Department, Mansoura University.

Background

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation [1]. Exacerbations are important events in COPD management because they negatively impact

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health status, hospitalization rates, and disease progression [2].

Common bacterial organisms causing COPD exacerbation are *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and *Pseudomonas aeruginosa* [3].

Atypical mycobacteria are opportunistic bacteria and are therefore more likely to cause disease when there are defects in local or systemic host immunity and have potential to cause respiratory disease, particularly in patients with pre-existing lung damage [4]. Atypical mycobacterial colonization of the lower respiratory tract is an independent stimulus to airway inflammation and can modulate the character and frequency of COPD exacerbations [5]. The potential role of fungal infection in the pathogenesis of COPD is poorly understood [6].

So, this study was planned to investigate the role of infectious pathogens (fungi and atypical mycobacteria in addition to the well-known bacteria) in patients with COPD exacerbation in our locality.

Methods

Study design

This is an observational cross-sectional study.

Duration of the study

This study was conducted at our department, over 24 months from May 2017 to May 2019.

The target population

This study included 100 patients with acute exacerbations of chronic obstructive pulmonary disease (COPDAE) diagnosed according to GOLD 2017 [7]. They were included only if they had acute worsening of respiratory symptoms that require an additional therapy [7]. Exclusion criteria include patients who refused participation or patients presented with other associated diseases such as bronchiectasis, history of tuberculosis, and bronchial carcinoma. Patient selection bias was avoided by the clear definition of study population, using standardized protocol to collect data such as questionnaires as modified British Medical Research Council (mMRC), get information from two different sources as participant and participant's spouse, and implement blinding by being clueless about the disease status of studied participants. Sample size was determined by Epi Info program version 20. Informed written consents were taken from all patients enrolled in the study after approval of our institutional research board under code (MD/17.02.88).

Data collected

Clinical data

Full history taking and clinical examination were done with attention to age, sex, residence, occupation, smoking history, smoking index, severity of airflow limitation, severity of COPD, degree of exacerbation, medications used, and other comorbid diseases.

Spirometry was done for patients who were able to do the test and patients who were not able to do it; their spirometric measures were recorded from their hospital profile of previous admissions. Assessment of airflow limitation was according to GOLD 2017 [7] based on post-bronchodilator fixed ratio FEV1/FVC > 0.70: GOLD 1, FEV1 ≥ 80% predicted; GOLD 2, 50% > FEV1 > 80% predicted; GOLD 3, 30% > FEV1 > 50% predicted; and GOLD 4, FEV1 > 30% predicted [7], severity of COPD according to GOLD 2017 (refined ABCD assessment tool).

COPD exacerbations are classified according to GOLD 2017 as follows: mild (treated with short acting bronchodilators only, SABDs), moderate (treated with SABDs plus antibiotics and/or oral corticosteroids), and severe (patient requires hospitalization or visits the emergency room). Severe exacerbations may also be associated with acute respiratory failure [7].

Radiological data

Chest X-ray was done for radiological assessment of the patients.

Sputum examination and culture for atypical mycobacteria, fungi, and other bacterial agents

Specimens were transported and processed immediately in the Microbiology Unit of our University. If delay was expected, specimens were preserved at refrigerator temperature (4 °C) for 24 h according to Mahon et al. [8].

Microscopic examination of sputum

A. Gram staining

Using a piece of stick, a purulent part of the sputum was transferred to a glass slide, and a thin smear was made, allowed to air-dry, heat fixed, and stained by the Gram technique .The Gram smear was examined also for the presence of predominant organisms among the pus cells [8].

B. Ziehl-Neelsen staining to detect acid fast bacilli (AFB)

To increase the chances of detecting AFB in sputum smears, the sputum was treated with 5% volume/volume sodium hypochlorite (NaOC1), left for 10–15 min at

room temperature followed by centrifugation at 250–1000 r/min for 20 min. Then, the supernatant was discarded, and a drop of the well-mixed sediment was transferred to a clean scratch-free glass slide and it was spread to make a thin preparation and allowed to air-dry. After dryness, the smear was heat-fixed and stained using the Ziehl-Neelsen technique and examined microscopically for AFB. The presence of thin, curved, single, pairs, or groups of pink bacilli that could be beaded on a blue background was reported as positive for AFB [9].

C. Potassium hydroxide (KOH) preparation to detect *Aspergillus* spp. [10]

Cultures of sputum

A. Bacterial culture

The purulent part of the sputum was washed from saliva in about 5 ml of sterile physiological saline [11]. Bacterial growth was identified systemically by the colony morphology, by Gram-stained film from the colonies examined for the characteristic morphology, and by biochemical reactions [12].

B. Culture of sputum for *Mycobacteria tuberculosis* (*M. tuberculosis*)

Sputum was decontaminated using sodium hydroxide, 40 g/l, before being cultured for *M. tuberculosis*. The Lowenstein-Jensen (LJ) egg medium was used for *M. tuberculosis* cultures. Decontaminated sputum was inoculated on LJ slopes and incubated aerobically at 35–37 °C for 2–6 weeks. The organism is slowly growing. When cultured on the Lowenstein-Jensen medium at 30–35 °C, *M. tuberculosis* produces raised, dry, cream (buff) colored colonies. Visible colonies are usually produced 2–3 weeks after incubation, but cultures should be incubated for up to 6 weeks before being discarded [8].

Non-tuberculous mycobacteria (NTM) can be differentiated from *M. tuberculosis* by their ability to produce pigment when cultured in darkness and light (scotochromogen), when only exposed to light (photochromogen) or non-pigment producing (nonchromogen), and by their ability to grow at 25 °C and in 4 (p)-nitrobenzoic acid (PNB) medium. Most NTM, like *M. tuberculosis*, are slow-growing except *Mycobacteria chelonae* and *Mycobacteria fortuitum* which are rapid-growers [13]. Species identification in case of growth of NTM would be done by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Choromosomal DNA of NTM isolates will be extracted using DNA extract kit according to the manufacturer's recommendations [14].

C. Sputum culture for fungi

For fungal isolation, sputum samples were plated on Sabouraud dextrose agar (SDA) containing 50 μg/ml chloramphenicol and incubated at 30 and 37 °C. Cultures were evaluated for growth every 24 h during the first 7 days and weekly till 28 days. If filamentous fungi were detected, colonies were cultured on potato dextrose agar and subcultures were incubated at 30, 37, and 42 °C to identify the species [15].

Differentiation between commensals and pathogenic organisms in this study was done by isolation of the same organism from repeated cultures [16] which showed a pure growth of the same organism and confirmation by identification of the pathogenic forms of the organism on a direct film and correlation of our culture results with clinical, radiological, and laboratory findings of the patients [17].

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) statistical software (SPSS for windows v. 16.0). Categorical data were presented in the form of numbers and proportions. According to the results of normality tests, continuous data were presented either in the form of means and standard deviations or in the form of median (min–max) in case of non-normal distribution.

T test was used to test significance in case of normal distribution, while the Mann-Whitney test was used in non-normally distributed data. Statistical significance was set at a level of $p < 0.05$.

Results

One hundred patients with COPD exacerbations (mean age 62 years old) were enrolled. Only 10% of them were nonsmokers (Table 1). Sixty-three percent of studied patients were COPD group D. Degree of exacerbation in most of studied patients (53%) was moderate and in about 37% was mild. Only 10% had severe exacerbation (Table 2).

As regards sputum bacteriology of studied patients, all sputum samples were negative for typical and atypical mycobacteria whereas bacterial culture revealed that *Streptococcus pneumoniae* was isolated from 16 patients (16%), *Klebseilla pneumoniae* was isolated from 14 patients (14%), *Staphylococcus aureus* was isolated from 9 patients (9%), *Pseudomonas* spp. and *Enterobacter* spp. were isolated from 5 patients for each (5%), *Hemophilus influenzae* was isolated from 3 patients (3%), and *Escherichia coli* was isolated from 3 patients (3%). However, normal flora (commensal flora) was isolated from 43 patients (43%), no bacterial growth was found in 8 patients (8%), and more than one organism was detected in 11

Table 1 Sociodemographic characteristics of studied cases

Age, mean (± SD)		62 (± 8)	
Smoking index (pack-year), median		39.4	
		Number	**Percent (%)**
Sex	Male	98	98.0
	Female	2	2.0
Smoking	Current	46	46.0
	Ex-smoker	44	44.0
	Nonsmokers	10	10.0
Smoking type	Cigarette	78	78.0
	Shisha	6	6.0
	Both	6	6.0
Occupation	Non-risky occupations	64	64.0
	Risky occupations	36	36.0
Residence	Urban	62	62
	Rural	38	38

Risky occupations considered as risk factor for COPD, e.g., cafe workers, bakers, carpenters, agriculture workers, painters, diesel workers, and welding workers

patients (11%). Also, there were no significant associations between the bacterial isolates and sociodemographic and clinical data of studied patients (Tables 3, 4, and 5).

As regards sputum examination for fungal growth, *Candida* was isolated from 67 patients (67%), *Aspergillus* was isolated from 27 patients (27%), *Alternaria* was isolated from 3 patients (3%), and other fungi were isolated from 4 patients (4%); no growth of fungi was found in 18 patients (18%); and more than one fungus was found in 19 patients (19%). Also, there were no significant associations between the fungal isolates and sociodemographic and clinical data of studied patients (Tables 6, 7, and 8).

Table 3 Isolated bacteria from sputum of studied cases

Bacterial culture	**Number**	**Percent**
Klebsiella pneumoniae	14	14.0
Hemophilus influenzae	3	3.0
Staphylococcus aureus	9	9.0
Streptococcus pneumoniae	16	16.0
Pseudomonas aeruginosa	5	5.0
E. coli	3	3.0
***Enterobacter* spp.**	5	5.0
Normal flora (commensals)	43	43.0
Other bacteria	5	5.0
No growth	8	8.0
More than one organism isolated	11	11.0

Bacteria are not mutually exclusive (overlapping). Other isolated bacteria include *Proteous* (1 case), *Citrobacter* (1 case), *Acinetobacter* (2 cases), and late lactose fermented bacteria (1 cases)

Table 2 Clinical assessment of studied patients

		Number	**Percent (%)**
Group (COPD severity)	A	13	13.0
	B	16	16.0
	C	8	8.0
	D	63	63.0
GOLD (severity of airway limitation)	1	12	12.0
	2	41	41.0
	3	25	25.0
	4	20	20.0
Exacerbation grade	Mild	37	37.0
	Moderate	53	53.0
	Severe	10	10.0
Comorbid diseases	Present	67	67.0
	Absent	33	33.0
Treatment			
Systemic steroids	Not used	98	98.0
	Used	2	2.0
Oxygen therapy	Not used	85	85.0
	Used	15	15.0
Non-invasive ventilation	Not used	97	97.0
	Used	3	3.0

Comorbid diseases: hypertension, ischemic heart diseases, renal impairment, chronic liver diseases, and heart failure

Table 4 Isolated bacteria in association to sociodemographic data among the studied cases

Parameter		Total	No growth/normal flora, *n* (%), 51 (51)	Bacterial growth, *n* (%), 49 (49)	Significance (*p* value)
Age mean (± SD)			62.6 ± 8.5	62.5 ± 7.6	0.547[d]
Sex, *n* (%)	Male	98	50 (51)	48 (49)	1[b]
	Female	2	1 (50)	1 (50)	
Occupation, *n* (%)	Non-risky	64	30 (46.9)	34 (53.1)	.271[a]
	Risky	36	21 (58.3)	15 (41.7)	
Residence, *n* (%)	Urban	62	31 (50)	31 (50)	.798[a]
	Rural	38	20 (52.6)	18 (47.4)	
Smoking, *n* (%)	Current smokers	46	21 (45.7)	25 (54.3)	R
	Ex-smokers	44	25 (56.8)	19 (43.2)	0.289[a]
	Nonsmokers	10	2 (20)	8 (80)	0.569[a]
Smoking index (pack-year), *n* (%)	Median	Median	40	45	.085[c]
	Range	< 40	15 (32.6)	11 (25)	
		40–60	18 (39.1)	17 (38.6)	
		> 60	13 (28.3)	16 (36.4)	

Risky occupations considered as risk factor for COPD, e.g., cafe workers, bakers, carpenters, agriculture workers, painters, diesel workers, and welding workers
R reference class
[a]Chi-square
[b]Fisher's exact
[c]Mann-Whitney
[d]*T* test

Discussion

Pathogenic bacteria are usually colonizing the airways of COPD patients, possibly contributing to increased airway inflammation, and have been implicated in COPD exacerbations (Lin et al. [18] and Erkan et al. [19]).

However, fungal and NTM colonization and their potential role in acute exacerbations of COPD are not widely investigated. This study is therefore designed to assess the role of infectious pathogens (fungi and atypical mycobacteria in addition to the well-known bacteria) in COPD exacerbations.

Table 5 Bacterial isolates in association to clinical and radiological data of studied cases

Parameter		Total	No growth/normal flora, *n* (%), 51 (51)	Bacterial growth, *n* (%), 49 (49)	Significance (*p* value)
Exacerbation grade, *n* (%)	**Mild**	37	19 (51.4)	18 (48.6)	R
	Moderate	53	27 (50.9)	26 (49.1)	0.97[a]
	Severe	10	5 (50)	5 (50)	0.94[a]
COPD groups, *n* (%)	**A**	13	8 (61.5)	5 (38.5)	R
	B	16	10 (62.5)	6 (37.5)	1[a]
	C	8	2 (25)	6 (75)	0.183[a]
	D	63	31 (49.2)	32 (50.8)	0.418[a]
GOLD (severity of airway limitation), *n* (%)	**1**	12	8 (66.7)	4 (33.3)	R
	2	41	20 (48.8)	21 (51.2)	0.275[a]
	3	25	12 (48)	13 (52)	0.386[a]
	4	20	9 (45)	11 (55)	9.234[a]
X-ray, *n* (%)	**Normal**	40	21 (52.5)	19 (47.5)	.918[a]
	Hyperinflation	49	24 (49)	25 (51)	
	Consolidation	11	6 (54.5)	5 (45.5)	

R reference class
[a]Chi-square

Table 6 Isolated fungi on cultures among the studied cases

Fungi	Number	Percent (%)
Candida	67	67.0
Aspergillus	27	27.0
Alternaria	3	3.0
Other fungi	4	4.0
No growth	18	18.0
More than one fungus isolated	19	19.0

Fungi are not mutually exclusive (overlapping). Other isolated fungi include *Trichosporon* (1 case), mucormycosis (2 cases), and *Basidiobalus* (1 case)

Sputum samples were utilized for the diagnosis of the offending organisms for COPD exacerbation, as it is an easy method for sampling in spite of its drawbacks in diagnosis. In a study of Bafadhel et al. [20], they used sputum samples and PCR in the diagnosis of fungal isolates, while Guinea et al. [21] used sputum, BAL, bronchial aspirate, and transbronchial lung biopsy samples and serological tests in their study.

In this study, TB and atypical mycobacteria could not be isolated in all studied cases, either by ZN staining or by culture on the Lowenstein-Jensen medium. In a study by Huang et al. [22], they investigated the role of NTM in the clinical course and progression of COPD; their study was done in Taiwan and included 251 patients using Bactec technique in NTM isolation and excluded patients less than 40 years old, nonsmokers, and smokers with smoking index less than 10 pack-years. Char et al. [23] found that 11% of their patients had evidence of mycobacterial infection (TB and NTM), and their study was done in the UK and included 126 patients who underwent LVRS or bullectomy at the Royal Brompton Hospital from 2000 to 2013 and depended on pathological methods in diagnosis (necrotizing granuloma with or without positive ZN staining for acid fast bacilli). These differences may be attributed to utilization of other media such as Bactec method for NTM or TB isolation or pathological examination, disparities in patient selection criteria, study designs, epidemiological factors, environmental factors, and total number of studied patients.

The most common isolated bacteria in this study was *Streptococcus pneumoniae* (16%), this is the same as that reported by Gupta et al. [24] as they isolated *Streptococcus pneumoniae* in 16% of their patients, and it is near to that reported by Sharma et al. [25] as they isolated *Streptococcus pneumoniae* in 13% of their patients.

The second most common organism isolated from the sputum of our patients was *Klebseilla pneumoniae*, it was isolated from 14% of patients, and it is near to that reported by Lin et al. [18] as they reported that *Klebseilla pneumoniae* was isolated in 19.6% of sputum samples via aerobic cultures, but in a study by Bari et al.

Table 7 Fungal isolates in association to sociodemographic characteristics of studied patients

Parameter		Total	No growth, *n* (%), 18 (18)	Fungal growth, *n* (%), 82 (82)	Significance (*p* value)
Age, mean (± SD)			59.9 ± 7.1	63.1 ± 8.2	0.128[d]
Sex, *n* (%)	**Male**	98	18 (18.4)	80 (81.6)	1[b]
	Female	2	0 (0)	2 (100)	
Occupation, *n* (%)	**Non-risky**	64	9 (14.1)	55 (85.9)	0.172[a]
	Risky	36	9 (25)	27 (75)	
Residence, *n* (%)	**Urban**	62	7 (11.3)	55 (88.7)	**.026**[a]
	Rural	38	11 (28.9)	27 (71.1)	
Smoking, *n* (%)	**Current smokers**	46	6 (13)	40 (87)	R
	Ex-smokers	44	10 (22.7)	34 (77.3)	.230[a]
	Nonsmokers	10	2 (20)	8 (80)	0.623[a]
Smoking index (pack-year), *n* (%)	**Median**	Median	40	40	.830[c]
	Range	< 40	8 (50)	22 (29.8)	
		40–60	7 (43.7)	24 (32.4)	
		> 60	1 (6.3)	28 (37.8)	

Risky occupations considered as risk factor for COPD, e.g., cafe workers, bakers, carpenters, agriculture workers, painters, diesel workers, and welding workers
R reference class
[a]Chi-square
[b]Fisher's exact
[c]Mann-Whitney
[d]*T* test

Table 8 Fungal isolates in association to clinical and radiological data of studied patients

Parameter		Total	No growth, *n* (%), 18 (18)	Fungal growth, *n* (%), 82 (82)	Significance (*p* value)
Exacerbation grade, *n* (%)	**Mild**	37	7 (18.9)	30 (81.1)	R
	Moderate	53	10 (18.9)	43 (81.1)	0.995[a]
	Severe	10	1 (10)	9 (90)	0.667[a]
COPD groups, *n* (%)	**A**	13	4 (30.8)	9 (69.2)	R
	B	16	3 (18.8)	13 (81.2)	0.667[a]
	C	8	0 (0)	8 (100)	0.131[a]
	D	63	11 (17.5)	52 (82.5)	0.273[a]
GOLD (severity of airway limitation), *n* (%)	**1**	12	3 (25)	9 (75)	R
	2	41	2 (4.9)	39 (95.1)	0.07[a]
	3	25	6 (24)	19 (76)	1[a]
	4	20	6 (30)	14 (70)	1[a]
X-ray, *n* (%)	**Normal**	40	7 (17.5)	33 (82.5)	1[b]
	Abnormal(hyperinflation and consolidation)	60	11 (18.3)	49 (81.7)	
Comorbid diseases, *n* (%)	**Present**	67	10 (14.9)	57 (85.1)	.254[a]
	Absent	33	8 (24.2)	25 (75.8)	

Comorbid diseases: hypertension, ischemic heart diseases, renal impairment, chronic liver diseases, and heart failure
R reference class
[a]Chi-square
[b]Fisher's exact

[26], they reported *Klebsiella pneumoniae* in 26% of their patients and Sharma et al. [25] in 6.3% of sputum samples via aerobic cultures.

The mean age of our patients with bacterial isolates was 62.5 ± 7.6 years, 49% were males, and the median of smoking index was 45 pack-years, while in a study of Papi et al. [27], they reported that the mean age of their patients was 70.6 ± 2.5 years, 87.5% were males, and the median of smoking index was 48.3 ± 5.7 pack-years. Bacterial isolates were associated in 48.6% of patients with mild exacerbation, 49.1% with moderate exacerbation, and 50% with severe exacerbation. In a study by Erkan et al. [19], they reported that COPD exacerbations increased by 88% with bacterial infection, while Sethi et al. [28] mentioned that bacterial isolates were associated with increase in the incidence of COPD exacerbation. As regards airway obstruction, bacterial isolates were associated in 33.3% of patients with mild airway obstruction, 51.2% with moderate obstruction, 52% with severe obstruction, and 55% with very severe obstruction, while Groenwegan and Wouters [29] reported bacterial isolates in 13% of patients with mild obstruction, in 32% of patients with moderate obstruction, and in 47% of patients with severe obstruction.

The most common fungal isolate in this study was *Candida albicans* that was isolated from 67% of patients, followed by *Aspergillus* that was isolated from 27% of patients and that is near to that reported by Mahmoud et al. [30], as they isolated *Candida* from 63.9% of their COPD patients with acute exacerbation, followed by *Aspergillus* which was isolated in 36% of the patients in spite of their use of sputum, BAL, and serological tests in the diagnosis of fungal infections and their use of Sabaroud agar for fungal growth. The explanation of this relatively high rate of fungal growth may be attributed to association of patients with comorbid diseases and the frequent use of COPD patients to antibiotics and steroids.

The mean age of our patients with fungal isolates was 63.1 ± 8.2 years, 81.6% were males, and 85.1% of patients were associated with comorbid diseases, while Mahomoud et al. [30] reported that the mean age of their patients was 57 ± 3.2 years, 89.5% of patients were males, and the prevalence of fungal isolates was higher with comorbid diseases. Fungal isolates were associated with mild exacerbation in 81.1%, moderate exacerbation in 81.1%, and severe exacerbation in 90%, while Mahmoud et al. [30] reported association of fungal isolates with mild exacerbation in 36.8%, moderate exacerbation in 36.8%, and severe exacerbation in 26.3%. As regards airway obstruction, fungal isolates were associated with mild airway obstruction in 75%, moderate obstruction in 95.1%, severe obstruction in 76%, and very severe obstruction in 70%, while Mahmoud et al. [30] reported association of fungal isolates with moderate obstruction in 58% and severe obstruction in 42% and no fungal isolates were found in cases with very severe obstruction. However, in this study, there was no statistical

significance in the association between the fungal isolates and sociodemographic and clinical data of studied patients.

There are limitations to this study. First, doing of extra tools for assessment of patients such as CT scan and using of other media for organism cultures and non-culture-based methods for fungal identification such as serological tests were limited due to the financial cost. Second, this study was done on hospital admitted patients that may represent high-risk patients with more comorbidities; consequently, the results may not be applicable to community-based settings. Third, fungal culture-based methods for organism identification had low sensitivity and low specificity and negative cultures cannot readily exclude fungal infection.

Conclusion

This study showed that fungal and bacterial isolates from the airway could have a role in COPD exacerbation. Non-tuberculous mycobacteria have no role in COPD exacerbation in our locality at the period from 2017 to 2019. These findings suggest that fungal, bacterial, and mycobacterial sputum cultures should be done for all patient of COPD exacerbation. Also, antifungal and antibacterial therapy should be considered in the treatment of COPD exacerbation, although the implication of this has not yet been conclusively established. Further investigations into the nature and consequences of the presence of NTM in COPD patients are required to confirm whether NTM have a role in COPD exacerbation or not.

Abbreviations

AFB: Acid fast bacilli; BAL: Bronchoalveolar lavage; COPD: Chronic obstructive pulmonary disease; FEV1: Forced expiratory volume second 1; FVC: Forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; HIV: Human immunodeficiency virus; KOH: Potassium hydroxide; LJ: Lowenstein-Jensen; *M. tuberculosis*: *Mycobacteria tuberculosis*; mMRC: Modified British Medical Research Council; NaOCl: Sodium hypochlorite; NTM: Non-tuberculous mycobacteria; PCR-PRFL: Polymerase chain reaction-restriction fragment length polymorphism; PNB: p-Nitrobenzoic acid; SDA: Sabouraud dextrose agar; SPSS: Statistical Package for the Social Sciences; TB: Tuberculosis

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Authors' contributions

E.A.F. had selected the patients, collected the data and samples from patients, and wrote the research parts; H.W.A. had revised the research parts; H.E.E. did the microbiological work and revised the research; and M.K.F.E. had supervised all the research. All authors have read and approved the manuscript.

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Availability of data and materials

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Ethics approval and consent to participate

Informed written consents were taken from all patients enrolled in the study after approval of our institutional research board under code (MD/17.02.88).

Consent for publication

Not applicable.

Competing interests

None.

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