

## ORIGINAL ARTICLE

# Microbiological Etiology of Chronic Cough Associated with Acute Exacerbation of Chronic Obstructive Pulmonary Disease (COPD): A Study from Karachi, Pakistan

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## ABSTRACT

**Background:** Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) worsens the respiratory symptoms that are usually triggered by infection with bacteria or viruses or by environmental pollutants. Therefore, the aim of this study was to determine the bacterial etiology from sputum culture in patients suffering from acute exacerbation of COPD, admitted in hospital.

**Methods:** The study was cross sectional observational, where sputum bacterial cultures were analyzed from the patients with Acute exacerbation COPD treated in the ICU of a tertiary care hospital for pulmonary disease from January 2019 to December 2019. Two sputum samples were collected from each patient for bacterial examination. The results of sputum bacterial culture findings were expressed as frequency and percentage by using SPSS.

**Results:** In the present study, there were 1296 patients, both males 749 (57.8%) and females 547 (42.2%). The mean age of patients was 57.39±19.74 years. 470 (36.3%) showed negative culture reports. 440 (34.0%) patients had *Moraxella* infection, which was most common organism in all patients, and 149 (11.5%) patients had *Pseudomonas* infection, 157 (12.1%) patients had *Yeast Albicans* and in only 1 (0.1%) patient *Enterobacter* infection were found. Other pathogens in low frequency identified were *Haemophilus parainfluenzae*, *Streptococcus pneumoniae*, *Escherichia coli* and *Haemophilus influenzae*. It was observed that the frequency of infections was linked with increasing age.

**Conclusion:** With increasing age, people are prone to acquire pulmonary infections specifically COPD. It is therefore very important to perform sputum culture to identify the causative agents and treat the patients with appropriate antibiotic to reduce the episodes of AECOPD.

**Keywords:** Bacteria; Sputum Culture; COPD; Antibiotic; Cough.

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## INTRODUCTION

Chronic cough is one of the frequent reasons for consultation with physicians, which is not only an important but also difficult clinical problem to deal with. This may account for 10-38% of respiratory outpatient practice<sup>1,2</sup>. However, epidemiological surveys depicted that a small portion of the population is willing to seek medical advice for such symp-

toms. There are different types of cough including "acute self-limiting cough", "cough for less than 3 weeks", "sub-acute acute cough which lasts for almost 3-8 weeks", and the "acute cough", due to upper respiratory- tract viral infection that usually clears within 2 weeks in most of the patients and "chronic persistent cough that lasts for more than 8 weeks". Non-viral causes of acute cough include exacerbation of existing asthma, and exposure to

environmental pollutants<sup>3</sup>. Chronic cough is commonly associated with different causes such as corticosteroid responsive airway diseases like asthma, cough variant asthma, and eosinophilic bronchitis, additionally linked with cough resistant to inhaled corticosteroids including gastro-esophageal reflux disease (GORD), and the postnasal drip syndrome or rhino sinusitis<sup>4-6</sup>.

Chronic cough is also commonly associated with chronic obstructive pulmonary diseases (COPD) which is highly prevalent in Asian countries including Pakistan, India, and China. Limited airflow in COPD is caused by obstructive bronchiolitis and emphysema that may vary in different people. COPD is progressive illness with remission and exacerbations. An exacerbation of COPD is characterized by patient's baseline dyspnea, cough, and/or sputum production<sup>7</sup>. In a study from East London, presence of bacteria in sputum was compared for the frequency of COPD exacerbations, it revealed that those with pathogens in their sputum were more likely to be frequent exacerbators, moreover, there was an increased level of interleukin-8 (IL-8) in the sputum of the these patients<sup>8</sup>. Exacerbations increase the airways inflammatory response usually triggered by bacterial or viral infections or by environmental pollutants<sup>9</sup>; however, the cause of severe exacerbations may remain unidentified in many cases<sup>7</sup>. Several previous studies depicted that during COPD exacerbations, bacterial concentration was found to be very high in lower airways in almost half of the patients<sup>10-12</sup>. It is not easy to diagnose a respiratory infection in a COPD patient because there are mild signs and symptoms that can be misunderstood with noninfectious exacerbations. Therefore, it is emphasized to perform laboratory examination to confirm the presence of any infection.

Although extensive studies have been performed but, still the prevalence of bacterial infection as well as the importance of antibacterial therapy in AECOPD are controversial<sup>13</sup>. This is because if 50% of the cases are due to bacterial infections the rest of the 50% exacerbations are either viral or nonbacterial<sup>14-17</sup>. This is highly important to perform a microbiological study for the identification, which could help for the management of bacterial infections in this disease.

Sputum Gram's stains have several advantages over other available microbiological tests. Due to the presence of neutrophils in the Gram's stain, it is indicated that bacteria are real culprit for inflammation, the antimicrobial treatment will be easy to select based on the type of bacteria, and the quantity of bacteria discriminates an infection from a noninfectious exacerbation of COPD<sup>13</sup>. However, the treatment decision cannot be made alone based on this result,<sup>18</sup> because sputum cultures may

vary from Gram's stain results<sup>13-14</sup>.

COPD is caused typically 25% by viruses, 26% by bacteria; 27% by a combination of the two; 22% have no ascertainable cause, hence, bacterial infections are dominant in causing acute exacerbation of COPD<sup>19</sup>. *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis*<sup>7,19</sup> are among the common bacterial pathogens found in the sputum of COPD and the type of pathogen depends upon the severity of airway disease. *Staphylococcus aureus* and *Pseudomonas aeruginosa* were detected in patients with more severe AECOPD<sup>19</sup>. A lot of research has been conducted worldwide but there is dearth of data are available in Pakistan. Therefore, in this study, we aimed to investigate the most common bacteria in sputum culture of patients having chronic cough.

## METHODS

A cross-sectional observational study of two consecutive sputum cultures performed during the Intensive Care Unit stay (ICU), on the patients with COPD being treated in the ICU for pulmonary diseases in a tertiary care hospital in between January 2019-December 2019. Patients admitted in the ICU, of belonging to all age groups and of either gender suffering from chronic cough were included in the study. The study was conducted through non-probability convenient sampling technique after taking ethical exemption from the ERC. The Ethical Review Committee of Ziauddin University granted ethical exemption (ERC Reference: 2310620IAFOR).

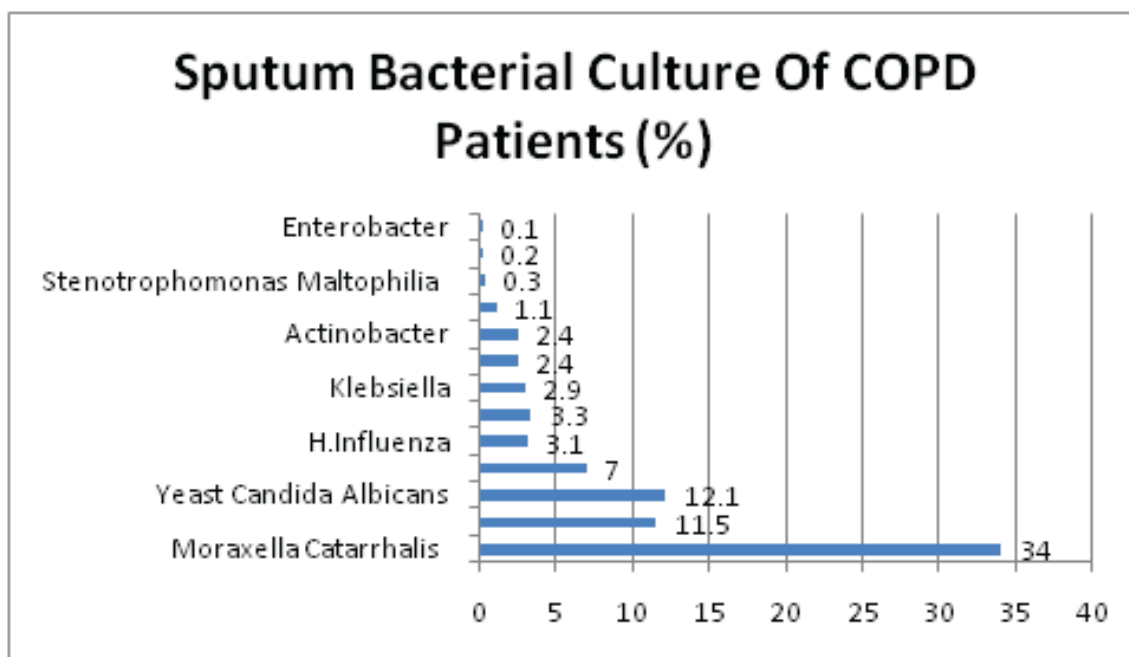
There were 1296 patients admitted with AECOPD belonging to both genders. Their FEV1 (forced expiratory volume) were less than 50% of standard normal values of FEV1 based on gender, age, weight, height. Patients were also suffering from respiratory failure (I or II type). Reports of two sputum sample cultures were collected from each patient admitted in the ICU with AECOPD. Then tests were performed to identify the bacterial infection. The Laboratory examinations were performed by microbiology department at Dr. Ziauddin Hospitals Clinical Laboratories, Karachi, Pakistan. Data was inserted and analyzed by using SPSS version 23.0. Descriptive analysis was performed, and the results findings were expressed as number and percentage of each type of bacteria. The data was collected from the hospital records and during the collection process; the reports were anonymized as advised by the ERC during the process of exemption.

## RESULTS

The findings revealed that among 1296 patients, the most frequent microorganism was *Moraxella*

*catarrhalis*, which was positive in 440 (34%) patients, and its frequency was high in all age groups. The second most frequent species was *Pseudomonas*,

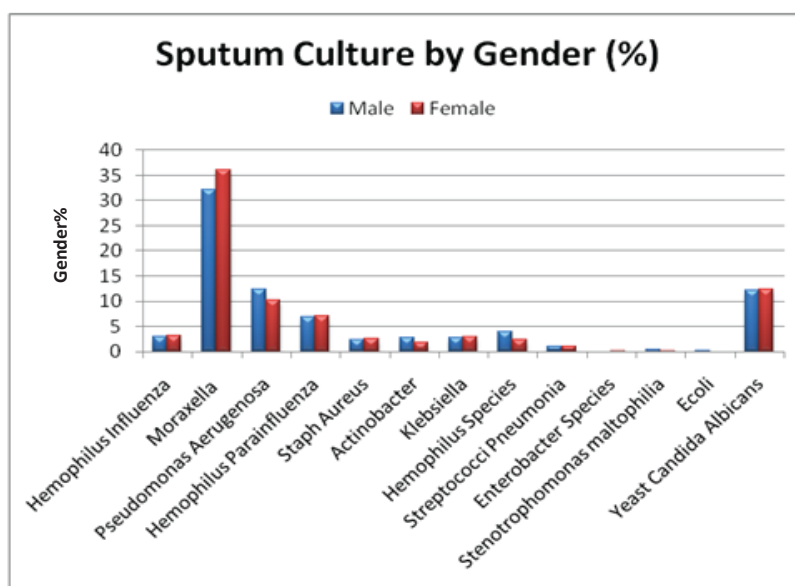
which was positive in 149 (11.5%) cases. The lowest frequency (Figure 1) was of *Enterobacter*, which was positive in 1 (0.1%), and *E. coli* in 2 (0.2%) cases.



**Figure 1: Frequency count (%) on x-axis of bacterial culture (on y-axis) in chronic obstructive pulmonary disease (COPD) sputum.**

Sputum bacterial cultures results of 1296 cultures showed *H. influenza* was positive in 40 (3.1%), *Moraxella catarrhalis* was positive in 440 (34.0%), *Pseudomonas aeruginosa* was positive in 149 (11.5%), *H. parainfluenza* was positive in 91 (7.0%), *S. aureus* was positive in 31 (2.4%), *Acinetobacter* species was positive in 31 (2.4%), *Klebsiella* species was positive in 37 (2.9%), *Haemophilus* species was positive in 43 (3.3%), *S. pneumoniae* was positive in

14 (1.1%), *Enterobacter* species was positive in 1 (0.1%), *Stenotrophomonas maltophilia* was positive in 4 (0.3%), *E. coli* was positive in 2 (0.2%). Yeast *Candida albicans* was positive in 157 (12.1%), Yeast *Candida glabrata* was positive in 3 (0.2%), Yeast *Candida tropicalis* was positive in 3 (0.2%) cases. It was observed that the culture was negative in 470 (36.3%) of the patients.



**Figure 2: Percentage of male and female (on y-axis) in bacterial culture (on x-axis) from sputum samples.**

With respect to the gender frequency (Figure 2), there were 749 (57.8%) males and 547 (42.2%) female patients. Mean age of patients was  $57.39 \pm 19.74$  years, whereas, the mean age of males was  $58.40 \pm 20.46$  years and that of females was

$56.0 \pm 18.63$  years. Patients were also divided into three sub-groups (Table 1) and there were 257 (19.8%) young age, 388 (29.9%) middle age and 651 (50.2%) old age patients. Majority of the patients were belonging to old age group.

**Table 1: Frequency of culture isolated organisms and their distribution in several age groups.**

Culture Isolated Organism	Total Cases n (%)	Cases Age (years)		
		( $\leq 40$ ) n (%)	(41-60) n (%)	(>61) n (%)
<i>H. influenza</i>	40 (3.1)	15 (1.2)	14 (1.1)	11 (0.8)
<i>Moraxella catarrhalis</i>	440 (34)	126 (9.7)	154 (11.9)	160 (12.3)
<i>Pseudomonas aeruginosa</i>	149 (11.5)	20 (1.5)	42 (3.2)	87 (6.7)
<i>H. parainfluenza</i>	91 (7.0)	28 (2.2)	33 (2.5)	30 (2.3)
<i>S. aureus</i>	31 (2.4)	3 (0.2)	11 (0.8)	17 (1.3)
<i>Acinetobacter</i> species	31 (2.4)	4 (0.3)	5 (0.4)	22 (1.7)
<i>Klebsiella</i> species	37 (2.9)	0 (0.0)	10 (0.8)	27 (2.1)
<i>Haemophilus</i> species	43 (3.3)	16 (1.2)	16 (1.2)	11 (0.8)
<i>Strep pneumoniae</i>	14 (1.1)	3 (0.2)	7 (0.5)	4 (0.3)
<i>Enterobacter</i> species	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)
<i>Stenotrophomonas maltophilia</i>	4 (0.3)	1 (0.1)	1 (0.1)	2 (0.2)
<i>E. coli</i>	2 (0.2)	0 (0.0)	1 (0.1)	1 (0.1)
<i>Yeast Candida albicans</i>	157 (12.1)	21 (1.6)	44 (3.4)	92 (7.1)
<i>Yeast Candida glabrata</i>	3 (0.2)	0 (0.1)	1 (0.1)	2 (0.2)
<i>Yeast Candida tropicalis</i>	3 (0.2)	0 (0.0)	0 (0.0)	3 (0.2)
Negative	470 (36.3)	86 (6.6)	127 (9.8)	257 (19.8)
<b>Total</b>	<b>1296 (100%)</b>	<b>257 (19.8%)</b>	<b>388 (29.9%)</b>	<b>651 (50.2%)</b>

## DISCUSSION

COPD is a life-threatening pulmonary disease and it is one of the leading causes of death worldwide. It has lethal effects of the patient's life and if left untreated may lead to death. Few symptoms of COPD include dyspnea, wheezing, cough, and sputum production<sup>20</sup>. COPD is a progressive illness and characterized by worsening symptoms, stated as exacerbations, which might be due to infection of the trachea-bronchial tree<sup>15</sup>. Either respiratory viruses cause these infections or bacteria, where 26% showed bacterial cause and 27% showed both viral and bacterial cause<sup>19</sup>. The prevalence of

bacterial infection and type of bacteria involve have been controversial<sup>13</sup>.

In present study, COPD patients were divided into three subgroups. The frequency of young age cases was 257 (19.8%), middle age was 388 (29.9%) and old age was 651 (50.2%). This result showed that with increasing age more people are prone to acquire pulmonary infections specifically COPD. Our results are comparable to previous study conducted for seven years and showed that smoking and age are risk factors for the incidence of COPD and it was significantly associated with increasing age<sup>21</sup>.

Additionally, *Moraxella catarrhalis* which was positive in 440 (34%), its frequency was highest in all age groups in our study. *Moraxella catarrhalis* is regarded as most dominantly affecting upper respiratory tract pathogen in humans<sup>22</sup>. Based on the results of study by Murphy et al., *Moraxella catarrhalis* is the second most common bacterial cause of exacerbations in patients of COPD after *H. influenza*<sup>23</sup>, which contrasts with our findings.

The other common pathogens were *Pseudomonas aeruginosa* with frequency of 149 (11.5%) and Yeast *Candida albicans* with frequency of 157 (12.1%). Results of our study are consistent with other previous studies except few pathogens are not common in our study specially *H. influenza*, however, other studies showed most common bacterial pathogens observed were *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Streptococcus pneumoniae* and *Moraxella catharralis*<sup>19,22,24-26</sup>. Furthermore, it is depicted that presence of different bacteria may also depend on the severity of airway disease. *Staphylococcus aureus* and *Pseudomonas aeruginosa* are more virulent and observed in patients with more severe AECOPD<sup>19</sup>.

Within this context, a study showed that *Haemophilus influenzae* and *parainfluenzae* was less frequent, which might be because these patients were already treated with antibiotics before admission in hospital due to respiratory failure<sup>26</sup>. There are limited studies about isolated bacteria in sputum culture in AECOPD but all of them indicate the importance of doing bacterial sputum culture in AECOPD because of large number of cases that is up to the 50% AECOPD is caused by bacterial infections. It is therefore very important to perform sputum test to identify the causative agents and treat the patients with appropriate antibiotic to reduce the episodes of AECOPD. We may suggest that the confirmation of infections etiology should be performed through sputum analysis for treatment selection. We also recommend the routine sputum bacterial culture application in each patient with COPD exacerbation.

### CONCLUSION

With increasing age people are prone to acquire pulmonary infections specifically COPD. Therefore, it is very important to perform sputum culture to identify the causative agents and treat the patients with appropriate antibiotic to reduce the episodes of acute exacerbations of chronic pulmonary obstructive disease (AECOPD). AECOPD badly deteriorates the patients' quality of life by disturbing mental, social, and economic life activities. Bacterial infections are contributing in almost 50% of the cases, but respiratory infections are quite difficult to

diagnose in a patient with COPD exacerbation because of being asymptomatic or symptoms may be confused with non-infectious exacerbations.

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### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### ETHICS APPROVAL

Ethical exemption was granted by the Ethical review Committee of Ziauddin University (ERC Reference Code: 2310620IAFOR).

### PATIENT CONSENT

Written consents were obtained from the participants of the search.

### AUTHORS' CONTRIBUTION

FS provided the concept and final approvals of the article and had a supervisory role. TA played her role in designing the research and literature review was also done by her. MIA was involved in drafting of the research article and was also the corresponding author. AAK helped by providing data analysis and result writing. MA contributed in the concept for research and by providing corrections in the discussion. NS was involved in literature review and revision of the research draft.

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