

## Frequency of *Streptococcus pneumoniae* and *Haemophilus influenzae* in acute exacerbation of chronic obstructive airway disease and their sensitivity to levofloxacin

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### Abstract

**Objective:** To determine the frequency of *Streptococcus pneumoniae* and *Haemophilus influenzae* in acute exacerbation of chronic obstructive pulmonary disease and their sensitivity to levofloxacin.

**Methods:** The cross-sectional study was conducted at the Department of Medicine, AbbasiShaheed Hospital, Karachi, between July 2009 and January 2010. Patients already diagnosed with chronic obstructive pulmonary disease and admitted with symptoms of acute exacerbation were included in the study and their sputum samples were sent for microbiological evaluation. SPSS 16 was used for statistical analysis.

**Results:** Of the total 105 patients in the study, 90 (85.17%) were males. Overall mean age at presentation was 62±10.2 years. *S.pneumoniae* was isolated from sputum culture of 33 (31.4%) patients, while 13 (12.4%) patients showed growth of *H. influenzae*. Out of the 33 sputum specimens of *S.pneumoniae*, 32 (97.0%) were sensitive to levofloxacin, while 1 (3.0%) was resistant. All the 13 isolates of *H. influenzae* were sensitive to levofloxacin.

**Conclusion:** *S.pneumoniae* and *H.influenzae* are still the most prevalent organisms isolated in acute exacerbation of chronic obstructive pulmonary disease in our population. Levofloxacin is still considered a highly sensitive antibiotic against these common micro-organisms in our population, but *S.pneumoniae* has started developing resistance against levofloxacin. Therefore, intermittent surveillance regarding development of resistance pattern of common micro-organisms against commonly prescribed antibiotics is required.

**Keywords:** COPD, Culture and sensitivity, Sputum, Bacteria. (JPMA 64: 399; 2014)

### Introduction

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of mortality worldwide and an important cause of the overall burden of disease. According to a study, worldwide prevalence of the COPD is 9.34/1000 in men and 7.33/1000 in women.<sup>1</sup> In Europe, incidence among adult population is 4-6% and it is a leading cause of death. In people aged 25-75 years in the USA, the estimated prevalence of the disease is 6.6%.<sup>2</sup> The estimated annual expenditure on the disease is \$24 billion, 70% of which is related to exacerbations requiring hospitalization.<sup>3</sup>

COPD is characterised by slowly progressing, irreversible airflow limitation caused by chronic inflammation in the bronchioles.<sup>4</sup> The disease is associated with intermittent exacerbations characterised by acute deterioration in symptoms, lung functions and quality of life.<sup>5</sup> The principal identified causes of COPD exacerbations include bacterial and viral infections, pollution events, cold

weather and interruption of regular treatment.<sup>6</sup>

At least half of the COPD exacerbations are due to pathogenic micro-organisms. An international study shows *Haemophilus influenzae* 32.5% and *Streptococcus pneumoniae* 20.3% isolated from sputum cultures in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).<sup>7</sup> A local study shows the prevalence of *S. pneumoniae* 48.7% and *H. influenzae* 14.6%.<sup>1</sup>

In infective exacerbations prompt antibiotic treatment shortens the duration of exacerbations and may prevent hospital admission and further lung damage.<sup>8</sup>

Several clinical trials support the clinical efficacy of fluoroquinolones in the exacerbation phase.<sup>7</sup>

The susceptibilities of organisms to antibacterial agents have changed dramatically over the past decade. The tracking resistance in the United States today (TRUST) study indicate that the susceptibility pattern continues to change and also shows geographic variation.<sup>9</sup>

The rationale of this study was to find out the sensitivity of levofloxacin to *S.pneumoniae* and *H. influenzae* in our population in order to optimise the use of antibiotics,

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avoid the emerging resistance and thus reduce the economic burden.

### Patients and Methods

The cross-sectional study with a non-probability purposive sampling technique, conducted at the Department of Medicine, Abbasi Shaheed Hospital, Karachi, from July 2009 to January 2010.

Patients aged between 50-70 years, already diagnosed on the basis of pulmonary function tests, having signs and symptoms of acute exacerbation suggested by increased intensity of cough, increased amount of sputum, change in the colour of sputum, increased intensity of shortness of breath and fever, and with positive sputum culture were included in the study. Patients having other concomitant chest disease, for example tuberculosis, bronchiectasis, pneumonia and lung abscess on chest X-ray and who were already on antibiotics or had taken antibiotics 3 weeks prior to the exacerbation, were excluded. After history and examination, informed consent was taken from the patients or their attendants. A fresh sample of sputum was collected into a sterile container and was sent for culture and sensitivity. All relevant information was filled in a proforma. The data was analysed using SPSS version 16. Continuous variable, that is patient's age, was expressed as mean  $\pm$  standard deviation. Qualitative variables, such as gender, sputum culture, sensitivity and resistance pattern of levofloxacin, were expressed as frequencies and percentages.

### Results

Of the 105 patients in the study, 90 (85.7%) were males and 15 (14.3%) females. The male-to-female ratio was 6:1. Overall mean age was  $62 \pm 10.2$  years and the age range was 50-70 years (Table). *S. pneumoniae* was isolated from sputum cultures of 33 (31.4%) patients, whereas

*H. influenzae* was isolated from 13 (12.4%). Besides, sputum samples of 59 (56.2%) patients showed other organisms. Out of 33 *S. pneumoniae* cases, 32 (97.0%) were sensitive to levofloxacin, while only 1 (3.0%) was resistant to it. All 13(100%) *H. influenzae* cultures were sensitive to levofloxacin. The cumulative sensitivity of *S. pneumoniae* and *H. influenzae* was 97.8% and the cumulative resistance was 2.2%.

### Discussion

In the present study, 85.7% were males and 14.6% females which are consistent with an international study that also showed male predominance with 83.1% males and 15.8% females.<sup>10</sup> However, a Canadian study showed that out of 150 patients there were 59 (39%) males and 91 (61%) females.<sup>11</sup>

In the present study the age range was 50-70 years and the mean age was  $62 \pm 10.2$  years which is consistent with a study done by Chin CL et al<sup>12</sup> which showed mean age of  $64.8 \pm 2$  years.

Sputum bacteriology of the patients in this study showed the frequency of *S. pneumoniae* to be 31.4% and *H. influenzae* 12.4% which is consistent with a study done previously in a tertiary care hospital in Karachi<sup>1</sup> which showed 48.7% *S. pneumoniae* and 14.6% *H. influenzae*.

However, in contradiction to these results, ongoing international studies are showing that the frequency of common bacteria isolated in AECOPD is now changing rapidly and it also changes with geographical variation. A study showed that *H. influenzae* was relatively more common (13-50%) followed by *S. pneumoniae* (7-26%) in AECOPD.<sup>13</sup>

As bacterial infection is considered a major factor in the etiology of AECOPD, several studies have been done on antimicrobial therapy in these patients. Numerous placebo-controlled trials of antibiotics have been published suggesting beneficial effect of antibiotics<sup>14</sup> but unfortunately there have been significant differences in the results of these individual studies.

The role of specific agent remains unclear and antibiotics are still prescribed on the basis of empirical evidence.

Some investigators have suggested a more rapid resolution of symptoms seen with quinolones in contrast to comparators<sup>15,16</sup> which is associated with a longer disease-free interval.<sup>17,18</sup>

The susceptibilities of *S. pneumoniae* and *H. influenzae* to antibacterial agents have changed dramatically over the past decade. But resistance of *S. pneumoniae* and

**Table:** General characteristics and frequency of organisms of patients with AECOPD.

General characteristics	Number	Percent
<b>Gender</b>		
Male	90	85.7
Female	15	14.3
M : F ratio	6 : 1	
<b>Age (years)</b>		
50 - 59	28	26.7
60 & above	77	73.3
Mean $\pm$ S.D	$62 \pm 10.2$	
<b>Frequency</b>		
<i>Streptococcus pneumoniae</i>	33	31.4
<i>Haemophilus influenzae</i>	13	12.4
Others	59	56.2

AECOPD: Acute Exacerbation of Chronic Obstructive Pulmonary Disease.

*H. influenzae* to levofloxacin is still low.<sup>8</sup> Results of different studies shows that fluoroquinolone resistance rates remain low in *S. pneumoniae* in most countries.<sup>19-21</sup>

In our series, the sensitivity of *S. pneumoniae* and *H. influenzae* to levofloxacin was 97.0% and 100% respectively which is in contrast to a study done previously in which no resistance was seen against levofloxacin.<sup>1</sup>

Dearth of local data suggests that new trials are needed to determine the frequency of different organisms and their susceptibility to different antibiotics in our society so that we can treat the patients effectively with minimum side effects of drugs and can minimise the development of resistance to these drugs and can effectively reduce the economic burden. Furthermore intermittent surveillance to see the resistance pattern of commonly prescribed antibiotics is needed as previously levofloxacin was considered highly sensitive against these microbial pathogens, but now, as is evident from this study, *S. pneumoniae* has started developing resistance against levofloxacin.

Limitations of this study included the fact that for the identification of potential pathogenic micro-organisms, simply a single sputum culture was done and more sensitive techniques, such as polymerase chain reaction (PCR) for molecular characterisation of micro-flora, were not used. Besides, contamination by upper airway secretions that may often contain potential pathogens is a major concern. Despite its limitations, sputum culture remains the predominant investigation performed in a clinical setting and it is still useful in locating the pathogenesis of exacerbation of COPD. It is important to note that all studies to date of bacterial causation of exacerbation have used a single culture of sputum at the time of presentation and standard or semi-quantitative culture techniques. No study has studied multiple sputum samples from each exacerbation or applied more sensitive techniques. It is quite possible that such studies may reveal that a larger proportion of exacerbations have a bacterial origin than the current data suggest.<sup>13</sup> Explanation to second limitation is that, in bronchoscopic studies of AECOPD, the bacterial species isolated represent a similar spectrum of pathogens commonly isolated from sputum culture.<sup>22,23</sup> These support easy-to-obtain method and the majority of studies have continued to use sputum as the primary non-invasive method of sampling.

## Conclusion

In AECOPD etiology, microbial infection plays an important role. In microbial infections, *S. pneumoniae* and

*H. influenzae* have high prevalence rate in our geographical region. As antibiotics are prescribed to treat the condition, the most important concern is the emerging resistance of common pathogenic organisms against these antibiotics. Quinolones still have low resistance rate against these organisms, but *S. pneumoniae* has already started developing resistance against levofloxacin. As such, intermittent surveillance is needed to monitor the resistance pattern of commonly prescribed antibiotics against these organisms. Therefore, in the treatment of AECOPD it is important to know the frequency of different bacteria and their sensitivity to commonly prescribed antibiotics according to the geographical location so that we can treat the patient effectively and can reduce the side effects, pharmacy cost, economic burden and antibiotic resistance.

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