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Impact of the COVID-19 Pandemic on Acute Exacerbation Frequency in COPD Patients (Postprint)

Authors: Shi Weijuan, Wang Fengyan, Yang Yuqiong, Xie Qingxiu, Li Yuqi, Li Shiyue, Chen Rongchang, Zhang Dongying, Zheng Jinping, Liang Zhenyu

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Abstract

Background: Respiratory viral infections are important triggers of acute exacerbations of chronic obstructive pulmonary disease (COPD). Following the outbreak of the 2019 novel coronavirus (COVID-19) pandemic, China implemented a series of preventive measures aimed at cutting the transmission chain of COVID-19. Multiple studies have shown that the frequency of hospitalizations for COPD exacerbations decreased during the COVID-19 pandemic period; however, research on the impact of preventive measures on the frequency of exacerbations of different severities is relatively lacking.

Objective: To investigate the impact of the COVID-19 pandemic context on the frequency of COPD exacerbations of different severities.

Methods: Patients were from the First Affiliated Hospital of Guangzhou Medical University, and COPD diagnosis met the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Data on exacerbation frequency and other clinical information were collected for patients during October 2016-May 2017 (Group), October 2017-May 2018 (Group), October 2018-May 2019 (Group), and October 2019-May 2020 (Group). We analyzed changes in COPD exacerbation frequency before and after the COVID-19 pandemic. Differences in exacerbation frequency during the same period were compared between Group and Groups , , and patients, respectively.

Results: COPD patients included 162 cases in Group , 157 cases in Group , 167 cases in Group , and 159 cases in Group . In Groups and , exacerbation frequency during the months corresponding to the post-COVID-19 outbreak period (October-January) was slightly higher compared with the months corresponding to the pre-pandemic period (February-May) ($p<0.05$); the difference

was not statistically significant in Group (p>0.05), whereas in Group , exacerbation frequency was lower after the COVID-19 outbreak than before (p=0.01). Exacerbation frequency in February-April 2020 was significantly lower than in February-April 2019, 2018, and 2017 (p<0.05). There was no significant difference in the frequency of monthly exacerbations without medical consultation among the four groups of COPD patients.

Conclusion: COVID-19 prevention and control measures have played a positive role in reducing the frequency of COPD exacerbations. This suggests that COPD patients should continue to limit gatherings, maintain social distancing, wear masks when going out, and practice frequent hand washing even after the pandemic.

Full Text

Preamble

Analysis of the Impact of the COVID-19 Pandemic Context on the Frequency of Acute Exacerbations in COPD Patients

Authors: Shi Weijuan[1], Wang Fengyan[1], *Yang Yuqiong*[1], *Xie Qingxiu*[1], *Pan Chengqin*[1], *Li Yuqi*[1], *Chen Rongchang*[1,2], *Zhang Dongying*[1], *Zheng Jinping*[1], Liang Zhenyu[1]*

Affiliations: 1. The First Affiliated Hospital of Guangzhou Medical University/National Clinical Research Center for Respiratory Diseases, Guangzhou 510030, China 2. Shenzhen People' s Hospital/Shenzhen Institute of Respiratory Diseases, Shenzhen 518020, China

Corresponding authors: Zheng Jinping, Professor, Chief Physician, PhD Supervisor; E-mail: 18928868238@163.com; Liang Zhenyu, Medical PhD, Chief Physician, Master' s Supervisor; E-mail: 490458234@qq.com

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Abstract

Background: Respiratory viral infections are important triggers of acute exacerbations of chronic obstructive pulmonary disease (AECOPD). Following the COVID-19 outbreak, China implemented a series of preventive measures to interrupt transmission chains. Multiple studies have shown that hospitalization rates for AECOPD decreased during the pandemic, but research on how these measures affect exacerbation frequencies across different severity levels remains limited.

Objective: To investigate the impact of the COVID-19 pandemic context on the frequency of AECOPD of varying severity.

Methods: Patients were recruited from The First Affiliated Hospital of Guangzhou Medical University and diagnosed with COPD according to GOLD criteria. Data on acute exacerbation frequencies and other clinical information were collected for four periods: October 2016–May 2017 (Group I), October 2017–May 2018 (Group II), October 2018–May 2019 (Group III), and October 2019–May 2020 (Group IV). Changes in AECOPD frequency before and after the COVID-19 outbreak were analyzed, with comparisons of exacerbation frequencies during equivalent time periods between Group I and Groups II, III, and IV.

Results: The study included 162 COPD patients in Group I, 157 in Group II, 167 in Group III, and 159 in Group IV. In Groups I and II, acute exacerbation frequencies during February–May were significantly higher than during October–January ($p<0.05$); Group III showed a similar trend without statistical significance ($p>0.05$). In Group IV, post-outbreak exacerbation frequency was significantly lower than pre-outbreak levels ($p=0.01$). The February–April 2020 exacerbation frequency was markedly reduced compared to the same months in 2019, 2018, and 2017 ($p<0.05$). No significant differences were observed in monthly frequencies of untreated exacerbations across the four groups.

Conclusion: COVID-19 prevention and control measures played a positive role in reducing AECOPD frequency. We recommend that COPD patients should continue to avoid crowded gatherings, maintain social distancing, wear masks when outdoors, and practice frequent handwashing even after the pandemic.

Keywords: Chronic obstructive pulmonary disease; COVID-19; Pandemic context; Follow-up cohort; Acute exacerbation

Introduction

Chronic obstructive pulmonary disease (COPD) is a common condition characterized by persistent airflow limitation that poses serious threats to human health. An acute exacerbation of COPD (AECOPD) is defined as a clinical event featuring worsening respiratory symptoms beyond normal day-to-day variation, leading to changes in medication [1]. These exacerbations reduce quality of life, accelerate lung function decline, and increase both economic and social burdens [2], making reduction of exacerbation frequency a critical therapeutic goal.

Viral infections are major triggers of AECOPD, with rhinovirus and common coronaviruses being the most frequently detected viruses during exacerbation episodes [3]. As a chronic respiratory disease, stable COPD management includes smoking cessation, regular pharmacotherapy, and influenza and pneumococcal vaccination [1], but does not typically incorporate measures common to acute respiratory infection control such as mask-wearing or social distancing.

COVID-19, also caused by viral infection, transmits through contact with droplets from infected individuals, contaminated surfaces (fomites), inhalation of virus-laden aerosols, and mucosal exposure [4]. Research indicates that a six-foot distance can prevent disease transmission [5]. Following the COVID-19 outbreak, China activated Level I public health emergency responses nationwide. Based on transmission characteristics, measures including home isolation, universal testing, restriction of public gatherings, social distancing, and mask mandates were implemented to control infection sources and interrupt transmission pathways. Studies comparing influenza activity indicators before and after COVID-19 public health measures to the previous three years showed significantly decreased influenza positivity rates, demonstrating that COVID-19 prevention measures effectively reduced transmission of viral respiratory diseases [6]. These measures decreased interpersonal contact and viral respiratory disease transmission. Multiple studies have reported decreased AECOPD hospitalizations during the pandemic [7-9], but research on impacts encompassing both treated and untreated exacerbations remains lacking. This study investigates the effects of COVID-19 prevention and control measures on AECOPD frequency.

Methods

1.1 Study Subjects

This prospective observational study was approved by the Ethics Committee of The First Affiliated Hospital of Guangzhou Medical University (Approval No.: 2017-22). Participants were recruited from a COPD follow-up cohort at the hospital, established in early 2016 with patient visits every three months to collect demographic and clinical data. Inclusion criteria were: (1) age $ $40 years; (2) COPD diagnosis meeting GOLD criteria; (3) ability to provide informed consent and comply with follow-up protocols. Exclusion criteria included: (1) other pulmonary diseases or severe $ $1-antitrypsin deficiency; (2) history of lung surgery or recent malignant tumor diagnosis; (3) participation in double-blind drug clinical trials.

The study selected four patient groups with follow-up time windows in June–August 2017 (Group I), June–August 2018 (Group II), June–August 2019 (Group III), and June–August 2020 (Group IV).

1.2 Data Collection

Acute exacerbation frequencies, medication use, symptom scores, and other information were collected for the following periods: October 2016–May 2017 (Group I), October 2017–May 2018 (Group II), October 2018–May 2019 (Group III), and October 2019–May 2020 (Group IV). For Group IV, October 2019–January 2020 represented pre-COVID-19 data, while February–May 2020 represented post-outbreak data. Changes in AECOPD frequency before and after

the outbreak were analyzed, comparing Group IV with Groups I, II, and III for overall exacerbation frequency, untreated exacerbation frequency, and medically attended exacerbation frequency (including outpatient, emergency, and hospital visits). According to GOLD guidelines, an acute exacerbation was defined as worsening respiratory symptoms requiring medication changes [1]. Group exacerbation frequency was calculated as the ratio of total exacerbation events to total group population. The study flow chart is shown in [Figure 1: see original paper].

1.3 Statistical Analysis

SPSS 22.0 software was used for statistical analysis. Normally distributed quantitative data were expressed as mean ± standard deviation (+S) and compared using independent samples t-tests. Non-normally distributed data were presented as median and interquartile range, with Mann-Whitney U tests for between-group comparisons. Categorical data were expressed as n (%). Wilcoxon signed-rank tests compared pre- and post-COVID-19 exacerbation frequencies within Group I. Chi-square tests compared monthly exacerbation frequencies between Group I and other groups, with Bonferroni correction (p$ $0.05/3=0.017 considered statistically significant).

Results

2.1 Baseline Characteristics

The study included 162 COPD patients in Group I, 157 in Group II, 167 in Group III, and 159 in Group IV. No significant differences were observed between Group IV and Groups I, II, or III in age, modified Medical Research Council dyspnea scale (mMRC) scores, COPD Assessment Test (CAT) scores, percentage of predicted forced expiratory volume in one second (FEV1%pred), smoking history, or inhalation medication history (P>0.017). Detailed baseline data are presented in .

Table 1 Comparison of baseline characteristics among the four groups

[The table shows demographic and clinical data including: male sex, age, mMRC scores (0-1 vs 2-4), CAT scores (<10 vs $ $10), FEV1%pred values and categories, smoking history (pack-years), and inhalation medication use (ICS+LABA, LABA+LAMA, ICS+LABA+LAMA), with statistical comparisons between Group IV and each of the other groups.]

2.2 Comparison of Acute Exacerbation Frequencies

2.2.1 Comparison of Exacerbation Frequencies Before and After COVID-19 in Group IV and Corresponding Months in Other Groups

Table 2 Comparison of acute exacerbation frequencies during October–January and February–May among the four groups

Group	October–January a (%)	February–May b (%)
I	43 (26.54)	68 (41.98)
II	34 (21.66)	54 (34.39)
III	45 (26.95)	61 (36.53)
IV	30 (18.87)	9 (5.66)

Note: a. October–January refers to the period from October of the previous year to January of the follow-up year. b. February–May refers to the period from February to May of the follow-up year.

Groups I and II showed significantly higher exacerbation frequencies in February–May compared to October–January ($p<0.05$), while Group III showed no statistically significant difference ($p>0.05$). During October 2019–May 2020, 39 exacerbation events occurred in Group IV, with 30 events (18.87% frequency) pre-COVID-19 and 9 events (5.66% frequency) post-outbreak. The post-outbreak frequency was significantly lower ($Z=-3.362$, $p=0.001$).

2.2.2 Comparison of Exacerbation Frequencies Between Group IV and Groups I, II, and III Monthly exacerbation frequencies from October to May for each group and comparisons between Group IV and the other three groups are shown in **Table 3** and **Figure 2**.

Table 3 Comparison of acute exacerbation frequencies (%) between Group IV and other groups during the same period

[The table presents monthly exacerbation frequencies for each group from October through May, with statistical comparisons showing that Group IV's frequencies in February–April were significantly lower than all other groups ($p<0.001$), while October–December differences were not significant.]

As shown in Table 3, no significant differences were observed between Group IV and Groups I, II, or III during October–December 2019 ($p>0.05$). However, Group IV' s exacerbation frequencies in February–April 2020 were significantly lower than all three comparison groups ($p<0.05$). The total exacerbation frequency for Group IV during October 2019–January 2020 was significantly lower than Groups I and III ($p<0.05$) but not Group II ($p>0.05$). The February–May 2020 total frequency was significantly lower than all comparison groups ($p<0.05$). Compared to the average of Groups I–III, Group IV showed no significant difference in October–December but significant reductions in January–May ($p<0.05$), with decreases of 7.56% in January, 7.39% in February, 9.43% in March, 9.05% in April, and 6.12% in May.

Figure 2 illustrates that while Groups I–III showed rising average exacerbation frequencies after January, Group IV demonstrated a clear downward trend.

2.2.3 Comparison of Untreated Exacerbation Frequencies Table 4 Comparison of untreated acute exacerbation frequencies (%) among the four groups

[The table shows monthly frequencies of untreated exacerbations, which were low across all groups with no significant differences.]

As shown in Table 4 and Figure 3, no significant differences were observed in monthly frequencies of untreated exacerbations among the four COPD patient groups.

2.2.4 Comparison of Medically Attended Exacerbation Frequencies Table 5 Comparison of medically attended acute exacerbation frequencies (%) among the four groups

[The table presents monthly frequencies of exacerbations requiring medical attention, showing significant reductions in Group IV during February–April compared to other groups.]

Table 5 shows no significant differences between Group IV and other groups during October–December 2019 ($p>0.05$). However, Group IV' s medically attended exacerbation frequencies in February–April 2020 were significantly lower than all comparison groups ($p<0.05$). Compared to the average of Groups I–III, Group IV showed no significant difference in October–December ($p>0.05$) but significant reductions in January–April ($p<0.05$), with decreases of 6.95% in January, 5.95% in February, 9.66% in March, and 6.79% in April.

Figure 4 demonstrates that while Groups I–III showed increasing trends in medically attended exacerbation frequencies after January, Group IV exhibited a marked decline.

Discussion

Acute exacerbations of COPD significantly impact patients through reduced quality of life, accelerated lung function decline, and increased economic burden. Studies show the average cost of AECOPD hospitalization is \$9,545±\$12,700 in the United States [10], while in Canada, treatment costs average \$1,673 per patient with 82% attributable to hospitalization [11]. In Beijing, China, hospitalization costs increased from ¥15,953.5 to ¥19,874.5 between 2008–2017 [12]. Reducing exacerbation frequency is therefore a primary goal of stable COPD management, which GOLD guidelines address through smoking cessation, regular inhalation therapy, and vaccination [1]. However, Beijing data from 2008–2017 show an inverted U-shaped trend in AECOPD hospitalization rates [12], indicating that exacerbations remain a heavy burden on healthcare systems and that reducing their frequency remains an urgent challenge.

This study analyzed follow-up data from four COPD patient groups. The AECOPD frequency during February–May 2020 (post-COVID-19 outbreak) was 5.66%, compared to 18.87% during October 2019–January 2020 (pre-outbreak), representing a 13.21% reduction. In contrast, February–May frequencies in 2017–2019 were higher than the preceding four months. The February–May 2020 frequency was 36.32%, 28.73%, and 30.87% lower than the same periods in 2017, 2018, and 2019, respectively, demonstrating a clear reduction following the COVID-19 outbreak.

We attribute this reduction to China' s control measures, which also limited influenza transmission due to shared transmission routes: (1) community lockdowns, home isolation, and social distancing restricted pathogen spread; (2) universal mask-wearing reduced droplet transmission risk; and (3) nucleic acid testing for suspected infections maximized identification of infection sources, reducing exposure [13]. Multiple studies confirm that COVID-19 public health measures effectively reduced viral respiratory disease transmission, advocating for their continued use in influenza prevention [14-17]. These measures also significantly reduced AECOPD frequency by controlling viral and bacterial transmission, major exacerbation triggers. The temporal pattern aligns with China' s control timeline: Wuhan' s lockdown began January 23, 2020, with strict measures effectively controlling COVID-19 transmission by early April [18].

Multiple studies report significantly reduced AECOPD admissions during the pandemic, coinciding with public health interventions. Simple preventive measures such as face masks, hand hygiene, and social distancing warrant further investigation for AECOPD prevention [19-22]. However, these studies note potential negative impacts on healthcare access, as patients might avoid seeking care due to fear of nosocomial COVID-19 infection. Our study, conducted in a routine follow-up cohort capturing all exacerbation events (both treated and untreated), found no significant difference in untreated exacerbation frequencies during February–April 2020 compared to previous years. This suggests that COVID-19 measures positively reduced AECOPD frequency without substantially impeding patients' access to medical care.

This study has limitations. First, baseline frequencies of untreated exacerbations were low in Groups I–III, and the relatively small sample size may have obscured differences. Second, Group IV' s untreated cases included both mild symptoms not requiring care and potential access barriers due to lockdown restrictions. However, the absence of increased untreated exacerbation frequencies suggests that lockdown-related access issues were either nonexistent or rare.

Reducing AECOPD frequency remains a top clinical priority. While contact reduction is not widely promoted for AECOPD prevention, particularly during high-risk seasons, China' s COVID-19 experience (February–April 2020) offers valuable insights: (1) COPD patients should avoid crowded places and maintain social distancing, especially during influenza season; (2) Masks should be worn outdoors except during exercise; (3) Handwashing should be frequent. These low-cost, easily implementable measures should be widely promoted for COPD

patients.

Author Contributions: Shi Weijuan: conceptualization, data curation, writing; Xie Qingxiu, Pan Chengqin, Li Yuqi: data collection; Liang Zhenyu, Wang Fengyan, Yang Yuqiong, Zhang Dongying: manuscript revision; Li Shiyue, Chen Rongchang, Zheng Jinping: resource provision.

Conflict of Interest: The authors declare no conflicts of interest.

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