RESEARCH

Corticosteroid and antibiotic use in hospitalized patients in Lebanon with acute exacerbation of chronic obstructive pulmonary disease

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Abstract

Background Chronic obstructive pulmonary disease (COPD) is currently one of the leading causes of death worldwide, with 90% of these deaths reported in low- and middle-income countries. In Lebanon, the prevalence of COPD is 9.7%. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommends the use of antibiotics and corticosteroids in inpatients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). The studies examining the level of conformity with the GOLD recommendations are rare, which increases the need for the current study.

Methods A 3-month cross-sectional study was done. Patients included were those diagnosed with acute exacerbations of COPD and admitted to one of the selected hospitals in Beirut, of various nationalities and sexes, aged 18 to 89. Data were selected from patient files admitted between January 2020 and June 2022 using a data collection sheet. The SPSS version 24 statistics software was used to conduct statistical analysis.

Results A total of 260 patients were recruited, with 86.7% receiving systemic corticosteroids, 24.3% respecting dose, and 81.8% respecting the appropriate duration of corticosteroid intake. 80% exhibited pulmonary indications for receiving antibiotics, and 56.53% had the necessary cardinal symptoms. Around 74.5% of patients use antibiotics for the recommended time of 5 to 7 days. Age (*p* value = 0.006), gender (*p* value = 0.049), alcohol consumption (*p* value = 0.018), and use of psychiatric medications (*p* value = 0.049) are correlated with the conformity index of corticosteroid administration. A correlation was observed between the duration of use of antibiotics with cardinal symptoms (*p* value = 0.003), CRP-value (*p* value = 0.007), and type of hospital (*p* value = 0.00).

Conclusion This investigation revealed a need for correction in a deviation from the guidelines, shed light on existing clinical procedures, and emphasized the growing concern about the uncontrollable rate of antibiotic use and inadequate corticosteroid dosing.

Keywords AECOPD, GOLD guidelines, Corticosteroids, Antibiotics

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Background

Chronic obstructive pulmonary disease (COPD) is currently one of the leading causes of death worldwide, with 90% of deaths reported in low- and middle-income countries [1]. Because of continuing exposure to COPD risk factors and population aging, the global burden of COPD is expected to rise in the future decades [2]. The first and so far, only national study to evaluate the prevalence of COPD in the adult Lebanese population indicated a prevalence of 9.7% [3]. Exacerbations of COPD are critical occurrences in COPD care because they have a harmful influence on health, hospitalization, and disease progression. Exacerbations of COPD include increased airway inflammation, increased mucus production, and significant gas trapping. Increased dyspnea is a key symptom of exacerbation, and these alterations contribute to it. Other signs and symptoms include increased sputum purulence and volume, as well as coughing and wheezing [4]. Appropriate guideline-based management of AECOPD should not only result in better clinical outcomes for the exacerbation itself, but it may also play a role in longer-term benefits like improved survival, improved quality of life, reduced morbidity, and a slower rate of decline in lung function [5]. The goals of treatment for COPD exacerbations are to minimize the negative impact of the current exacerbation and prevent the development of subsequent events [6]. For most patients with moderate-to-severe exacerbations, systemic corticosteroids are prescribed to decrease inflammation and improve symptom control. The recommended period of corticosteroid medication has been lowered from 7–14 days to 5–7 days. Antibiotics are recommended for individuals who have three cardinal symptoms: increased dyspnea, sputum volume, or sputum purulence; two of the cardinal symptoms with increased sputum purulence being one of the two symptoms; or mechanical ventilation (invasive or noninvasive) [7]. Treatment for 5 to 7 days is indicated, depending on the patient's reaction [6].

Conformity with treatment plays a key role in the course of COPD [8]. Failure to adhere to a patient's treatment plan might result in deteriorating health to eventual death [8]. In addition, non-conformity has negative effects on the economy and the health of the entire society [8]. Numerous studies have revealed low rates of prescribing AECOPD medications in care settings all over the world that are consistent with guideline recommendations [7].

The need for corticosteroids and antibiotics cannot be overstated. Long-term corticosteroid and antibiotic use have far-reaching impacts, and the healthcare system must deal with high levels of resistance brought on by the uncontrolled use of antibiotics.

There are not many studies being done in the Middle East and North Africa region to assess how well exacerbated COPD patients conform with GOLD recommendations. In addition, both public and private healthcare systems in Lebanon were significantly impacted by the pandemic and economic collapse which makes this study more essential to assess the effectiveness of hospitals in Lebanon in following all the important changes to the healthcare system and spotting any areas that require improvement. This study aims to evaluate the conformity with 2020 GOLD recommendations upon administering antibiotics and corticosteroids to hospitalized patients with COPD exacerbation.

Methods

Study design and period

An observational cross-sectional study was carried out in two Lebanese hospitals in Beirut. One hospital is a public hospital, and the other is a private hospital.

Data collection sheet and pilot study

A data collection sheet was developed to study the conformity of therapy according to the recommendations of GOLD 2020 guidelines. A preparatory step was taken to ensure the validity and reliability of the data collection sheet before the data collection began. Ten clinical pharmacists were requested to conduct the evaluation. The pilot study was done on 10 respondents to determine whether the survey questions were clear. Additional adjustments were made in response to participant comments. Data from the piloting were not included in the analysis.

Study population

Inclusion criteria

Patients admitted to one of the selected hospitals in Beirut, of different nationalities and genders, aged between 18 and 89 years, and diagnosed with an exacerbation of COPD.

Exclusion criteria

Patients who have a history of asthma, have radiologically diagnosed pneumonia, have pulmonary embolisms, or have pneumothoraxes were excluded. patients with significant comorbidity who have an anticipated survival time of fewer than 6 months or died during hospitalization. patients who have been hospitalized in intensive care units or who have had hospital stays of up to 2 days only. patients with apparent immunodeficiency (e.g., acquired immunodeficiency syndrome or immunosuppressive drugs) and those with other infectious diseases who need antibiotic treatment. patients who are pregnant or lactating.

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Data collection
Patients were identified using the computerized information system of the hospital's pharmacy. Medical records of patients admitted between January 2020 and June 2022 were selected for data extraction and analysis.

Index for conformity with GOLD guidelines upon administering corticosteroids
An index was developed using the five dichotomous variables that were deemed essential because there was no index from prior studies to calculate the conformity with GOLD Guidelines after administering corticosteroids. Every "yes" response earns a "1," but every "no" response earns a "0." According to Table 1, the final index is "5".

Factor analysis for the conformity index
Exploratory factor analysis using the five dichotomous items provided for the conformity index was done. There were no correlations found. Additionally, the anti-image correlations were greater than 0.5, and the Kaiser–Meyer–Olkin (KMO) measure of sampling adequacy was assured to be adequate (0.702 > 0.7). After administering corticosteroids, the mean index was 1.88 (SD = 1.05).

Statistical analysis
The data analysis was carried out using the SPSS version 24. The descriptive data were analyzed using mean/standard deviation for quantitative data and frequency/percentage for qualitative data. The index was computed for conformity to GOLD guidelines upon administrating corticosteroids. Bivariate analysis was done to see the factors affecting the index that was taken as the dependent variable as well as the duration of use of antibiotics. Multiple linear and logistic regressions were carried out after entering the variables.

Results
Sociodemographic characteristics
For this study, 260 patients in total who met the inclusion requirements were enrolled as subject cases. They were equally obtained from two hospitals. Their ages ranged from 47 to 89, with the most ranging between the ages of 61 and 70 (30.3%). Most of the patients (52.3%) were males, were current smokers (56.9%), and abstained from alcohol (68.07%). Baseline and medical socio-demographic characteristics are presented in Tables 2 and 3.

Prescribing patterns of corticosteroids
Overall, there was low conformity (21.1%) with oral prednisone treatment recommendations. Other systemic corticosteroids were used in place of prednisone, primarily methylprednisolone (58.1%) or dexamethasone (7.7%). Only 21.2% of patients received the 30–40 mg dose that was suggested. Concerning the duration of treatment, the GOLD recommended less than 7 days. 185 patients (71.2%) were prescribed oral prednisone or an alternative for an adequate duration. 25.3% of patients reported an increase in eosinophil count to > 2%, and 50.4% of patients received additional inhaled corticosteroids. The detailed results are shown in Table 4.

Descriptive analysis for conformity index
Based on Fig. 1, the conformity index with GOLD Guidelines showed that 43.5% of patients had an index of 1, whereas 24.22% had an index of 2, 23.2% had an index of

Table 1 Variables of the index measuring conformity with GOLD guidelines upon administering corticosteroids

Variable	Yes	No
Oral Prednisone administration	1	0
Dose of 40 mg or alternative	1	0
5 to 7 days duration of treatment	1	0
Addition of inhaled corticosteroid	1	0
Eosinophil count > 2%	1	0
Total index	5	

Table 2 Baseline socio-demographic characteristics of patients

Variable	*n* (%)
Age class	
≤ 50	34 (13.1%)
51–60	63 (24.2%)
61–70	78 (30.3%)
71–80	45 (17.3%)
81–90	40 (15.4%)
Gender	
Female	124 (47.7%)
Male	136 (52.3%)
Smoking status	
Current smoker	148 (56.9%)
Ex-smoker	35 (13,4%)
Nonsmoker	77 (29.6%)
Alcohol intake	
No	177 (68.07%)
Quit alcohol intake	14 (5.38%)
Yes	69 (26.5%)
Admitting season	
Fall	44 (16.9%)
Spring	64 (24.6%)
Summer	56 (21.5%)
Winter	96 (36.9%)

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Table 3 Medical sociodemographic characteristics of patients at admission

Variable	n (%)
Heart failure	24 (9.2%)
Hypertension	115 (44.23%)
Anxiety and depression	9 (3.4%)
Chronic heart disease	62 (23.8%)
Obesity	2 (0.7%)
Diabetes	73 (28.07%)
Chronic kidney disease	30 (11.5%)
A patient infected with SARS-COV 2	
Yes	79 (30.4%)
No	181 (69.6%)
Oxygen saturation	
<88%	117 (45%)
>92%	67 (25.7%)
88–92%	76 (29.2%)
White BLOOD CELLS (Cells/l)	
<4.5 x 10^9	25 (8.87%)
>11 x 10^9	93 (36.29%)
4.5 to 11$\times$10^9	142 (56.04%)
Neutrophils (neutrophils/microlite)	
<2500	19 (9.6%)
>7000	153 (58.8%)
2500–7000	88 (33.8%)
C-reactive protein value	
<20 mg/l	76 (29.2%)
>40 mg/l	123 (47.3%)
20–40 mg/l	61 (23.4%)
Temperature	
<37	127 (48.8%)
37–38	119 (45.7%)
38–39	8 (3%)
>39	6 (2.3%)

Table 4 The prescribing patterns of corticosteroids and antibiotics

Variable	N = 260 (%)
Systemic corticosteroid received:	
Oral prednisone	55 (21.1%)
Methylprednisolone	151 (58.1%)
Dexamethasone	20 (7.7%)
None	34 (13.1%)
Adequate administered dose of 40 mg prednisone or alternative	
Yes	55 (21.2%)
No	205 (78.8%)
Duration of treatment between 5 to 7 days	
Yes	185 (71.2%)
No	75 (28.8)
Add on the administration of inhaled corticosteroids	
Yes	131 (50.4%)
No	129 (49.6%)
Eosinophil count ≥ 2%	
Yes	66 (25.3%)
No	194 (74.6%)
Antibiotics administration	
Yes	206 (79.3%)
No	54 (20.7%)
Cardinal symptoms appeared at admission	
Increased shortness of breath	88 (33.8%)
Increased shortness of breath, increased sputum purulence	35 (13.46%)
Increased shortness of breath, increased sputum volume	25 (9.6%)
Increased shortness of breath, increased sputum purulence, increased sputum volume	112 (43.07%)
5–7-day duration of treatment	
Yes	158 (60.7%)
No	102 (39.3%)

3, 5% had an index of 4, and 1.5% had an index of 5. Seven patients had a zero index (2.7%).

Bivariate analysis for corticosteroid conformity index with GOLD

The independent variable gender (*P* value = 0.01) is significantly associated with the conformity index with GOLD Guidelines with females (2.064 ± 1.117) having a higher index. In addition, there is a strong association between both diagnosing bacterial cause of exacerbation (*P* value = 0.025) and oxygen saturation (*p* value = 0.003) with the index with patients being diagnosed with bacterial exacerbation (2.006 ± 1.12) and patients with oxygen saturation < 88% (2.237 ± 1.184) having higher indexes for conformity to corticosteroid treatment. The type of primary payer upon administration (*P* value = 0.02) is also correlated with the index with private insurance being the one with the highest index (2.421 ± 0.837). furthermore, this index was associated with alcohol intake (*P* value = 0.031) where those who drink alcohol had the highest association (2.169 ± 1.257).

The medication history showed that the previous use of either corticosteroid (2.279 ± 0.751) or both antibiotics and corticosteroids (2.055 ± 1.109) led to a greater index of conformity with this variable being significantly correlated with the index with *P* value = 0.01. finally, diastolic blood pressure is weakly associated with greater conformity (*P* value = 0.043).

Antibiotics prescribing patterns

The three cardinal symptoms (increased shortness of breath, increased sputum purulence, and increased sputum volume) appeared in the highest percentage of patients upon administration, accounting for 43.07

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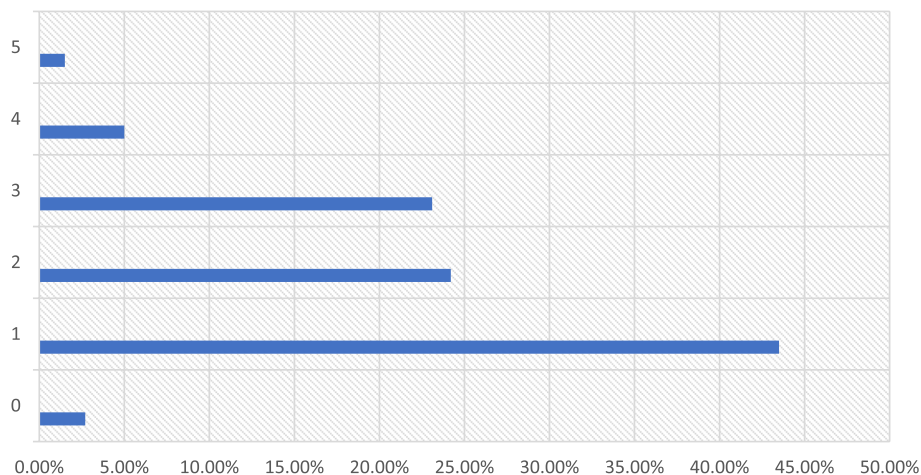
Conformity Index

Fig. 1 Descriptive analysis for conformity index with corticosteroids therapy in GOLD

of all cardinal symptoms. Only 33.8% of patients had increased shortness of breath, 13.46% had increased shortness of breath and increased sputum purulence, and 9.6% had increased shortness of breath and increased sputum volume. 74.5% of patients used antibiotics for the appropriate duration of time following GOLD recommendations (Table 4) The bivariate analysis for the duration of use of antibiotics showed a significant correlation with CRP value (p value = 0.007), cardinal symptoms (p value = 0.003), and type of hospital (p value = 0.00) (Table 5). The multivariate analysis reassured the association with the CRP value (Table 6).

Discussion

Practitioners' knowledge of the critical elements of COPD exacerbation management is seriously lacking. Systemic corticosteroids should be the initial option in treating acute exacerbations to speed up recovery and lower treatment failure rates [9]. In this analysis, the percentage of patients receiving systemic corticosteroids was high (86.7%) which is similar to a study done in Australia where 89% of patients received systemic corticosteroids [10]. The proportion of patients receiving glucocorticoids parenterally was three times higher than that of individuals receiving the medication orally (66.81% for IV versus 24.32% for oral). Results are comparable to those from China (48.65% for IV versus 15.31 for oral) [11]. This might be because many medical professionals believe that administering corticosteroids intravenously results in a quicker onset of action and better outcomes [11]. However, recent research suggests that oral and IV glucocorticoids have similar efficacy [11]. A variety of glucocorticoids, such as Methylprednisolone and Dexamethasone, do not have a specific dose guideline [9]. This

Table 5 Bivariate analysis for the duration of use of antibiotics

Variable	Adequate duration of use		P value
	No	**Yes**	
Cardinal symptoms			**0.003**
Increased shortness of breath	21(39.6%)	32 (60.4%)	
Increased shortness of breath, increased sputum purulence	3 (8.8%)	31 (91.2%)	
Increased shortness of breath, increased sputum volume	8 (38.1%)	13 (61.9%)	
Increased shortness of breath, increased sputum purulence, increased sputum volume	21 (20.6%)	81 (79.4%)	
C-reactive protein			**0.007**
< 20 mg/l	17 (41.5%)	24 (58.5%)	
20–40 mg/l	5 (11.9%)	37 (88.1%)	
> 40 mg/l	24 (23.8%)	77 (76.2%)	

Table 6 Multivariate regression for the duration of use of antibiotics and conformity index

Variables with duration of use of antibiotics	Standardized beta	P value	Exp (B)	95% CI
C-reactive protein value	− 0.747	**.0048**	2,110	[0.975, 4.568]
Variables with conformity index				
Gender	0.414	**.049**	0.178	[0.001, 0.827]
Age	− 0.226	**.006**	− 0.247	[− 0.386, − 0.067]
Alcohol	− 0.472	**.018**	− 0.227	[− 0.861, − 0.084]
Psychiatric drugs	− 0.214	**.049**	− 0.172	[− 0.428, 0.000]

study's findings, which were comparable to those of studies conducted in China and Iran where doses diverged from the prescribed standards [11, 12], showed that only 24.70% of patients took the recommended amount of prednisone or an alternative. This exposes patients to the adverse events of unnecessary high doses of steroids and higher hospital costs without appearing to relate to any evident clinical benefit. This could be explained by a lack of knowledge in pharmacokinetics. Additionally, after the actual or apparent failure of low-dose oral medication initiated in the ambulatory setting, some patients may first undergo high-dose intravenous therapy. Also, this study demonstrated conformity with the recommended duration of corticosteroid use, with 81%. This is comparable to a study from China, where the average duration appeared to be within the recommended range [11] but different from a study in Iran, where there was no conformity with the recommended duration of corticosteroid use. A dose of glucocorticoids given over a long period can have a potent anti-inflammatory impact, for this reason, some practitioners could choose longer periods of use. Other factors, such as a lack of familiarity with some GOLD guidelines or recent updates, or inadequate training may be to blame for this deviation. In cases with AECOPD where the eosinophil count is equal to or higher than 2%, studies are evaluating the necessity of adding inhaled corticosteroids (ICS) [13]. which was not the case in either our study or in a study done in Colorado, where nearly half of the inpatients received ICS despite the eosinophil count [14].

Reasons for such administration could include the pulmonologists' preferences, the accessibility of medications on the market, the long marketing history and information provided by pharmaceutical companies, the automatic renewal of a prior prescription without an updated assessment or ICS withdrawal after they were introduced, or the belief that ICS is the most beneficial in real life compared to clinical trials. Based on the conformity index, only 4 patients out of 260, or 1.5% of cases, had complete conformity to the GOLD Criteria after receiving corticosteroids. This is similar to a study conducted in the USA, where only 3 patients out of 94 (3.2%) had complete conformity to the guidelines [15]. Some of the underlying causes of inadequate conformity are unfamiliarity with a specific recommendation, disagreement with a specific recommendation, low self-efficacy for carrying out a specific recommendation, low perceived benefit of a specific recommendation, and time constraints on the ability to carry out a specific recommendation. Due to the lack of previous studies conducted in Lebanon, it is impossible to determine the exact extent to which the economic crisis and financial collapse, as well as the short-cutting of medication and the weakened national pharmaceutical industries, may also be responsible for the low conformity levels while administering medication to AECOPD patients in Lebanese hospitals, but it plays a critical role. This study showed a negative correlation between using glucocorticoids and getting older, drinking alcohol, and taking psychiatric medications. Given their complex comorbidity and disability, elderly patients with AECOPD should, nevertheless, be treated with caution while using glucocorticoids. However, more research should be done on psychiatric medications because Lebanese hospitals do not offer psychiatrists to follow up with regular patients, and statistics are only gathered based on nurses' daily notes and medications administered during hospitalization. When it comes to the level of association with age, our findings are comparable to a previous Chinese study; however, gender in the study showed no correlation.

Antibiotic misuse results in resource waste, bacterial resistance, and a negative effect on the patient's microbiome. However, antibiotics are frequently utilized for AECOPD. Of most patients admitted (80% (206/260) received antibiotic treatment throughout their stay, but 31.9% did so without an indication (i.e., did not exhibit the three cardinal symptoms (43.07%): increase in dyspnea, sputum volume, and sputum purulence; did not exhibit the two cardinal symptoms if increased sputum purulence is one of the two symptoms (13.46%).

This is comparable to numerous studies from Australia, Canada, and Iran, where antibiotics are prescribed more often than necessary despite the listed cardinal symptoms

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[7, 10, 12]. Doctors may prescribe antibiotics based on prior exacerbations that were of bacterial origin or to satisfy the beliefs and expectations of patients even though they may not be clinically indicated. According to the GOLD recommendations, an antibiotic course should last 5 to 7 days. According to our study, more patients (74.5%) than those in Australia (59%) [10] received antibiotics for the whole recommended duration. This difference may be related to longer hospitalization days and higher costs. Sputum purulence, as one of the two cardinal symptoms observed, was associated with the highest adequate duration (91.2%), while the presence of all three cardinal symptoms showed 79.4% of cases with adequate duration of use. In contrast, the correlations with the other cardinal symptoms are less strong. This study is comparable to one conducted in China, where positive sputum etiology was associated with the most adequate treatment duration [2]. The weak correlation between sputum volume and antibiotic prescription may suggest that clinicians are less certain about an increase in sputum volume as a sign of bacterial infection. This is consistent with the GOLD recommendation that, among the criteria, sputum purulence is the best predictor of bacterial infection and that, in the absence of purulence, sputum volume, and increasing dyspnea should not be highlighted [9]. CRP levels and antibiotic use duration were correlated in bivariate and multivariate analyses. The bivariate analysis revealed that patients with CRP values between 20 and 40 mg/l (88.1%) and patients with CRP values over 40 mg/l (76.2%) had the highest rates. This is in line with a recent study that found a link between overall CRP levels and the duration of antibiotic use [16]. In cases of AECOPD, this correlation might be explained by having guidance that said antibiotics are likely to be beneficial and should typically be prescribed (save for patients with a CRP > 40 mg/l), but are unlikely to be beneficial for patients with a CRP 20 mg/l, but may be beneficial for patients with a CRP 20–40 mg/l [17].

Strengths and limitations

The current study is the first to be undertaken in Lebanon to evaluate the conformity with GOLD 2020 guidelines while administering corticosteroids and antibiotics in hospitalized patients with AECOPD. Random patient selection helped to lessen admission selection bias, and multivariate analysis helped to lessen confounding bias. Additionally, because this study is cross-sectional, recall and follow-up biases are not present. Although the procedures employed to obtain the data were sufficiently transparent to minimize the possibility of nondifferential measurement bias, the used data collection sheet and index had not undergone validation from previous studies. The bias in sampling selection is exacerbated by the removal of patients who passed away while being treated in a hospital and by non-randomization.

Although the sample size calculation was clearly and carefully explained, it was not thought to be sufficient to attain external validity. Additionally, because just two tertiary care hospitals were used for data collection, it is not representative of the clinical practices. As a result, the sample size was insufficient, and it might not be representative. Finally, because the researcher was not blinded, differential measurement bias may be found.

Conclusion

This study investigated primarily the level of conformity with GOLD 2020 guidelines and the patterns of antibiotic and corticosteroid prescriptions for AECOPD patients in two Lebanese hospitals. Despite its many limitations, it demonstrated a deviation from the recommendations that need to be corrected, provided insight into current clinical practices, and highlighted the increasing concern over the uncontrollable rate of antibiotic use and insufficient corticosteroid dosing, which is consistent with existing studies. Age, gender, alcohol consumption, and use of psychiatric medications are among the characteristics that have a significant impact on the conformity index of corticosteroid administration. It also stated a connection between the CRP level, cardinal symptoms, and type of hospital with the duration of antibiotic use.

Abbreviations

AECOPD	Acute exacerbation of chronic obstructive pulmonary disease
CI	Confidence Interval
COPD	Chronic obstructive pulmonary disease
COVID-19	Coronavirus disease-19
CRP	C-reactive protein
GOLD	Global Initiative for Chronic Obstructive Lung Disease
ICS	Inhaled corticosteroid
KMO	Kaiser-Meyer-Olkin
MENA	Middle East and North Africa
SARS-COV-2	Severe Acute Respiratory Syndrome Coronavirus-2
SD	Standard deviation
SPSS	Statistical Program for Social Sciences

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The approval for this study was waived to ensure that this study respects patient's confidentiality and anonymity. Reference 2022–0804. Date: 16-August-2022.

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