Original Article

The Role of C – Reactive Proteins as Indicator of Antibiotic Therapy among Patients with Acute Exacerbation of Chronic Obstructed Pulmonary Disease

Muhammad Mujtaba Ali[1], Rashid Ali[2] and Hafiz Muhammad Taha Waqas[3]

ABSTRACT

Objective: This study was conducted to define role of CRP as indicator of antibiotic therapy among patients with COPD.

Study Design: Descriptive case series Study

Place and Duration of Study: This study was conducted at the Department of Pulmonology, Shalamar Medical and Dental College Lahore from June, 2019 to January, 2020.

Materials and Methods: The study included 100 cases fulfilling inclusion criteria. Serum CRP levels were measured in all patients and were categorized as: low CRP (<40 mg/L) and high CRP (>40 mg/L). Patients in both groups received antibiotic therapy (Levofloxacin 500mg twice daily per oral) for 7 days. Patients were assessed for clinical success (absence of dyspnea and sputum).

Results: High CRP level was observed in 65(65%) patients and low in 35(35%) patients. Clinical success was achieved among 14(40%) patients in low CRP group and 56(86.2%) patients with high CRP group ($p<0.05$).

Conclusion: Majority of patients had high CRP level (>40mg/L). So, CRP level can be used as an indicator for commencement of antibiotic therapy among patients with acute exacerbation of COPD.

Key Words: Chronic obstructive pulmonary disease; C–reactive Proteins; antibiotic therapy

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the 4th principalreason of mortality globally.[1,2] It is a escapable and curable ailment, for which physicians have to inaugurate a impulsive and precise verdict and management, comprising teaching for prophylaxis.[3] COPD is a chief source of morbidity and mortality worldwide.[4,5] The exact incidence of COPD all over the world is basically unidentified, however approximations have wide-ranging from 7-19%.[6]

[1.] Department of Medicine, Tehsil Head Quarter Hospital, Shakargarh.
[2.] Department of Pulmonology, Akhtar Saeed Medical and Dental College, Lahore.
[3.] Department of Pulmonology, Shalamar Medical and Dental College, Lahore.

Correspondence: Dr. Hafiz Muhammad Taha Waqas, Senior Registrar of Pulmonology, Shalamar Medical and Dental College, Lahore.
Contact No: 03327392024
Email: taha_waqas06@hotmail.com

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It is generally a progressive illness, categorized by exacerbation of symptoms.[7] Exacerbations signify a substantial financial problem, however, additional significantly, it can lead to augmented lung function deterioration, in addition to amplified mortality.[8] In the attention of refining the analysis of COPD, numerous kinds of biomarker have been measured that are connected to respiratory pathophysiology.[2,8]An acute phase protein i.e. CRP is hepatic in origin and formed in response to IL-6 stimulation.[9] CRP is elevated in most disorders related with inflammation, infection or tissue destruction, for which it is a sensitive marker.[10,11] CRP in blood is stated to be higher during exacerbation compared with the baseline state.[12,13]

So far, there are no clear guidelines regarding the use of antibiotics in acute exacerbation of COPD. The disease burden is still very high in our population and a large number of patients with exacerbations are attended in primary care, and definitive evidence to support the use of antibiotics in such patients is lacking. Many studies in the past had shown relationship of CRP with acute exacerbation of COPD, but its clinical utility as indicator of antibiotic therapy is still debatable. Objective of the study was to determine the frequency of patients showing CRP > 40 mg/L among patients presenting with exacerbation of COPD and to compare the clinical Success Rate of Antibiotic therapy among

COPD patients with low CRP (<40) versus high CRP (>40).

MATERIALS AND METHODS

This Descriptive case series Study was conducted in in Department of Pulmonology, Shalamar Medical and Dental College Lahore from June, 2019 to January, 2020. The study included 100 patients of both gender,between20 – 80 years of age, with acute exacerbation of COPD. We excluded all the patients with antibiotic use in the previous 2 weeks, Bronchial asthma, pulmonary neoplasm, History of surgery on respiratory tract i.e. tracheotomy, Patients on steroid use and Patients with history of hypersensitivity to b-lactams, clavulanate or lactose.

Demographic features, history and physical examination were noted. All the patients had their serum CRP level done. The patients were categorized to have low CRP (i.e. < 40 mg/L) and high CRP (i.e. >40 mg/L). The patients in both groups had received antibiotic therapy (Levolfloxacin 500 mg per oral OD) for a period of 7 days. After 7 days of treatment, the patients were assessed for the absence of dyspnea and absence of sputum and were labeled as clinical success. All the collected data was entered into SPSS version 20 and analyzed. Study variables were analysed by simple descriptive statistics. Mean and standard deviation were calculated for numerical variables (age), CRP level and duration of COPD. Frequency and percentage were calculated for gender, number of patients with low & high CRP, presence of clinical success (yes or no) was presented as frequency distribution and percentage. Both the groups were compared each other for the clinical success. Effect modifiers like smoking (pack year, duration of COPD were controlled by stratification of data with clinical success.

RESULTS

Table No.I: Distribution of patients by CRP level and Comparison of patients by clinical success among patients with low (<40mg/L) and high (>40mg/L) CRP level

CRP level	No. of patients (%)	Clinical Success N(%)	P-value*
<40 mg/L	35 (35%)	14 (40%)	0.001 **
> 40 mg/L	65 (65%)	56 (86.2%)	
Total	100 (100%)	70 (70%)	
Mean ±SD	46.51±7.79		

* Chi-square test

** Statistically significant

There were total one hundred patients included in this study. The mean age of the patients was 65.04 + 14.75 years [range 46 – 80]. There were 85 (85.0%) male patients and 15 (15.0%) female patients (M:F; 5.2:1).The mean distribution of patients by duration of smoking (pack-year) was 56.22+8.99. The mean distribution of patients by duration of COPD was 11.89+3.78 years. Distribution of patients by CRP level and Comparison of patients by clinical success among patients with low and high CRP levels, Stratification of data (clinical success) with duration of smoking and COPD were shown in table 1, 2& 3, respectively.

Table No.2: Stratification of data (clinical success) with effect modifier (duration of smoking)

Duration of Smoking (Pack years smoking)	Clinical success n (%)
20 – 30 (n=12)	8 (66.7%)
31 – 40 (n=18)	11 (61.1%)
41 – 50 (n=45)	35 (77.8%)
51 – 60 (n=25)	16 (64%)
p-value*	0.517**

* Chi-square test

** Statistically not significant

Table No.3: Stratification of data (clinical success) with effect modifier (duration of COPD)

Duration of COPD (years)	Clinical success n (%)
1 – 5 (n=22)	18 (81.8%)
6 – 10 (n=67)	47 (70.1%)
11 – 15 (n=11)	5 (45.5%)
p-value*	0.732**

* Chi-square test

** Statistically not significant

DISCUSSION

The most common decision a pulmonologist has to make when treating a patient with an acute exacerbation in COPD is whether to prescribe antibiotic therapy. This prospective study investigated the role of CRP as an indicator of antibiotic therapy and revealed an important observation that commencement of antibiotic therapy with elevated CRP (> 40mg/L) may be more beneficial (more clinical success).

The mean age of the patients in our study was 65.04+14.75 years with an age range of (46 – 80 years). In a study by Arslan RS, et al,[14] the mean age of patients was 63.70±7.81 years. In another study by Iqbal S, et al, [15] the mean age of patients was 59.3 years ±10.76SD while in literature; the mean age of patients has been reported as 70 years ± 8.0SD years and 62.1 years ± 9.8SD. In the study conducted in China,[16] the mean age reported is 73.4 years.

There was a male dominancy in our study (85% were male and 15% were female). This male dominancy has

also been observed in other studies. In study by Iqbal S, et al[15] there were 67.10% male with a male to female ration of 2.03:1. In an Indian study, there were 80.7% male.[17] In another study, there were 87.9% male patients with acute exacerbation of COPD.[18] The reason for male dominancy in our study is related to prevalence of smoking in our population. Smoking is more common in males with resulting in higher incidence of COPD. In our study, we included all the patients who were smokers. The female patients in our study were also smokers. This reflects that smoking is not very uncommon among female in our population.

Smoking history was present in all of the patients included in the study. However, there has been found variability in frequency of smoking among different authors. Ahmad H, et al[19] found that 37.5% patients in their study were smokers. Alam SE [20]et al, reported that prevalence of smoking was 21.6%.COPD varies with age and smoking status, occurring rarely in individuals more than 40 years old, and less frequently in non-smokers. In our study, the majority of smokers (45%) had history of 41-50 years pack smoking. The mean duration (pack years) was 56.22+8.99 pack-years. Arslan RS, [14] documented a mean smoking history (Pack-years) 59.89±6.60 years among their study population. Nearly all physicians acknowledge that the first step in patient management is the cessation of smoking.[21] The mean duration of COPD was 11.89+3.78 years in our study while in study by Ahmed H, [22]et al the mean duration of 8.81(± 5.72 SD) years.

We observed that a CRP level of < 40 mg/L was observed in 35% of the patients, while majority of the patients had high level of CRP. In our study, the cut off value was 40 mg/L, which was similar to that of study by Llor, et al. [11] However, Peng C, et al [7] also used a cut of value as low as 15.6mg/L among patients with a sensitivity of 81.5% and a specificity of 77.8%.

In our study, the clinical response was achieved in 86.2% patients with CRP >40mg/L and 40% among patients with CRP <40mg/L. The results were statistically significant ($p<0.05$). A study by Llor[11]et al have shown that the clinical success rate among patients with a CRP <40 mg/L was 87.6%, while only 34.5% of patients with a CRP >40 mg/L experienced clinical success ($p <0.05$). The clinical success rate (87.6%) achieved in with an antibiotic is quite comparable with that of observed in previous placebo-controlled trials, particularly 68% in the study by Anthonisen and colleagues,[23] 80% in the study by Daniels and colleagues,90 and 86.4% in the study by Allegra and colleagues,[24] all of which included patients with severe COPD.

In our study, we selected levofloxacin as an antibiotics. Amoxicillin, trimethoprim/sulfamethoxazole, tetracy-line, and erythromycin were not chosen because failure rates with their use may almost double in outpatients with COPD exacerbations compared with amoxicillin/ clavulanate, azithromycin, or ciprofloxacin.[24]

Our study had certain limitations. This was carried out in a single centre and in a limited population size.

CONCLUSION

The results of the study demonstrate use of antibiotic therapy among patients with elevated CRP level (>40mg/L) showed better clinical response as compared to that of low CRP level. So, elevated CRP level (>40mg/L) may be used as an indicator of antibiotic therapy among patients with acute exacerbation of COPD. However, there is still need of double blind randomized controlled trial to document its role.

Author's Contribution:

Concept & Design of Study:	Muhammad Mujtaba Ali
Drafting:	Rashid Ali, Hafiz Muhammad Taha Waqas
Data Analysis:	Hafiz Muhammad Taha Waqas
Revisiting Critically:	Muhammad Mujtaba Ali, Rashid Ali
Final Approval of version:	Muhammad Mujtaba Ali

Conflict of Interest: The study has no conflict of interest to declare by any author.

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