C-Reactive Protein in Community Acquired Pneumonia

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Abstract

C-reactive protein (CRP) is an acute phase protein synthesized by hepatocytes. In response to infection or tissue inflammation, CRP production is rapidly stimulated by cytokines, particularly interleukin (IL)-6, IL-1 and tumor necrosis factor. The aim of the present study is to evaluate the prognostic value of CRP levels at admission as an indicator of the severity or complication of CAP. Fifty patients with primary diagnosis of community-acquired pneumonia during March 2013 to February 2014. A-25 patients were males and 25 females. The CRP measured by CRP-latex Slide agglutination method. Also, patient underwent chest-x ray and patients were categorized into patients with CRP ≥ 100 mg/L and CRP < 100 mg/L22, and the complications (pleural effusion and lung abscess) were correlated to possible risk factors (HT, DM) and smoking. There is a significant increase in complication of CAP in patients with high CRP level (CRP ≥ 100 mg/L), so that CRP is highly sensitive, specific and accurate test to predict complication in CAP. The CRP affected by gender (female), age and diabetes mellitus in patient with CAP. There are no significant correlations between CRP level and smoking and hypertension in patient with CAP.

Keywords: C-reactive protein (CRP); CAP; Diabetes Mellitus

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Introduction

C-reactive protein (CRP) is an acute phase protein synthesized by hepatocytes. In response to infection or tissue inflammation, CRP production is rapidly stimulated by cytokines, particularly interleukin (IL)-6, IL-1 and tumor necrosis factor, although its exact function in vivo is not known, it probably has a role in opsonisation of infectious agents and damaged cells [1, 2]. Pneumonia is defined as infection of the lower respiratory tract parenchyma by agents such as bacteria, viruses, fungi, or even parasites, microbial agents can be introduced to the lungs through several routes, the most common route is by aspiration of oropharyngeal secretions [3]. Legionella species, mycobacteria, endemic fungi, Mycoplasma pneumonia, Chlamydia pneumonia and most viral infections are examples of pneumonia caused by direct inhalation of organisms, resulting in geographic and seasonal clustering of cases [4]. Much less commonly pneumonia can arise from hematogenous or embolic spread of infection from infected heart valves or venous clot. The small vessels of the pulmonary circulation act as filters for venous blood carrying small clusters of bacteria from the source [3,4]. Diagnosis and therapy are dependent on clinical, imaging, and laboratory data, patients usually exhibit respiratory symptoms, including productive cough, dyspnea, chest pain, and occasionally hemoptysis [5]. The chest radiograph plays an important role in the diagnosis, aparenchymal opacity is observed in the patient with pneumonia however, noninfectious disorders that mimic pneumonia exist, and no radiographic finding is entirely specific for infection [5]. Pneumonia is most commonly classified by where or how it was acquired: community-acquired, aspir-ation, healthcare-associated, hospital acquired, and ventilator-associated pneumonia, it may also be classified by the area of lung affected: lobar pneumonia, bronchial pneumonia and acute interstitial pneumonia; or by the causative organism [6]. Community-acquired pneumonia (CAP) was defined as the presence of a new infiltrate on the chest radiograph along with appropriate clinical history and physical signs of lower respiratory tract infection in a patient not hospitalized within the previous month and in whom no alternative diagnosis emerged during

follow-up [7]. Death rates from CAP increase with the presence of co morbidity and increased age; the condition affects persons of any race or sex equally [8]. The decrease in death rates from pneumonia and influenza are largely attributed to vaccines for vulnerable populations (e.g., older and immune compromised persons) [8, 9]. Pneumonia can be classified as typical or atypical, although the clinical presentations are often similar, several symptoms commonly present in patients with pneumonia [9]. Common clinical symptoms of CAP include cough, fever, chills, fatigue, dyspnea, rigors, and pleuritic chest pain, depending on the pathogen, a patient's cough may be persistent and dry, or it may produce sputum, other presentations may include headache and myalgia, certain etiologies, such as legionella, also may produce gastrointestinal symptoms like nausea vomiting and upper abdominal discomfort [10]. Chest radiography (postero anterior and lateral views) has been shown to be a critical component in diagnosing pneumonia.11 According to the latest American Thoracic Society (ATS)guidelines for the diagnosis and treatment of adults with CAP, "all patients with suspected CAP should have a chest radiograph to establish the diagnosis and identify complications (pleural effusion, multilobar disease) [11]. Sputum Gram stain, two sets of blood cultures, and urine antigens [12]. Furthermore, sputum samples are adequate in only 52.3% of patients with CAP, and only 44 % of those samples contain pathogens [13]. Nonetheless, initial therapy often is guided by the assumption that the presenting disease is caused by a common bacterial pathogen, blood cultures, however, are not necessary for outpatient diagnosis [11]. Legionella antigens were found in the urine of 48 % of patients with suspected Legionella pneumophila [14]. Most patients with CAP are treated empirically based on the most common pathogen(s)associated with the condition [15, 16]. Consensus guidelines from ATS, Infectious Diseases Society of America and Canadian Guidelines for the Initial Management of Community-Acquired Pneumonia recommend initial empiric therapy with macrolides, fluoroquinolones, ordoxycycline [17]. Although data are limited on duration of CAP therapy, current research recommends 7 to 10 days of therapy for

S. pneumonia and 10 to 14 days of therapy for Mycoplasma pneumonia and Chlamydia pneumonia [18, 19]. From complication of CAP is para pneumonic effusion which is a neutrophilic exudative effusion adjacent to a lung with pneumonia [19, 20, 21]. The aim of the present study is to evaluate the prognostic value of CRP levels at admission as an indicator of the severity or complication of CAP.

Patients and Methods

Fifty patients with primary diagnosis of community-acquired pneumonia who had admitted to Al-Sader medical city were enrolled in this study during the period from March 2013 to February 2014.These patients were admitted to medical ward,(25) patients were males and (25) patients were females .Their ages ranging from (30 – 70) years the mean was(57.52) yr. Detailed history and physical examination were obtained and blood samples were drawn(two milliliter) from all patients and CRP to each patient was measured by CRP-latex Slide agglutination method using CRP-Latex by SPINREACT. The normal value was up to 6 mg/L. Also patient underwent chest-x ray by using (FLEXAVISION-SHMADZU machine) The patients were categorized for purpose of statistical analysis into patients with CRP ≥ 100 mg/L and CRP < 100 mg/L[22], and the complications (pleural effusion and lung abscess) were correlated to possible risk factors (HT, DM) and smoking

Exclusion Criteria:

Patients with these conditions are excluded:

- Hospital-acquired pneumonia
- chronic obstructive pulmonary disease
- Active thoracic or extra thoracic malignancy.
- Immuno suppression (iatrogenic or acquired).
- Chronic liver disease or cirrhosis.
- Pulmonary oedema
- Pulmonary infarction
- Vasculitis

Statistical analysis

Statistical analysis was done by using chi square test, and P value of less than 0.05 was considered statistically significant, using SPSS-20 (Statistical Packages for Social Sciences –version 20). Sensitivity calculated as the following (true positive/true positive + false negative), specificity calculated as the following (true negative/ true negative + false

positive), accuracy calculated as (true positive + true negative /total)

Result

C-reactive protein in relation to complication of CAP

By follow up of 50 patients with CAP included in this study, 6(12%) patients developed complication (one patient developed lung abscess and five patients developed pleural effusion), and 44(88%) patients without complication, 10(20%) patients had CRP ≥ 100 mg/l and 40(80%) had CRP < 100 mg/l. Among the patients who developed complications; 5(83.3%) patients had CRP ≥ 100 mg/l(16.7%) & 1 patient was CRP < 100 mg/l & the P value statistically significant (<0.001). CRP test had high sensitivity, specificity and accuracy.

Table 1:

Validity of CRP in prediction of complication in CAP

CRP	Complication	No complication	Total
≥ 100 mg/l	5(50%)	5(50%)	10
< 100 mg/l	1(2.5%)	39(97.5%)	40

P value < 0.001

Sensitivity = 83.3%

Specificity = 88.6%

Accuracy =88%

C-reactive protein in relation to sex

Among 50 patients included in this study, 25(50%) patients were male, and 25(50%) patients were female so, among 25 males,2 had CRP level ≥100 mg/l, among 25 female 8 had CRP level ≥ 100 mg/land the P value statistically significant (0.034) as shown in table 2.

Table 2:

Relation between CRP and sex

sex	CRP ≥ 100 mg/l	CRP < 100 mg/l	Total
M	2 (8%)	23 (92.5%)	25
F	8 (32%)	17 (68%)	25

P value = (0.034)

C-reactive protein in relation to age

The age of 50 patients included in this study categorized as 13 patients ≥ 65 years, 37 patients < 65 years with their mean age (57.52) (SD ±10.38). The P value was statistically significant (0.006) as shown in table 3.

Table 3:

Relation between age & CRP

Age	CRP ≥ 100 mg/l	CRP < 100 mg/l	Total
≥65	6(46%)	7(54%)	13
<65	4(11%)	33(89%)	37

P value = 0.006

C-reactive protein in relation to CAP with diabetes mellitus:

Among 50 patients with CAP,24 (48%) patients have diabetes mellitus, from them only 8 patients had CRP level ≥ 100 mg/l and 16 patients had CRP level <100 mg/land the P value statistically significant (0.024) as shown in table 4

Table 4:

Relation between CRP and DM

	CRP ≥ 100 mg/l	CRP < 100 mg/l	Total
Diabetic	8 (30%)	16 (70%)	24
Non-Diabetic	2(8%)	24 (92%)	26

P value = (0.024)

C-reactive protein in relation to CAP with hypertension

Among 50 patients with CAP,29 patients had hypertension (58%), from them only 5 patients had CRP level ≥ 100 mg/l and 24 patients had CRP level <100 mg/l and the P value statistically non-significant (0.567) as shown in table5

Table5:

Relation between CRP and HT

	CRP ≥ 100 mg/l	CRP < 100 mg/l	Total
Hypertensive	5 (17%)	24 (83%)	29
Non-Hypertensive	5 (24%)	16 (76%)	21

P value = (0.567)

C-reactive protein in relation to CAP with smoking

Fifteen (30%) patients were smoker, from them 3 patients had CRP level ≥ 100 mg/l and P value was statistically non-significant (1.0) as shown in table 6.

Table 6: Relation between CRP and smoking

	CRP ≥ 100 mg/l	CRP < 100 mg/l	Total
Smoking	3 (20%)	12 (80%)	15
No smoking	7 (20%)	28 (80%)	35

P value = (1.0)

Discussion

Many studies showed different uses of CRP in clinical practice. Firstly; as a diagnostic tool to distinguish between noninfectious and infectious conditions and within the latter between viral and bacterial or superficial and deep infections. Secondly, as a prognostic and follow-up test, as serial measurements may be useful to evaluate the response to antibiotic treatment and to detect complications in patients with infections [1, 3].

In this study it was found that CRP≥ 100 mg/L increase risk of severity and complication of CAP. Chalmers et al., [22] found that CRP values <100 mg/ L in CAP patients on the day of admission and four days later were independently associated with a low 30-day mortality rate, low probability for mechanical ventilation and/or inotropic support and low rates of complicated pneumonia. Jordi Almirallet al., [23] found that high CRP values are suggestive of severity, which may be of value in deciding about the inpatient care.

The current study showed that CRP level increase in female with significant p value this agrees with Amit Khera et al., [24] who found that CRP levels increased to a greater degree with variation in fat quantity and are more affected by fat distribution in women compared with men. Ford ES, et al.25 and Lakoski SG et al., [26] show that CRP level more in woman than in men.

The present study found significant correlation between CRP and age group, where CRP levels increased with age group ≥ 65 years, this agree with Earl S. Ford et al., [27] that show the median CRP concentration increased with age. This study showed that CRP levels increase in patients of CAP with diabetes mellitus with significant p value. The

current study shown no significant correlation between CRP and CAP with hypertension. Regarding smoking, the present study found no significant correlation with CRP.

Conclusion

- There is a significant increase in complication of CAP in patients with high CRP level (CRP ≥ 100 mg/L), so that CRP is highly sensitive, specific and accurate test to predict complication in CAP.
- CRP affected by gender (female), age and diabetes mellitus in patient with CAP
- No significant correlations between CRP level and smoking and hypertension in patient with CAP.

Recommendation

As a cheap and readily available, CRP test is better to be used in patients with CAP to detect early complications.

Conflict of interest

None. No support from any organization for the submitted work. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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