ISSN- O: 2458 - 868X, ISSN –P: 2458 - 8687

International Journal of Medical Science and Innovative Research (IJMSIR)

IJMSIR : A Medical Publication Hub

Available Online at: www.ijmsir.com

Volume – 3, Issue –1, January - 2018, Page No. : 289 - 294

Role of CRP as an independent predictor of severity in community acquired pneumonia.

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Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Introduction

CAP is commonly defined as an acute infection of the pulmonary parenchyma that is associated with at least some symptoms of acute infection, accompanied by the presence of an acute infiltrate on a chest radiograph or auscultatory findings consistent with pneumonia (such as altered breath sounds and/or localised rales), in a patient not hospitalised or residing in a long-term-care facility for ≥14 days before onset of symptoms. Symptoms of acute lower respiratory infection may include several (in most studies, at least 2) of the following: fever or hypothermia, rigors, sweats, new cough with or without sputum production or change in colour of respiratory secretions in a patient with chronic cough, chest discomfort, or the onset of dyspnea. Most patients also have nonspecific symptoms, such as fatigue, myalgias, abdominal pain, anorexia, and headache(1)Pneumonia is the leading cause of death in world and sixth most common cause of death in the United States. From 1979 through 1994, the overall rates of death due to pneumonia and influenza increased by 59% (on the basis of ICD-9 codes on death certificates) in the United States [2]. Much of this increase is due to a greater proportion of persons aged ≥65 years; however, age-adjusted rates also increased by 22%, which suggests that other factors may have contributed to a changing epidemiology of pneumonia, including a greater proportion of the population with underlying medical conditions at increased risk of respiratory infection. Annually, 2–3 million cases of CAP result in ~10 million physician visits, 500,000 hospitalisations, and 45,000 deaths in the United States [3, 4]. The incidence of CAP that requires hospitalisation is estimated to be 258 persons per 100,000 population and 962 per 100,000 persons aged ≥65 years [4]. Although mortality has ranged from 2% to 30% among hospitalised patients in a variety of studies, the average is ~14% [5]. Mortality is estimated to be <1% for patients not hospitalised [5,6]. The incidence of CAP is heavily weighted toward the winter months.community acquired pneumonia is a common disorder with an incidence of 20 % to 30 % in developing countries compared to 3% to 4% in developed countries[7].C-reactive protein (CRP) is an acute phase protein produced primarily in the liver and is stimulated by cytokine release, primarily interleukin-6. Small studies suggest that an elevated CRP is relatively nonspecific and is not directly related to severity[8,9]on the basis of this evidence, the 2004 update of the British Thoracic Society (BTS) guidelines does not recommend admission CRP as a marker of severity. However, the guidelines recommend measurement of CRP as a useful marker of treatment

failure in community- acquired pneumonia[10] A CRP that fails to fall by 50% or more within 4 days of admission is indicative of adverse outcomes such as empyema[11]It is well recognised that elevated concentrations of pro inflammatory cytokines correlate with severity and outcome of sepsis[12,13] and it has been shown that elevated CRP is an independent predictor of mortality in acutely ill patients[14]This has not been specifically examined in community- acquired pneumonia. No previous studies have examined whether a low CRP can exclude severe community-acquired pneumonia.

Aims and objectives

To study role of CRP as an independent predictor of severity in community acquired pneumonia.

Materials and methods

This prospective study was conducted in department of pulmonary and internal medicine skims soura. All patients who attended medical out patient department (opd) and the patients who were admitted with provisional diagnosis of community acquired pneumonia were taken in the study and the total of 60 patients were studied All the eligible patients with diagnosis of CAP who did no required hospitalisation were put on empirical antibiotic therapy and were followed on old basis and were contacted on telephone. Patients admitted directly to internal medicine ward or through emergency were assessed within 4 hours of admission. The initial assessment included detailed history and clinical examination. Routine investigation at admission included complete blood count with ESR ,kidney function test ,liver function test ,LDH ,arterial blood gas analysis , chest roentgenogram, ECG, thoracocentisis with analysis of pleural fluid (ph, total cell count , differential cell count , LDH , amylase ,gram staining and culture). Gram staining and culture of respiratory secretions and blood culture were performed where ever feasable /indicated . A semi quantitative test for CRP was performed at admission and repeated at day 4. The CRP kit used was manufactured by Randox laboratories ltd.

Inclusion criteria

The main inclusion criteria was presentation to hospital with diagnosis of community acquired pneumonia(CAP) . CAP was defined as per idea guidelines

Exclusion criteria

Hospital acquired pneumonia ,active thoracic or extra thoracic malignancy ,conditions likely to cause diagnostic confusion or where chest radiographic changes are equivocal (pulmonary fibrosis ,allergic bronchopulmonary aspergillosis) , chronic lung disease (copd, bronchiectasis ,chronic asthma), immunosuppression ,solid organ transplant ,chronic liver disease ,hematological disorders including malignancies ,other acute comorbid illness leading to physiological or metabolic derangements such that pneumonia severity assessment would be inappropriate (eg acute pulmonary embolism ,cystic fibrosis , steroid use)

Statistical Analysis

All data were analyzed using SPSS version 20 (SPSS Inc., Chicago, Ill). Descriptive statistics of demographic and clinical variables are presented as median (interquartile range) unless otherwise stated. The Mann-Whitney U test was used for the comparison of 2 groups of continuous data. Sensitivity, specificity, negative predictive value, positive predictive value, and the area under the receiver operator characteristic (ROC) curve was use for comparison of predictive tests. A 2 2 table using the Fisher's exact test was used to compare readmissions before day 4. For all analyses, a 2-tailed P value of <.05 was considered statistically significant. We used multiple logistic regression to compare the outcomes of interest in patients with elevated CRP (100 mg/L) compared with

patients with lower CRP levels (100 mg/L).outcome to be seen the primary outcome of interest was 30-day mortality. Secondary outcomes were need for mechanical ventilation and/or inotropic support and development of complicated pneumonia (lung abscess, empyema, or complicated para- pneumonic effusion).

Results

Table 1 Presenting symptoms in studied patients n=60		
Symptoms	Number n1 =	Percentage (%)
Cough with expectoration	60	100
Breathlessness	39	65
Altered sensorium	27	45
Hemoptysis	6	10
Pleuritic chest pain	2	3

Total number of patients was 60 with age of patients ranged from 16 to 80 years with mean age of 48.70 ±17.15 years ,there were 32 females (53%) and 28 males (47%). The youngest patient was 16 yrs old female.Presenting symptoms in studied patients are shown in table 1.

Table 2 clinical examination of patients n=60		
Clinical finding	Number n1=	Percentage (%)
Crepts	54	90
Bronchial breathing	24	40
Pleural rub	12	20

Table 2 clinical examination of patients n=60		
Signs of effusion	10	16
Wheeze	6	10
Tachycardia	30	50
Encephalopathy	27	45
Fever	48	80
Hypotension	18	30
Hepatomegaly	3	5

Clinical examination of patients showed findings on presentation as shown in table 2.

It was observed that CRP levels were significantly increased in 45% of patients . The raised CRP levels and outcome within 30 days of admission are shown in table 3.

Table 3 CRP levels in studied patients and outcome within 30 days of admission n=60			
	CRP > OR = 100 mg/L	CRP <100mg/l	P value
Total	n=27(45%)	n=33(55%)	
Mortality	11(41%)	1(3%)	<0.0001
Ventilation need/inotropic support	11(41%)	1(3%)	<0.0001
Complicated pneumonia	2(7%)	2(7%)	0.85

C reactive protein levels and adverse outcomes within 30 days of admission shown in table4

Table 4 CRP levels and 30 days adverse events				
CRP(mg/l)	n=60	Complicated pneumonia (%)	Invasive ventilation/ionotropic support (%)	Mortality (%)
>or=200	7	15	86	86
150-199	16	6	19	25
100-149	4	0	25	25
<100	28	4	4	4
<50	5	0	0	0
Statistical analysis	Chi-square	0.043	12.979	12.979
	Df	4	4	4
	P value	.839(ns)	<.0001	<.0001

CRP as an independent predictor of severity in cap shown in table 5

Table 5 CRP as independent predictor of severity in cap			
	Mortality		
CRP >100 mg/l	No	Yes	Total
Test positive	16	11	27
test negative	32	1	33
Total	48	12	60
	Estimated value	**95% confidence interval**	
		Lower limit	Upper limit
Prevalence	0.2	0.111901	0.327037
Sensitivity	0.91667	0.597539	0.995635
Specificity	0.666667	0.514865	0.79192
Likelihood ratio(LR+)	2.75	1.78	4.248
Likelihood	0.125	0.019	0.825

Table 5 CRP as independent predictor of severity in cap			
ratio(LR-)			
Positive predictive value(ppv)	0.407	0.245	0.593
Negative predictive value(npv)	0.97	0.847	0.995
Odd ratio (or)	22	2.500	497.114
Relative risk (rr)	13.444	2.080	277.602
	Chi square tests		
Test	CHI -SQUARE		P value
Pearson uncorrected	13.199		<0.0001
Yates corrected	10.974		<0.0001
Mantel -haenzel	12.979		<0.0001

Discussion

In the present study the mean age of patients was 48.70±17.15 years and the age range was 16 to 80 yrs with 32 females and 28 males . In our study the most common symptoms of the patients were cough with expectoration (100%) followed by breathlessness(65%),altered sensorium (40%),hemoptysis (10%), and pleuritic chest pain (3%),which was consistent with study carried by Naoyuki Miyashita et al(15) and other study is Shah et al (16). Clinical examination on day 1 revealed 80% patients were febrile ,30% had hypotension ,50% had tachycardia ,crepts were present in

90% patients ,40% had bronchial breathing ,20% pleural rub ,16% had signs of effusion same results were found in study by S.Bansai et al (17). In our study group of all patients 20% required invasive ventilation and /or inotropic support , complicated pneumonia developed in 7% of patients ,hospital stay was prolonged in 20% of patients .the 30 day mortality was 20% .the mortality rate of CAP varied in different centres from 5.7% in British thoracic society multi centric study (18) to a higher mortality of 21% to 25% in other (19,20). In our study elevated CRP more than or equal to 100mg/l was associated with no only increased 30 day mortality but also a marker of invasive ventilation and or inotropic support . The high negative predictive value of CRP below 100mg/l for each of these outcomes can reassure clinicians and has potential to aid the initial decision to admit or discharge patient from hospital, the findings were also consistent with studies by Garcia Vazquez E, Martinez JA et al(21). One more observation noted in our study was that seen and as recommended by British thoracic society using repeat measurement of CRP on day 4 patients can be differentiated as high risk or low risk currently ,on admission risk scoring is seen but in hospital risk severity scoring is not used , there is no reason why severity assessment should not be used in admitted patients and the finding in our study that patients in whom CRP falls by 50% or more in 4 days have low 30 days mortality ,need for mechanical ventilator and/or inotropic support and complicated pneumonia should be of value to clinicians, these findings were consistent with James D.Chalmers et al(22).

Conclusion

1. Low admission CRP levels <100 mg/l effectively excludes severe community acquired pneumonia and can be used as an adjunct to clinical judgement to identify low risk patients who may be safely discharged .CRP <100 provides high negative predictive value for mortality.
2. In patients admitted to hospital a CRP level that falls by 50% or more in four days indicate a low risk of 30 days mortality , use of mechanical ventilation and/or inotropic support or development of complicated pneumonia .

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