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Medicine

MONITORING OF COMMUNITY-ACQUIRED PNEUMONIA USING HIGH SENSITIVITY C - REACTIVE PROTEIN (HS CRP) AS A MARKER

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ABSTRACT Pneumonia is a leading cause of death affecting all age group especially young adults, old and chronically ill individuals. C-reactive protein is an acute phase protein which is synthesized in liver and its level rise in response to inflammation. Interleukins (IL) -6 released by macrophages and adipocytes triggers the synthesis of C-reactive protein in liver although tumor necrosis factor (TNF)-alpha, IL-1, and other cytokines are thought to be involved in the release of C-reactive protein. Evidence of a relationship with severity is still unclear, with some studies showing no correlation of TNF-alpha, IL-6, and soluble interleukin-2 receptor (IL-2R) do with severity. In present study we have determined a correlation between estimation of hsCRP levels and and outcome of patients with pneumonia.

KEYWORDS : HsCRP, interleukins, pneumonia

Introduction

Community-acquired pneumonia (CAP) is a major issue estimating around 2-12 cases/1,000 population per year (1).The largest number of deaths have been reported in the first few days of hospitalization (2), so the early detection of CAP help in the early initiation of antibiotic treatment and adequate supportive care. It has been noticed that approximately 10-25% of patients with CAP fail to resolve within the anticipated time (3). Treatment failure can be a result of poor response by host due to complications developed by infections such as post-obstructive pneumonia, empyema, or lung abscess (4). Some serum markers of infection such as C-reactive protein (CRP) and interleukins (IL) have been used in monitoring the response to the antibiotic treatment (5, 6). Plasma CRP is an acute phase-protein which is synthesized by the liver largely under transcriptional control of IL-6 (7). An increase in CRP levels can be noticed in response to several inflammatory stimuli and bacterial infection being one of the most potent. The level of CRP starts increasing within 4-6 hours of the stimulus response, get doubles in every 8 hours, reaching at its peak at 36-50 hours and start decreasing rapidly with a half-life of 19 hour after removal of stimulus (8). In present study, patients were subjected to quantitative estimation of hsCRP levels and its correlation with severity and outcome of patients with pneumonia.

Material and methods

This study was conducted on100 patients with pneumonia admitted in medicine department, Muzaffarnagar Medical College and Hospital. A detailed clinical history from the patient was recorded. The hematological and biochemical investigations along with blood cultures and sputum cultures were carried out. Chest X-ray and arterial blood gas analysis was also done. hsCRP levels were measured by ELISA method. The hsCRP levels were measured on day 1 and again on day 5 to day 7. The hsCRP levels were correlated with the outcome of patients. Patients with pneumonia aged not less than twelve year were included in the study irrespective to gender. Patients with acute inflammatory condition other than pneumonia, associated chronic medical illness which may lead to rise in hsCRP, coronary artery disease, autoimmune disorders and chronic kidney disease were excluded from the study.

Results

1. hsCRP concentration at two different time points

Table 1: hsCRP level at day 1(hsCRP1) and at day 5-7 (hsCRP2)

	hsCRP1	hsCRP2
No. of patients	100	100
Minimum	65.32	10.20
Maximum	98.90	99.9

Figure 1: Scatter diagram representing distribution of hsCRP levels at day 1 in different age groups.

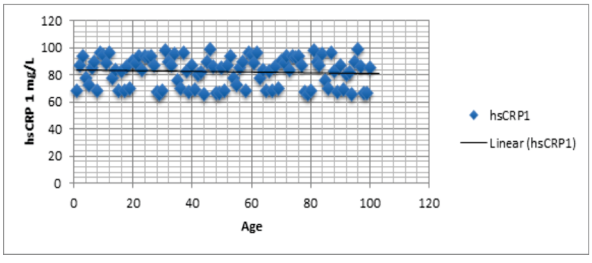
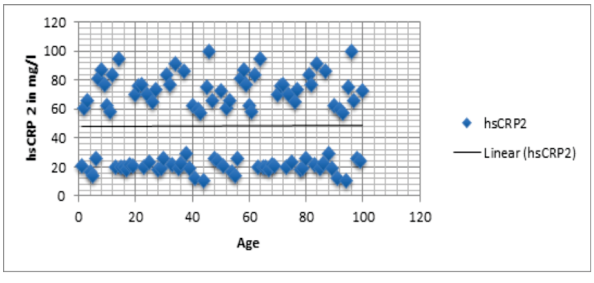


Figure 2: Scatter diagram representing distribution of hsCRP levels at day 5 in different age groups.



2. Outcome of the patients:

Table 2: Descriptive analysis of outcome of patients

Outcome of patients	No. of patients
Discharged	46
Antibiotic switch	14
Prolonged hospital stay	18
Shifted to ICU	12
Not survived	10
Total	100

Forty six out of 100 patients without any complication were discharged. Antibiotics were switched in 14 patients due to failure to response. Eighteen patients experienced a prolonged hospital stay. Twelve patients were shifted to ICU and 10 patients could not survive due to complications. Outcome of the patients were further categorized in to discharged and morbid group where all the patients of different morbidities were clubbed into a single group for the ease of statistical analysis. (Table 3)

Table 3: Classification on the basis of outcomes of patients

Patients Outcome	No. of patients
Discharged	46
Prolonged morbidity (antibiotic switch, prolonged hospital stay, shifted to ICU, not survived)	54
Total	100

3. Analysis of hsCRP levels in patients with pneumonia

Patients were grouped into hsCRP>70 mg/L and hsCRP <70 mg/L to determine if there was any significant correlation with patient outcome. 72 out of 100 patients with hsCRP level >70mg/L and 28 patients with hsCRP level < /=70 mg/L were observed.

4. Correlation of baseline hsCRP levels with patient outcome

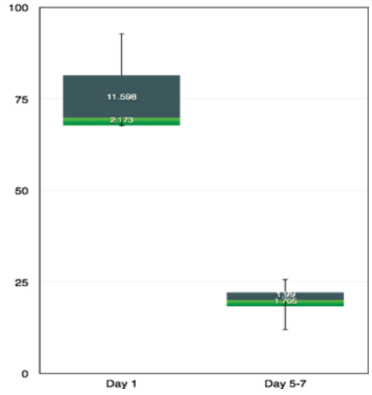
Table 4: hsCRP level versus outcome

Groups	Outcome					p value 0.001
	Discharged	Antibiotic Switch	Prolonged hospital switch	Shifted to ICU	Not survived	
No. of patients with hsCRP> 70 mg/L	20	14	18	12	8	
No. of patients with hsCRP< 70 mg/L	26	0	0	0	2	

Out of 72 patients who had hsCRP value more than 70 mg/L, 52 patients had prolonged morbidity and out of 28 whose hsCRP levels was less than 70mg/L, only one patient had prolonged morbidity. This correlation was proved to be statistically significant with p<0.001 using Pearson chi square test. (Table: 4)

5. Mean hsCRP1 and hsCRP2 in the discharged group.

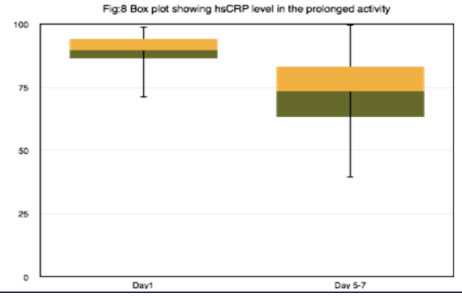
Figure 3: Box plot showing the hsCRP in the patients whose stay in ward was uneventful and were discharged. The hsCRP2 (day 5-7) shows drastic decline compared to hsCRP1 (day 1).



6. Mean hsCRP1 and hsCRP2 in the prolonged morbidity group

Figure 4: Box plot showing hsCRP levels in the prolonged morbidity group,

hsCRP2 (hsCRP day 5-7) levels showing a broad range of values ranging 99.9mg/L- 60mg/L.



7. The mean hsCRP values at day1 between the two groups (discharged and prolonged morbidity) were compared

Table 5: Comparison of mean hsCRP1 between two groups

Patient outcome	Mean hsCRP1	p value
Discharged	73.96	0.001
Prolonged morbidity (antibiotic switch, prolonged hospital stay, shifted to ICU, expiry)	89.49	

The mean hsCRP1 (hsCRP day 1) levels were found to be significantly higher in prolonged morbidity group.

8. The mean hsCRP values at day 1 between the two groups (discharged and prolonged morbidity) were compared

Table 6: Comparison of mean hsCRP 2 between two groups

Pateint outcome	Mean hsCRP2	p value
Discharged	19.78	0.001
Prolonged morbidity (antibiotic switch, prolonged hospital stay, shifted to ICU, expirty)	72.66	

The mean hsCRP2 (hsCRP day 5-7) levels were found to be significantly higher in the prolonged morbidity group.

Discussion

Smith and colleagues studied 28 CAP patients after prescribing antibiotics from day 1 until day 5 of therapy to assess the serial changes of the plasma CRP, tumour necrosis factor alpha and interleukin- 6. Two patients died. The mean (+/- SD) CRP values for days 1,2,3,4, and 5 were 136 +/- 43, 96 +/- 44, 53 +/- 36, 54 +/- 43, and 44 +/- 31 mg/L respectively for those patient who survived. CRP levels on day 1 in patients undergone antibiotics treatment prior to hospital admission were significantly lower than those who were not on antibiotic treatment, 107 +/- 42 and 152 +/- 44 mg/L ($p < 0.05$). A continuous rise in CRP value despite of antibiotic treatment was associated with infective complications or death. (6). Chalmers et al showed that low CRP levels <100 mg/L was found to lower down 30-days mortality, requirement for invasive ventilation and/or inotropic support, and complicated pneumonia and Patients showing failure of CRP level more than 50% or more at day 4 are at higher risk of severity and development of complicated pneumonia (9). Menendez et al have demonstrated that patients with high CRP level on day 1 and day 3 was found to be asoociated with higher risk of treatment failure. (10) Bruns et al proved that an inappropriate antibiotic treatment was associated with delayed normalisation of CRP. Patients showing a fall of 60% in CRP levels in 3 days or a fall of 90% in 7 days had a 4-7 times increased risk of having received unsuitable antibiotic therapy. A higher risk of treatment failure was also observed in patients showing an inadequate decline in CRP, however, this result was statistically insignificant (11). Daga et al conducted a prospective study on 83 patients (48 patient of pneumonia and 35 patient of COPD with acute exacerbation) to determine the CRP value. The mean value of CRP was 75.87 mg/L and maximum value was 600mg/L. The mean value in COPD patients was 16.71 mg/L, median was 0 mg/L. and maximum value was 90 mg/L. The CRP values in the two groups were found to be highly significant (p=0.0012). They concluded that, that CRP could be considered as an important parameter in doubtful cases in a particular clinical setting (12). Another study conducted in the patients with lower respiratory tract infections revealed that CRP level > 100mg/L acted as independent marker associated with higher risk of death (13). Similarly, we found a definite correlation between hsCRP levels and outcome of the patient that concluded the higher hsCRP value is related with more severe condition. Patients with hsCRP1 >70mg/L met with prolonged morbidity like antibiotic switch, prolonged hospital stay, shifted to ICU and death. Patients on day 5- day 7 hsCRP did not show a decrease >50% of day 1 hsCRP which predicted prolonged morbidity (P<0.001).

Conclusion

High admission hsCRP >70 mg/L effectively predicts poor outcome in severe CAP and can be used as an adjunct to clinical judgment for identifying high-risk patients who need hospital admission. The time course characteristics of hsCRP, unlike other cytokines, make it ideally

suited for use as a peripheral marker in pneumonia. Consecutive CRP measurements are useful in the first week in follow-up of antibiotic treatment for severeCAP. A delayed decline in CRP levels is related with a higher risk of having received inappropriate antibiotic treatment.

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