

## Original Article

### Correlation of changes in CRP levels and APACHE II in critically ill patients

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#### Abstract

**Background:** Sepsis is one of the main causes of morbidity and mortality in the intensive care unit.[1] C Reactive Protein (CRP), is an acute-phase reactant, which increases markedly within hours after tissue injury.[4] Changes in plasma CRP levels can be useful in the diagnosis and followup.[5]

**Objective:** To investigate the relation between CRP level and APACHE II score over the duration of illness in critically ill.

**Material & Methods:** A prospective, randomized study was conducted, including 200 patients, aged 25-65 years, of either sex, fulfilling the systemic inflammatory response (SIRS)/sepsis criteria based on ACCP/SCCM definitions.[5] Patients were divided into two groups (I & II) based upon their outcome. Group I included patients who expired in the I.C.U and Group II patients were those who improved and were shifted from the ICU to their respective wards. At the time of admission and each day thereafter APACHE II scores and CRP levels were carried out till the patients were either shifted from the ICU to wards or expired. Collected data was divided into two groups. Serum CRP levels were measured using an immunochemistry analyzer.

**Results:** Observations showed that the mean CRP values declined beyond day 4 in group II while, the values kept on increasing in group I (table 2, figure 1). The difference between the groups was significant ( $p < 0.01$ ).

**Conclusion:** The degree of sepsis and organ dysfunction cannot be identified by a single marker; rather a combination of parameters is more useful.

#### Introduction

Sepsis is one of the main causes of morbidity and mortality in the intensive care unit.[1] A delay in making the diagnosis and instituting appropriate therapy has been associated with increased mortality.[2] C Reactive Protein (CRP), is an acute-phase reactant synthesized by the liver following stimulus by various cytokines including tumor necrosis factor- and interleukin (IL6).[3] Its plasma concentration is normally under 10mg/litre, which may increase markedly within hours after infection, trauma, ischemia, burns, and other inflammatory conditions.[4] Changes in plasma CRP levels can be useful in the diagnosis of infection and in follow-up of the clinical course.[5]

However, in critically ill patients with symptoms of systemic inflammation or

shock, the above may not be true. Medline search did not reveal any information regarding the clinical and outcome correlation of changes in CRP levels in 'critically sick' patient. Thus we planned this study to investigate the relation between CRP concentrations and Acute Physiological Age and Chronic Health Evaluation II (APACHE II) score over the duration of illness in critically sick patients. We concluded that the degree of sepsis and organ dysfunction cannot be identified by a single marker; rather a combination of parameters is more useful.

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## Materials and methods

After approval from the institute's ethical committee and written informed consent from a responsible family member of each patient, this prospective, randomized study was conducted. The study included 200 patients, aged 25-65yrs, of either sex, fulfilling the systemic inflammatory response (SIRS)/sepsis criteria based on ACCP/SCCM definitions.[5] All patients were admitted in our mixed ICU during July 2007 to June 2008 (108 in group I and 92 in group II). Patients with rheumatic diseases, inflammatory bowel disease, malignancy, high level of alcohol consumption, and those on hormone replacement therapy were excluded from the study.[6,7] Patients were divided into two groups (I & II) based upon their outcome. Group I included patients who expired in the ICU and Group II patients were those who improved and were shifted from the ICU to their respective wards. At the time of admission and each day thereafter APACHE II scores and CRP levels were carried out till the patients were either shifted from the ICU to wards or expired. Day-one (D-1) was defined as the first observational day, D-2 as second, D-3 as third day, and so on. Collected data was divided into two groups. Serum CRP levels were measured using an immunochemistry analyzer (IMModular; Hitachi; Tokyo, Japan).

SPSS 9.0 (SPSS Inc, Chicago, IL) software was used for statistical analysis. Comparison of CRP value between the groups was done by unpaired t-test.  $p < 0.05$  was considered as significant.

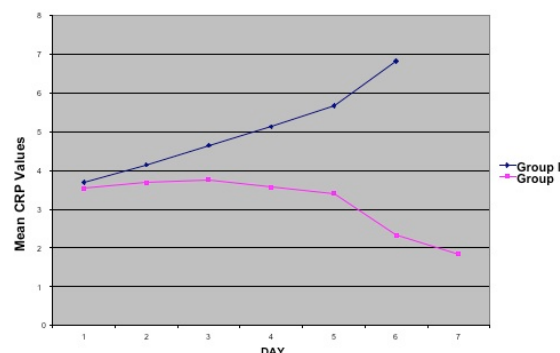
## Results

Data regarding age, sex, weight, and height amongst the groups was similar (Table 1).

**Table 1:** Demographic data

Groups	I	II
n	108	92
Age	40.3 ± 13.9	42.2 ± 12.3
Sex(M:F)	56:52	48:44
Weight (kg)	50.6 ± 9.2	55.8 ± 8.6
Height (Cm)	158 ± 9	156 ± 8

For ease of calculation the mean serum CRP values of all patients in a group were calculated at the end of study for each observational day. The values were then compared between the two groups by applying chi square test and calculating the p values. Observations showed that the mean CRP values declined beyond D-4 in group II while, the values kept on increasing in group I (Table 2 and Figure 1). The difference between the groups was significant ( $p < 0.01$ ). Likewise, Table 3, shows comparison of observed mortality in our patients with that of the predicted mortality based on their day 1 APACHE scores.



**Figure 1:** Mean CRP levels

## Discussion

Studies have reported higher CRP values in patients with bacterial infection as compared to those with viral infection, autoimmune disorders, or other nonbacterial infection-related inflammatory disease. Unfortunately, very few studies reported in literature correlate with severity of organ dysfunction or outcome with CRP value. CRP level on admission is a useful marker for early infection but not for outcome in critically ill patients admitted to the ICU.[8] However, elevated concentrations of serum CRP at admission have been reported to correlate with an increased risk of organ failure and death.[4] In the present study we tried to correlate the trends of CRP values with the prognosis during the course of patient's stay in the ICU.

We not only observed an elevated CRP levels on admission (within 24 hours of admission) to ICU in patients with SIRS/sepsis, but also there was a significant

**Table 2:** Mean CRP values (mg/litre) for each observational day and their comparison between the groups

	MEAN±SD (n)					
	D-1	D-2	D-3	D-4	D-5	D-6
Group I (n=108)	36.92±20.39	41.40±17.30	46.47±17.72	51.34±18.28	56.67±11.89	68.20±14.42
Group II (n=92)	35.41±21.17	36.82±15.99	37.61±14.77	35.68±14.05	34.15±12.37	23.30±16.97
Unpaired t-test Gp I vs Gp II	t=0.26  p=0.08  NS	t=0.97  p=0.06  NS	t=1.93  p=0.05  NS	t=3.41  p=0.008  HS	t=4.82  p=0.001  HS	t=4.86  p=0.001  HS

**Table 3:** Comparison of mortality in our patients with the predicted APACHE II mortality

APACHE II Score	Predicted APACHE II Score mortality		Observed mortality in our patients (percentage)	
	Non-operative	Postoperative	Non-operative	Postoperative
0-4	4	1	-	-
5-9	6	3	3/9(33.3)	0/3(0)
10-14	12	6	2/4(50)	0/3(0)
15-19	22	11	9/16(56.2)	-
20-24	40	29	6/8(75)	-
25-29	51	37	3/3(100)	-
30-34	71	71	3/3(100)	1/1(100)
>35	82	87	-	-

and serial increase in the CRP levels in patients, who later deteriorated and expired. Whereas, the patients who recovered and got shifted out of I.C.U to their wards showed a maximum rise until D2-D3, after which the values showed a decreasing trend though they still often remained elevated over normal values for several days.

We also observed that the predicted mortality in their patients as per the APACHE II score was far lower than the mortality observed. So, it can be assumed that isolated APACHE II score is a poor

predictor of mortality when used alone and it would be better if combined with other parameters, such as serial CRP levels.

### Conclusion

We conclude that the degree of sepsis and organ dysfunction cannot be identified by a single marker. Recently simultaneous measurement of procalcitonin levels and daily use of sepsis scores like SOFA have been suggested to increase the sensitivity and specificity of CRP as a marker for diagnosis, outcome and progression of sepsis/SIRS.[9]

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