Impact of CRP Test in Management of COVID-19

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Abstract :

Aims: The corona virus disease 2019 (COVID-19) caused by SARS CoV -2, is characterized as highly contagious and deadly; however there is no credible and convenient biomarker to predict the severity of the disease. The aim of the present study was to estimate whether the CRP level is able to act as a marker in indicating the severity of COVID-19, establish comparison between CRP level with other biomarkers and how it will be helpful in management of COVID-19 cases. **Methods:** Patients who complained of any respiratory symptoms i.e. cough or breathlessness with or without fever after laboratory confirmed of SARS-CoV-2 viral nucleic acid via RT-PCR were enrolled in study. RT-PCR for SARS-CoV-2 negative having respiratory symptoms were included as control group. **Results:** CRP getting raised in significant number of COVID 19 cases with significant titre in both severe and mild cases which was evaluated by χ^2 with p-value <0.0001 which was highly statistically significant and unpaired t test with statistically significant p value respectively. About 8% (8/100) of non severe adult COVID-19 patients progressed to severe cases after admission. Compared with non severe patients, the aggravated patients had much higher levels of CRP (mean ± SD: 64.5 ± 59.2 mg/L vs 245.75 ± 179, p-value 0.034) showed that CRP was significantly associated with aggravation of non severe COVID-19 patients. **Conclusions:** The level of plasma CRP was positively correlated to the severity of COVID-19. Our findings could assist to discern patients of severe COVID-19 from the non severe ones. Our findings may be useful as an earlier indicator for severe illness and help physicians to stratify patients for intensive care unit transfer.

Key Words : Biomarker, COVID-19, CRP

Introduction :

The current outbreak of corona virus disease 2019 (COVID-19) caused by SARS CoV -2 was first reported in Wuhan, China, in December 2019 [1, 2] that broke out worldwide, affecting over 227 countries. By the end of February 2020, more than 78,631 cases infected with SARS-CoV-2 and more than 2747 deaths were confirmed in China,[3] World Health Organization (WHO) declared it a pandemic in March, 2020.[4] Owing to the rapid increase in the number of COVID-19 patients, the hospitals in many regions face huge challenges. Generally, severe patients are treated in the intensive care unit, while mild patients are hospitalized in the usual isolation ward. However, a small subset of non severe patients may develop into severe cases.

Therefore, the problem of how to identify this group of patients in early stage, active monitoring and timely treating them is critical for reducing mortality and improving outcomes of COVID-19 patients. Therefore, one reliable and convenient biomarker is needed to predict the severity of COVID-19. Various previous studies[5] show that, C-Reactive Protein (CRP) rises significantly in patients those progress to severe & even fatal disease. This study was aimed to evaluate the prognostic ability of CRP in estimating the severity of COVID-19.

Materials and methods :

Study design

Present study was conducted at Department of Microbiology laboratory of tertiary Health Care Centre, Ahmedabad. This study was conducted over 100 patients during period of July-August 2020 & presented with respiratory symptoms i.e. cough, breathlessness with or without fever, which were screened by RT-PCR for SARS-CoV-2 with positive results. RT-PCR for

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SARS-CoV-2 negative having respiratory symptoms were included as control group. SARS-CoV-2 positive patients with carcinoma, inflammatory bowel disease and arthritis were excluded from the study. Anonymous clinical data was collected and analyzed to facilitate better clinical decisions and treatment. Upon admission, patients underwent blood routine investigations, including CRP quantification. [5]

Sample collection

Throat swab and nasopharyngeal swab were collected in viral transport media (VTM) and sent for RT-PCR at reference laboratory.

Blood samples were collected for various investigations i.e. CBC, CRP, S.ferritin, S.LDH, D-dimer. Sample were also collected for detection of COVID-19 antibody.

Statistical analysis

The analysis was performed by trial version of SPSS software. Significance of CRP concentration with COVID 19 disease management was analyzed and combined standard difference in mean and P-values were calculated

Results and Discussion:

During study period, 100 cases of SARS CoV-2 infection were included based on selection criteria, these comprised 71 (71%) males and 29 (29%) were females. Their gender and age distribution are displayed in Figure 1 & 2.

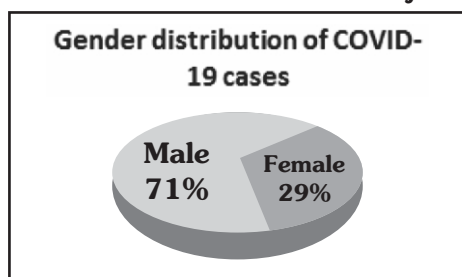**Figure 1: Gender distribution of subject studied**

Fig. 2 shows that most of the cases of COVID-19 were belong to age group of 41-80 years. Out of 18 severe COVID19 cases admitted in ICU and on ventilator support, 17 (94.45%) were of more than 50 years of age; the similar finding was also observed in the study by Wang D et al.[7] Significant increase in level of CRP was detected in test group (Mean ± SD: 98.17 ± 91.70) as

compared to control group (Mean ± SD: 28.73 ± 22.78) which was evaluated by unpaired t test and p-value was 0.0001; which implies that the result was statistically significant; that also match with the previous studies. [7]
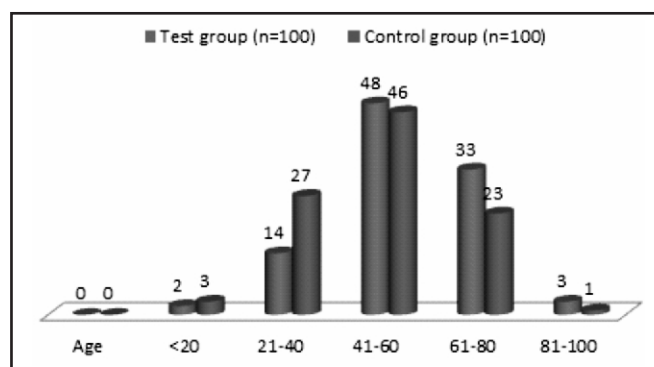
Figure 2: Age distribution of subject studied

Table 1: Performance of CRP test for diagnosis of COVID 19 infections

Test	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Serum CRP (≥ 6mg/L)	81	44	59	69

Table 2: Number of COVID 19 cases having increase in CRP level

CRP value	Number of cases in test group (n=100)	Number of cases in control group (n=100)	X^2test	p-value
Positive (≥ 6mg/L)	82	56		
Negative (< 6mg/L)	18	44	15.80	<0.0001
Total	100	100		

Out of 100 cases of COVID 19, 82 cases having increase in CRP level (≥ 6 mg/L) suggesting that COVID 19 causes increase in CRP level in significant number of cases which was evaluated by ϵ^2 and p-value was <0.0001 which was statistically highly significant. [8,9]

Significant increase in level of CRP in severe cases of test group (Mean ± SD: 144.24 ± 78.82) as compared to control group (Mean ± SD: 44.25 ± 34.45) which

Table 3: Comparison of Mean and SD of CRP level in severe and mild COVID 19 cases

Test group	Test group (CRP mg/L)	Control group	Control group (CRP mg/L)	p-value	t-value
Severe cases (n=18)	144.24 ± 78.82	Severe cases (n=4)	44.25 ± 34.45	0.0237	2.44
Mild cases (n=82)	65.63 ± 87.48	Mild cases (n=96)	15.71 ± 20.63	<0.0001	5.39

was evaluated by unpaired t test with p-value was 0.0237 which implies that the result was statistically significant. The similar findings were also observed in previous studies.[10,11]

While in mild cases of test group CRP level (Mean ± SD: 65.63 ± 87.48) also high as compared to mild cases of control group ((Mean ± SD: 15.71 ± 20.63) which was evaluated by unpaired t test with p-value was <0.0001 which was highly statistically significant.

Table 4: Correlations of CRP with other bio markers in COVID 19

Biomarker	Percentage of COVID 19 cases show significantly high / detectable value
CRP	81%
Total leukocyte count	27%
D-DIMER	22%
S.FERRITIN	36%
S.LDH	37%
COVID 19 antibody	39%

Table 4 shows in most of the cases of COVID 19, CRP get raised (in 81% cases) followed by S.LDH (37%), S.ferritin (36%) and D-dimer (22%).

Total 8 cases were progress from non severe course to severe course of COVID 19 during treatment.

In all 8 cases, who were progress from non severe course to severe course of COVID 19 during treatment had significant increasing level of CRP, which was evaluated by applying paired t test and p-value was 0.034 - which was statistically significant.

Out of 18 severe cases of COVID 19 admitted in ICU, 03 cases were deteriorated in condition having raised CRP level. Remaining 15 cases were recovered from

Table 5: Increase in level of CRP titre in non severe to severe course of COVID 19

Variable	Initial CRP level (mg/L)	Subsequent CRP level (mg/L)
Raised CRP level in patients progress non severe to severe course of COVID 19	138	250
	56	115
	24	643
	52	75
	2	142
	49	178
	25	316
	172	247
Mean	64.5	245.75
SD	59.2	179
p-value	0.034	
t-value	2.63	

severe to non severe course with significant decreasing in CRP level which was evaluated by paired t test and p-value was <0.00001, which was highly statistically significant. Thus monitoring CRP level can be helpful to determine outcome of COVID 19 course.

CRP is a type of protein produced by the liver that is elevated in response to inflammation.[12] Generally, CRP level is much higher in bacterial infections than in viral infections.[12] In our study, many COVID-19 patients showed elevated CRP levels which are co related with other studies.[11,12] Moreover, severe cases in this study showed significantly higher levels of CRP than non

Table 6: Decrease in CRP level in severe cases after treatment

Variable	Initial CRP level (mg/L)	Subsequent CRP level (mg/L)
Decrease in CRP level in patients progress severe to non severe course of COVID 19	202.49	1
	272	2
	48	1
	141	50
	113	1
	96	1
	71	2
	217	97
	261	35
	165	1
	76	1
	227	2
	129	40
	243	28
	89	2
Mean	156.699	17.6
SD	75.2	27.8
p-value	<0.00001	
t-value	7.5	

severe patients. The CRP level was also found to increase significantly in all those cases which progressed from non-severe to severe course of COVID 19. These suggested that CRP may be a serum marker of disease aggravation in COVID-19 patients.

Conclusion :

Elevated CRP level could be a valuable marker to predict the possibility of aggravation of non severe COVID-19 patients, which could help health care workers to identify those patients at an early stage for proper & timely management. However, multicenter studies with a large sample size may help to confirm these results.

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