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SERUM C-REACTIVE PROTEIN (CRP) IN PATIENTS WITH SARS COV-2 IN KAMRUP (ASSAM)

Biochemistry

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ABSTRACT

Background: The ongoing novel coronavirus (COVID-19) pandemic is shaping the world on an unprecedented scale affecting more than 10.3 million individuals across the globe . Various studies have found that C- reactive protein (CRP) levels could reflect disease severity and should be used as a key indicator for disease monitoring .

Objective: To assess the level of C reactive protein(CRP) in initial stage of COVID-19 cases and its correlation with clinical presentation of disease.

Materials and method: This retrospective case-control study includes 60 RT- PCR (reverse transcriptase-polymerase chain reaction) confirmed positive cases above the age of 18 years who were subsequently admitted between May- June, 2020, at Mahendra Mohan Choudhury Hospital(MMCH) –an annexe hospital of Gauhati Medical College and Hospital(GMCH), Kamrup, Assam.

Result: The mean CRP value in the case group was 6 ± 2.36 mg/L while in control group it was 3.03 ± 1.20 which was found to be significantly raised ($p<0.005$)

Conclusion: CRP may be an important index for prognosis and assessment of early stage of COVID-19. CRP levels can also be used in the treatment and management of positive cases.

KEYWORDS

COVID-19, SARS CoV-2, CRP, Assam.

INTRODUCTION

The coronavirus disease (COVID-19) also known as SARS-CoV-2 is a human beta corona virus,which originated in the city of Wuhan, China.It was first identified in Dec 2019. The pandemic then quickly spread to various countries, with many cases being reported worldwide.On January 30th, 2020, the WHO declared COVID-19 a Public Health Emergency of International Concern .[1]The first SARS-CoV-2 positive case in India was reported in the state of Kerala on January 30th, 2020. In Assam the first case of the COVID-19 pandemic was reported on 31 March 2020.[2]

COVID -19 scenario in Assam as on 28th June 2020:[3]
Positive cases:7165
Recovery rate:71%
Death rate:0.15%

COVID-19 infection displays a wide range of clinical manifestations. like cough, sputum production, diarrhoea, nausea/vomiting, and shortness of breath as more frequent clinical phenotypes in critical/non-survived COVID-19 patients, and in contrast, fever and headache were less prevalent.[4]The pathogenesis of the diseases is regulated by several host factors. C-reactive protein (CRP) has been reported to be upregulated during severe acute respiratory syndrome (SARS) outbreak in 2002 and associated with respiratory dysfunctions and death of the patients [5]

CRP (C- reactive protein) is a cytokine induced acute phase protein that increases in concentration as a result of acute inflammation.CRP level in the body has been used as a marker or indicator of infection and cancer.CRP is produced as a homopentameric protein, which consist of five identical non glycosylated polypeptide subunit noncovalently linked to form a disc shaped cyclic polymer with a molecular weight of 115kda.[6]CRP is synthesized primarily in liver hepatocytes but also by smooth muscle cells, macrophages,endothelial cells, lymphocytes, and adipocytes.Studies have revealed that CRP plays important roles in inflammatory processes and host responses to infection including the complement pathway, apoptosis, phagocytosis, nitric oxide (NO) release, and the production of cytokine particularly interleukin-6 and tumor necrosis factor-α.In the presence of calcium, CRP binds to polysaccharides such as phosphocholine (PCh) on microorganisms and triggers the classical complement pathway of innate immunity by activating C1q [7]

Interleukin-6 regulates the acute-phase response and is synthesized in the initial stages of inflammation and induces a number of acute-phase proteins, including CRP [8]. Many studies have found a correlation between increasing levels of IL-6 during inflammation and increasing levels of CRP [9]. Based on these observations, we carried out a study in SARS CoV-2 patients and assessed the CRP levels as one of the possible biomolecules linked with the severity of the disease process.

MATERIALS AND METHODS:

It was a retrospective case control study done in MMCH an annexe hospital of GMCH. Laboratory reports of diagnosed COVID -19 patients admitted in MMCH during the period May-June 2020 were taken up for the study.

Case group consisted of 60 confirmed (by RT-PCR) COVID-19 patients admitted in MMCH- a COVID hospital and matched with 60 age and sex matched healthy controls. Laboratory values of CRP were obtained from Hind Lab Kamrup(Metro), MMCH after taking due permission from the authority.

CRP was analysed by Nephelometry technology in SMART NEPHELO plus of Orbit diagnostics Pvt Ltd.

The normal biological reference value as per the above method is CRP < 8mg/L

After all the calculations and the biochemical estimations, the results obtained were statistically analyzed and compared between different groups of the study. Baseline characteristics of the study participants are expressed in mean ± SD (standard deviation). Student t test was used whenever applicable to analyze differences in baseline characteristics between the control and the test group. The results were considered significant when the probability (p value) was less than 0.05 % .Statistical analysis was done using GraphPad InStat version 3.00. All the statistical graphs were prepared using Microsoft Excel 2007.

RESULTS AND OBSERVATION

From our study we found that the maximum number of cases fall in the age group 46-55 years category followed by 36-45 years category and this trend corresponds to the positive travel history given by students, migrant workers and other professionals who have returned

back to Assam after the initial lockdown period. Among the 60 RT-PCR confirmed cases 42 are males and 18 are females ,while in control group 40 are males and 20 females.The mean CRP value in the case group is significantly raised (p< 0.0001) than in the control group.We further divided our case group into symptomatic and asymptomatic group depending on their clinical presentation.Out of the 60 positive cases, 12 cases presented with mild symptoms while 48 were asymptomatic.On comparing the CRP values between the symptomatic and asymptomatic group,the mean CRP value was raised significantly in the symptomatic group.

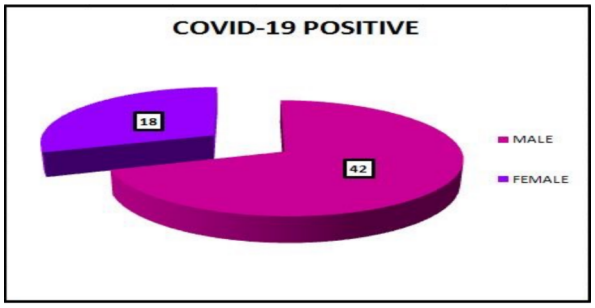

Fig1: Pie diagram showing sex distribution in case group

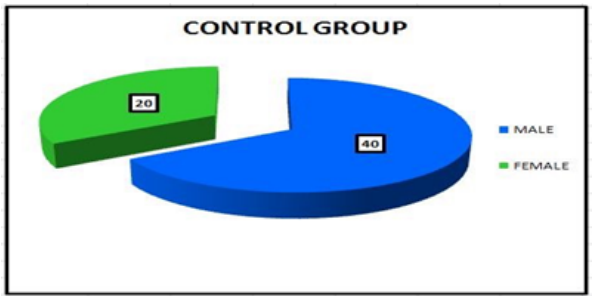

Fig2: Pie diagram showing sex distribution in control group

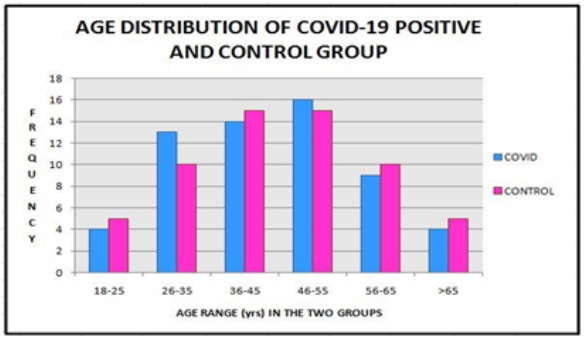

Fig 3: Bar diagram showing age distribution in both case and control group

Table 1:comparing The Crp Values Between Case And Control Group

PARAMETER (mg/l)	COVID CASES (N=60) MEAN ± S.D.	CONTROL (N=60) MEAN ± S.D.	COMPARISON
CRP	6 ± 2.365	3.033± 1.207	p < 0.0001
			HIGHLY SIGNIFICANT

TABLE 2:Comparing the CRP values between asymptomatic cases and Control group

PARAMETER (mg/l)	ASYMPTOMATIC COVID-19 CASES (N=48) MEAN ± S.D.	CONTROL(N=60) MEAN ± S.D.	COMPARISON
CRP	5.04 ± 1.071	3.033± 1.207	p < 0.0001
			HIGHLY SIGNIFICANT

Table 3: Comparing The Crp Values Between Symptomatic Cases And Control Group

PARAMETER (mg/l)	SYMPTOMATIC COVID-19 CASES (N=12) MEAN ± S.D.	CONTROL(N=60) MEAN ± S.D.	COMPARISON
CRP	9.83 ± 2.250	3.033± 1.207	p < 0.0001
			HIGHLY SIGNIFICANT

Table 4: Comparing The Crp Values Between Asymptomatic Cases And Symptomatic Cases

PARAMETER (mg/l)	ASYMPTOMATIC COVID-19 CASES (N=48) MEAN ± S.D.	SYMPTOMATIC COVID-19 CASES (N=12) MEAN ± S.D.	COMPARISON
CRP	5.04 ± 1.071	9.83 ± 2.250	p < 0.0001
			HIGHLY SIGNIFICANT

DISCUSSION

There is a global rise in the number of patients with COVID-19 and asymptomatic patients are also the source of infection[10]. COVID-19-related case fatality is also rapidly increasing. Early monitoring of key indicators is an important basis to guide treatment strategies, and also in assessing the severity of patients' condition [11]. The main pathological changes of COVID- 19 are related to lung and immune system damage [12].

Few studies have found a significant increase of CRP levels on average 20-50 mg/Lin patients with COVID - 19[13,14,15] A recent study done by Wang G et al showed that about 7.7% of non– severe COVID– 19 patients progressed to severe disease courses after hospitalization, and compared to non– severe cases, the aggravated patients had significantly higher concentrations of CRP (median 43.8 vs 12.1 mg/L)[16]. In another study, the mean concentration of CRP was significantly higher in severe patients (46 mg/L) than non– severe patients (23 mg/L)[17].Jin et al also conducted a study where the mean CRP level in severe cases of COVID -19 with gastrointestinal symptoms was 15.7mg/L while in non severe cases without any gastrointestinal symptom was 7.9 mg/L[18].In our study we found a significant rise in CRP level even in asymptomatic COVID-19 cases when compared with the normal control group; moreover, the mean CRP level in the symptomatic cases was significantly high when compared with the asymptomatic cases.The elevated levels of CRP might be due to the overproduction of inflammatory cytokines in patients with COVID– 19. Normally cytokines fight against the microbes but when the immune system becomes hyperactive, it may damage lung tissue. Thus, CRP production is induced by inflammatory cytokines and by tissue destruction in patients with COVID– 19.

CONCLUSION:

COVID– 19 patients with elevated levels of CRP need close monitoring and treatment even though they do not develop symptoms to meet the criteria for the severe disease, as they may progress to severe form in due course .So,elevated level of CRP may be a valuable early marker in predicting the possibility of disease progression in non– severe patients with COVID– 19, which can help the health workers to identify those patients at an early stage for early treatment. However, more studies in large scale multi centric institutions with larger case groups are required to further validate our findings. It is also seen that production of CRP is controlled by genetic makeup of the subject [19] and hence, it would leave us with a future scope to investigate individual genetic approach in different populations to obtain a firm conclusion.

Conflict of interest:

There is no conflict of interest

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