C-Reactive Protein (CRP) in Post COVID Major Depressive Disorder-

A Pilot Study

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Abstract:

Introduction: The COVID-19 infection is associated with an aggressive inflammatory response known as "cytokine storm." This overwhelming inflammation, may lead to many adverse outcomes or even death. The impact of the pandemic is not only limited to case numbers and mortality rates, but also deeply extends into the mental health of the global population. Depression appears to be a common complication in patients during and post–COVID-19 infection. In recent, many studies have revealed role of inflammation in pathophysiology of depression.

CRP is an acute phase glycoprotein secreted by the liver in response to systemic inflammatory cytokines. So, measurements of Serum CRP can be used to assess the severity of COVID 19 infection , depression and can also be used to assess response of treatment.

Aims & Objectives: To compare serum CRP level between post COVID patients with depression and post COVID patients without depression.

Material And Methods: This is a case control study included 10 diagnosed patients of depression attending post COVID psychiatry OPD after getting discharged from hospital (case group) and 10 age and gender matched post COVID patients without depression (control group) for study. Serum CRP levels were measured for both the groups.

Results: The mean CRP level in the control group and the case group were 7.26 ± 0.73 and 82.73 ± 22.23 mg/l respectively .The difference was found to be statistically significant (P < 0.01).Thus our study yielded higher levels of serum CRP in case group than in control group.

Conclusion: CRP can be used as a biomarker in COVID patients to assess severity of depression and these patients could be screened for early identification of depression and counseled for prevention of depression during and post COVID period.

Keywords: COVID-19, Depression, CRP, Post-COVID

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INTRODUCTION:

The COVID-19 infection is associated with an aggressive inflammatory response with the release of a large amount of pro-inflammatory cytokines including procalcitonin, ferritin, LDH,

CRP, IL-6, IL-1, TNF- α, and interferon known as "cytokine storm." This overwhelming inflammation, may lead to many adverse outcomes or even death. These inflammatory markers could be correlated with disease severity to predict COVID-19 mortality. [1]

The worldwide impact of the COVID-19 pandemic is significant and leading to increased mortality and morbidity of patients who survive .The impact of the pandemic is not only limited to case numbers and mortality rates, but also deeply extends into the mental health of the global population. According to the latest data, among its after-effects post-COVID depression is affects up to 39 % of people who had SARS-CoV-2 infection.

Depression appears to be a common complication in patients during and post–COVID-19 infection. It is important for the mental health of the population is to look for the cause of depressive episodes during and after COVID-19. This will help in faster diagnosis and effective treatment of the affected patients. In recent, many studies have revealed role of inflammation in pathophysiology of depression. A meta-analysis study by **Dowlati Y et al.,** [2] has shown an increase level of proinflammatory cytokines, such as TNF-α and IL-6 in people suffering from depression.

CRP is an acute phase glycoprotein secreted by the liver in response to systemic inflammatory cytokines. Serum CRP level is directly related to the severity of acute and chronic inflammation. [3] So, serial measurements of Serum CRP can be used to assess the severity of inflammatory disease and response to treatment.

In our study, we focused on inflammatory biomarker CRP, which is also present in excess in serum of COVID-19 patients and may influence the development of post-COVID depression.

RATIONALE OF THE STUDY:

This study is an attempt to assess the relationship between the serum CRP levels and depression related to COVID 19 infection. So if any association is found it will be helpful in the development of alternative treatment and preventive strategies for depression during and post COVID period.

AIMS & OBJECTIVES:

To compare serum CRP level between post COVID patients with depression and post COVID patients without depression.

MATERIAL AND METHODS:

This pilot study was conducted in the department of Biochemistry and department of Psychiatry of Chhindwara Institute of Medical Sciences (C.I.M.S.), Chhindwara (MP). This was a case control study included 10 diagnosed patients of depression attending post COVID psychiatry OPD after getting discharged from hospital were taken as cases and 10 age and gender matched post COVID patients without depression were taken as control for study.

Inclusion criteria: Post COVID diagnosed cases of depression attending psychiatry OPD. Age group between 18-50 yrs. Patients ready to give written informed consent.

Exclusion criteria: Patients on antidepressant drugs, patients having dependence of alcohol or smoking, patients with any inflammatory autoimmune disease such as diabetes, ankylosing spondylitis, rheumatoid arthritis.

Investigation Procedure: Venous blood (5 ml) sample was withdrawn from the antecubital vein following overnight fasting. The blood sample was collected in clot activator tube and serum was

collected. The serum was analysed for biochemical investigations on same day and remaining samples were preserved for further biochemical investigations at -20°C.

Serum CRP level was estimated by immunoturbidimetry method using CRP turbilatex kit on biosystem BA400 biochemistry fully automated analyzer.

Data Collection and Statistics: Results were expressed as mean ± S.E.M. The data were analyzed by one-way analysis of variance (ANOVA) tracked by Tukey's multiple comparison tests. Probability values less than 0.05 were considered statistically significant.

RESULTS:

The mean CRP level in the control group was 7.26 ± 0.73 mg/l while in the case group it was 82.73 ± 22.23 mg/l (Table 1& Figure1) .The difference was found to be statistically significant ($P < 0.01$).Showing a higher serum CRP level in post COVID depressive patients in comparison to post COVID patients without depression.

Table 1. Comparison of biochemical parameter between Case & Control

Parameter	Control (n=10) {Post COVID patients without depression} (Mean ± S.E.M.)	Case (n=10) {Post COVID patients with depression} (Mean ± S.E.M.)	p value
Age (years)	34.9 ± 7.91	36.4 ± 8.41	P > 0.05
Gender (M : F)	5:5	6:4	P > 0.05

CRP (mg/l)	7.26 ± 0.73	82.73 ± 22.23	P < 0.01

*P value <0.05 was taken as statistically significant

Figure 1. Comparison of Serum CRP between control and case groups.

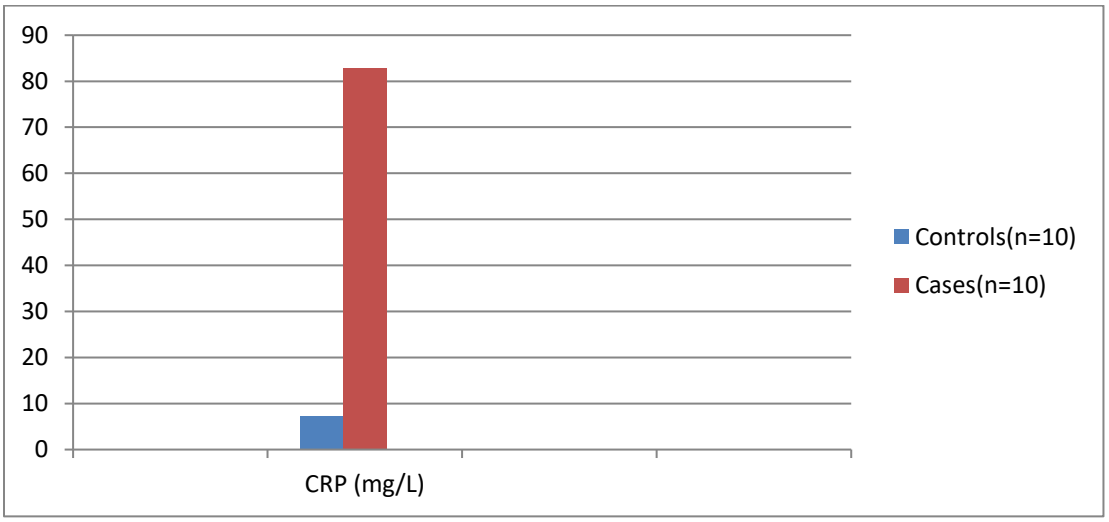
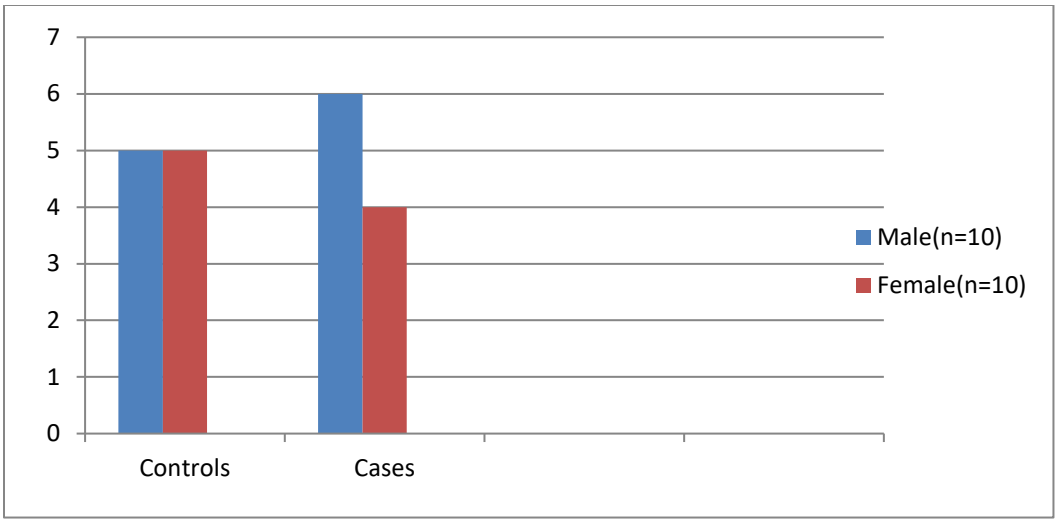


Figure 2. Distribution of subjects according to gender in both the groups.



DISCUSSION:

In our study, the levels of CRP in Post COVID patients with depression was found significantly higher than the Post COVID patients without depression (p value < 0.01). Findings of our study was in concordance with the study by **Yuan B et al.** [4] who found raised levels of serum CRP in post-COVID depressive patients as compared to COVID-19 patients without depression and study by **Guo Q. et al.** [5] who also found decrease in baseline CRP levels in COVID-19 patients in whom the severity of depression symptoms decreased as compared to COVID-19 patients in whom depression symptoms were not significantly reduced.

Depression is one of the most common mood disorder which can manifest as a single episode or as recurrent episodes. Depression affects individual emotional and psychological well-being with low self-esteem and ultimately resulted in social isolation

CRP is a biomarker used clinically to measure systemic inflammation and is increased in a subset of patients with major depressive disorder. **Haapakoski, et al., [6]** in their study found a significant association between increased serum CRP level and major depressive disorder.

Many studies describe, increased serum CRP concentration in COVID 19 infection and its concentration, correlates with the severity of COVID-19. **[7, 8]**

Early assessment CRP levels in post COVID depressive patients, could modify the disease progression and limit co-morbidities associated with it. Therefore, we assessed the level of CRP in our study .The relationship of CRP to COVID-19 infection is well documented, but further studies with large sample size must be undertaken to demonstrate its utility as a marker of post-COVID depression.

CONCLUSION :

Our pilot study showed a significant increase in serum CRP level in post COVID depressive patients and revealed that the etiopathogenesis of post-COVID depression analogous to the inflammatory hypothesis of Depression. So CRP can be used as a biomarker in COVID patients to assess severity of depression and these patients could be screened for early identification of depression and counseled for prevention of depression during and post COVID period.

Conflict of interest: Nil

Funding: Nil

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