

Original Research Article**To assess the severity of COVID-19 in relation to clinical value of immune inflammatory markers: An observational study****Dr. Preeti Motiyani¹, Dr. RS Meena², Dr. Dileep Dandotiya³, Dr. Mamta Meena^{4*},
Dr. Jitendra Rai⁵**¹Senior Resident (MD Medicine), Department of Cardiology, Gandhi Medical College, Bhopal (M.P.)²Associate Prof. (DM Cardiology), Department of Cardiology, Gandhi Medical College, Bhopal (M.P.)³Demonstrator (MD Community Medicine), Department of Community Medicine, Chhindwara Institute of Medical Sciences, Chhindwara (M.P.)⁴Assistant Prof. (MD Microbiology), Department of Microbiology, Gandhi Medical College, Bhopal (M.P.)⁵Postgraduate (MD Medicine), Department of General Medicine, Gandhi Medical College, Bhopal (M.P.)***Correspondence author:** Dr. Mamta Meena, Assistant Professor, Department of Microbiology, Gandhi Medical College, Bhopal (M.P.) 462001, mamtameena74@gmail.com

Background: Since December 2019, a novel type of pneumonia emerged in Wuhan, China, and rapidly transmitted to the whole globe. This pneumonia was verified to be caused by a different strain of coronavirus and named as coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO). Based on phylogeny, taxonomy and established practice, this novel coronavirus was designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Objectives: To show the co-relation between inflammatory markers and the severity of COVID-19 disease

Materials and Methods: A total of 250 patients were selected who are microbiologically COVID positive and ready to give consent were included in the study. Their basic test will be done.

Result- There is preponderance of male gender among the patients 147 were male 103 were female. The mean age of participant is 43 ± 2.825 ($\pm 6.57\%$) 65 patients were immediately required either oxygen or mechanical ventilation, among all this 26 patients were died. Among this entire 65 patients, 21 patients have raised CRP level, 14 have raised IL-6 Level among them all 26 were have raised D-Dimer.

Conclusion- Our study showed that high level of D-Dimer, IL-6 and CRP was independent risk factors for assessing the severity of COVID-19. IL-6 played a determining role in the severity of SARS-CoV-2 and had a potential value for monitoring the process of severe cases.

Key words- COVID-19, Inflammatory Markers, Severity, SARS-CoV-2, Outcome

Introduction- Since December 2019, a pneumonia emerged from China, and quickly have a grip over the world^[1,2]. This pneumonia was validated to be brought about through a special variant of coronavirus and named as coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO). Based on speciation, categorization and set up practice, this

distinctive variant of coronavirus was specified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) via the Coronavirus Study Group (CSG)^[3]. Which is akin to former two pathogenic coronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) Middle East respiratory syndrome coronavirus (MERS-CoV) during the first decade of this century^[4], SARS-CoV-2 is probable originated from bat^[5], and have the ability to transmit from to person^[6], cause pneumonia and respiratory disease^[7] with a glass appearance on imaging^[8]. COVID-19 is become a threat to human existence and health. Up to 27 March, 2020, 509299 people have been infected by means of SARS-CoV-2 worldwide, with mortality among 23338 cases^[9]. Regardless of most COVID-19 patients are having mild symptoms, affected person with severe type of symptoms may quickly progress to acute respiratory distress syndrome (ARDS), multiple organ dysfunction (MOD) and even mortality^[10]. Therefore, exploring plausible elements for the severity of COVID-19 is quintessential for extend or halt the development of the disease. Several researches have revealed that sufferers with advance age and co-morbidity are prone for severe disease^[11,12], and rogue immune-inflammatory response and cytokine storm may also be a reason in the sickness progression^[13]. Therefore, study was performed to compare the clinical features, immune-inflammatory parameters and cytokines between the severe and non-severe groups.

Objectives: To show the co-relation between inflammatory markers and the severity of COVID-19 disease

Materials and Methods- This cross-sectional study was done in a tertiary care hospital of central India among 250 consecutive hospitalized patients. All sufferers were identified in accordance to diagnosis and treatment guideline issued through MoHFW India and WHO. All the confirmed cases whom were ready to give written consent were recruited. Patients were labeled into mild, moderate, severe and critical type based on the severity of symptoms. Severe patients have to meet at least one of the following criterion's:

First, shortness of breath with respiration rate (RR) >30 times/min.

Second, oxygen saturation <93% in resting state.

The statistical analysis was done using microsoft excel 2007 and free on-line reachable website.

Observation and Results - In this study on the basis of our criteria we classified patients in two categories non-severe and severe a total 250 affected person have been participated in study 65 patients have been fall in severe category and 185 patient were in the non-severe category, there is preponderance of male sex in the study as well as in severe group. The mean age of all patient was 43 ± 2.8 in severe(S) group its higher 51.47 ± 5.8 while in non-severe(NS) group it is 40.02 ± 3.0 , Mean BMI 24.01 ± 3.53 for all the patients, in S-group it is 26.04 ± 5.63 which is higher than NS-group. Most common symptoms among all the cases is anorexia present in 94%, followed by headache 88.4%, bitter/loss of taste 87.2%, fatigue in 86%, sore throat 80.4%, dizziness and night time sweating 79.2% anxiousness among 78.4% , cough 77.6% and dyspnea 71.2%. fever is symptoms among 68% myalgia among 66.4%. other symptoms of gastrointestinal symptoms are much less regularly observed.

Immune- Inflammatory Markers like D-Dimer observed among NS-Group 366.2162 ± 33.583 and amongst S-Group 629.1071 ± 177.167 the p value observed <.001. The mean value of C-reactive protein among NS-Group 16.0445 ± 4.747 and S-Group 60.2797 ± 23.546 the p value observed <.001. The mean value of the Interleukin-6 (pg/ml) NS-Group 17.6792 ± 27.08 and S-Group 97.6515 ± 96.032 the p value observed is .005. Out of 65 patient from S-Group and

39 patients were discharged. While 26 were unfortunate and died during the treatment 21 have increase CRP level, 14 have raised IL -6 level amongst and all 26 had been having raised D-Dimer. There is no mortality amongst the NS group.

Discussion- In present study, among 65 patients in severe group, data of 65 patient analysed and mortality was in 26 (40%) patients. Which is comparable with a study done by Chilimuri et, al in New York found mortality in 43% cases of COVID 19 patients.^[14] In present study, mean age patients of Severe Group is (51.47 \pm 5.8 years) used to be considerably higher as in contrast to Non-Severe group (40.02 \pm 3.0). which is comparable with a study done by Mahase et. al mentioned considerably higher risk of mortality in advanced age population as compared to young.^[15] Yang et al also reported significantly higher mean age amongst Severe (64.6 \pm 11.2 years) as in contrast to that of non-severe (51.9 \pm 12.9 years)^[16]. Severe ARDS is the fundamental pathophysiology occur in COVID 19 infection and elder people have high risk of developing ARDS.^[17] Literature suggest that SARS-CoV infections among older individual results in sturdy immune response as in contrast to younger adults.

As a result, this immune response lead to increase in differential expression of pro-inflammatory genes and diminished in expression of type I interferon beta was once reduced.^[18] Also, the age dependent changes in T-cell and B-cell function along with excess production of type 2 cytokines may also be associated with deficient control of viral replication and more prolonged pro-inflammatory responses, potentially leading to negative outcome.^[19] In our study mortality found solely in the severe group cause for this can be vast injury to lung tissues does happen earlier than the patients develop dyspnea or low SPO2 levels, leading to poor prognosis and increased chance of developing ARDS and death. Similar to findings of our study, Du RH et. al also noticed presence of dyspnea, fatigue, sputum production was significantly associated with increased risk of mortality in COVID 19.^[20] In our study the inflammatory markers like IL6,CRP and D-Dimer had been substantially raised among the Severe group the mortality determined in this group is 40% Previous studies have suggested that the severe and aberrant host immune response are responsible for the severity of COVID-19^[13] Liu et.al^[21] took a further step to analyze the a study of Channappanavar and Perlman, in year 2017^[22], and corroborations has shows that cytokine storm may be a cause for deleterious consequence during SARS-COV-2 infection.^[23] Gupta et. al also advocate that IL-6 performs a key function in cytokine storm because of its pleiotropic property.^[24] D-Dimer, C- reactive protein and ferritin levels were significantly associated with mortality in a study by Chilimuri et. al.^[14] raised D-dimer levels in cases with COVID 19 represents alteration of the coagulation cascade which might also lead to development of extremesevere microembolic disease. Microembolic thrombi have been viewed in blood vessels of lung and other critical organs on autopsy of COVID 19 sufferers suggesting the coagulation activation in such patients.^[25] Matsumoto et. al in their study additionally indicates CRP tiers to be drastically associated with severity i.e. CRP levels have been substantially correlated with dimension of lung lesions and severity of COVID disease.^[26]

Conclusion- Our study demonstrated that high level of peripheral blood cytokine IL-6 and CRP were independent risk elements for assessing the severity of COVID-19. IL-6 played a pivotal function in the severity of COVID-19 and had a potential value for monitoring the process of severe cases. It reminds us to emphasize the cytokine storm in the progression of

COVID-19, and IL-6 blockade treatment possibly a therapeutic strategy for treating the severe patients.

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