How to Cite:
Singhal, S., Uniyal, N., Tiwari, D., & Maheshwari, S. (2022). Co-relation between inflammatory biomarkers and COVID-19 progression: A retrospective study . *International Journal of Health Sciences*, *6*(S2), 1407–1415. https://doi.org/10.53730/ijhs.v6nS2.5213

Co-relation between inflammatory biomarkers and COVID-19 Progression: A retrospective study

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***Abstract*---**Background & Objective: - Coronavirus Disease-19 (COVID-19) disease has caused considerable morbidity and mortality worldwide. The present study aims to investigate the prognostic significance of the inflammatory markers and to augment our present knowledge of these biomarkers to help in risk stratification. Methodology - The proposed study is a retrospective observational study on COVID-19 positive patients admitted in the ICU of Hospital of Government Doon Medical College, Dehradun, India from November 2020 to January 2021. Patients were categorized in to three groups moderate, severe and critical as per the criteria mentioned in methodology section in detail. Statistical Analysis- To explore the risk factors associated with illness severity of COVID-19, we categorized the patients into two groups, and one is moderate and severe and second is critical. Potential predictive variables included the following case characteristics on admission: demographic features and, comorbidity, clinical signs and symptoms and laboratory findings.

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
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Manuscript submitted: 27 Jan 2022, Manuscript revised: 18 Feb 2022, Accepted for publication: 09 March 2022

Results- Sixty-two patients were enrolled in this study with mean age of 63.24±20.12 of which 44(70.96%) were males and 18(29.03%) were females. Multiple number of patients had comorbidities with diabetes 36(58.06%) patients, followed by hypertension in 24(38.70%). Conclusion - Single prognostic inflammatory marker indicating the progression to disease severity early in disease timeline is the C - reactive protein. Neutrophil (NEU)-to-lymphocyte (LYM) ratio (NLR) with CRP together can have a good predictability of disease outcome.

***Keywords*---**inflammatory markers, COVID-19, retrospective study.

Introduction

COVID-19 disease has caused considerable morbidity and mortality worldwide. In spite lots of ongoing research, many facts about this novel coronavirus are unknown. Many lines of therapies have been instituted for the management of COVID-19 disease. COVID-19 is a pandemic with a wide spectrum of clinical presentation varying from asymptomatic to severe COVID-19 pneumonia and mortality [1, 2].

In a number of well published studies a co-relation has been found between the levels of inflammatory markers at time of presentation and the outcome of disease on individual basis [3,4, 5]. A number of inflammatory markers like TLC (Total leucocyte Count), CRP (C reactive Protein), Serum Ferritin, IL-6 (Interleukin- 6), D -dimer, procalcitonin have been implicated as the prognostic indicators for disease progression.

This study is being undertaken for academic purpose to see the prognostic significance of the inflammatory markers and to augment our present knowledge of these biomarkers to help in risk stratification. This would be helpful in instituting treatment guidelines as per risk group to provide timely intervention and mortality reduction in COVID-19 patients. Another objective is to single out a test with most important prognostic significance which can be made available at various primary health care centres facilitating the better management of COVID-19 cases at these areas, especially in the developing nation like India where the health care system is already burdened due to poor economic resources and thus not all battery of tests can be undertaken due to financial constraints.

Materials and Methods

The proposed study is a retrospective observational study on COVID-19 positive patients admitted in the ICU of Hospital of Government Medical College, Dehradun, Uttarakhand, India from November 2020 to January 2021. The institution is a dedicated COVID- 19 hospital which caters the moderate, severe and critically ill COVID- 19 patients of the Uttarakhand state. The study was approved by Research Review Board, (RRB/ GDMC/2021/1153) of GDMC. At the time of admission, all patients were screened for COVID- 19 infection by real time reverse transcriptase polymerase chain reaction (RT-PCR) assay. The data of

COVID- 19 positive patients who were admitted to ICU during the stated period was obtained from the Medical Record Section of the Institution.

Total Sixty-Two patients were enrolled for the study as per the following inclusion criteria: a) Age 18 and above. b) Patients tested RT-PCR SARS-CoV-2 positive. c) Admitted in ICU. d) Hospitalized patient with duration more than 48 hours. Patients who had chronic kidney disease (CKD), coronary artery disease (CAD), Immunosuppressed disease, autoimmune disease, Chronic Lung Disease and pregnant patients were excluded from the study to maintain a uniform cohort and remove any confounding factors so that the effect of associated disease on the prognosis can be removed.

All the COVID 19 positive patients admitted to ICU were assessed at the time of admission, on day 7 and at the time of discharge or death. Data collected included demographic profile (age, sex); history of present illness; history of comorbidities such as diabetes mellitus, CAD, CKD, COPD or any other chronic illness; clinical parameters such as heart rate (HR), blood pressure (BP), respiratory rate (RR), oxygen saturation (SpO2), temperature, conscious level (alert/ drowsy/ unconscious), source of oxygenation (nasal cannula/ face mask, non-rebreathe mask, non-invasive ventilation/ invasive ventilation); laboratory parameters such as complete blood counts (CBC), liver function test (LFT), kidney function test (KFT), random blood sugar (RBS), C reactive protein (CRP), interleukin 6 (IL-6), serum ferritin, procalcitonin, D- dimer. The laboratory tests were conducted in the Department of Biochemistry at Institution using standard protocols.

Adults with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma and/or convulsions) were given emergency airway management and oxygen therapy during resuscitation to target SpO2 ≥ 94%. Once the patient is stable, SpO2 is targeted to > 90% in non-pregnant adults. Appropriate oxygen delivery devices were used (nasal cannula for flow rates up to 5 L/min; Venturi mask for rates 6-10 L/min; and face mask with reservoir bag for flow rates 10-15 L/min). Disease severity grading was done based on WHO 10-point clinical progression scale modified as per the available modes of oxygen therapy in our institution as per the protocol. Ethical approval was sought and obtained from the GDMC, Government Doon Medical College, Research Review Board (RRB/ GDMC/2021/1153), and all study methods were performed per the Declaration of RRB regulations.

Statistical Analysis

Continuous variables were presented as median with interquartile range (IQR). Categorical variables were expressed as frequency. All patients were divided into moderate, severe and critical illness groups on three time point. To explore the risk factors associated with illness severity of COVID-19, odds of illness severity in critical patients with respect to moderate and severe patients was calculated. Potential predictive variables included the following case characteristics on admission: demographic features and, comorbidity, clinical signs and symptoms and laboratory findings. Potential predictors of severity were investigated using univariate logistic regression. A two-sided α of less than 0.05 was considered

statistically significant. All statistical analyses were conducted using SPSS software (V. 22) (IBM Institute Inc., USA).

Results

Sixty-two patients were enrolled in this study with mean age of 63.24±20.12 of which 44(70.09%) were males and 18(29.03%) were females. Multiple number of patients had comorbidities with diabetes 36(58.06%) patients, followed by hypertension in 24(38.70%). Patients with other comorbidities were excluded from the study. Mean of all the laboratory markers is shown in Table *2*.

Table *3* presents the median of age along with IQR (inter quartile Range), for categorical variables frequency was mentioned. For non- normally distributed variables median value along with inter quartile range was given. Based on disease severity for different time period (Day0, Day 7 at the time of discharge or death). The mean age is increasing with severity of disease in all three time segments. Number of patients having Chronic Respiratory Disease, Hypertension, Coronary Artery Disease, Diabetes Mellitus were more in severity. The median value of S. Ferritin is more in severe patients at the time of admission but at day 7 and at the time of discharge or death the value was decreased as compared to mild patients. N/L ratio, Urea, IL6, SGOT, SGPT, ALP, RBS, CRP , NLR and TLC had increased according to disease severity and time. The value of BIL was decreasing with time, however increasing with disease severity. S. PROCAL, S. Creatinine had increased from Day 0 to Day 7, but had decrement from day 7.

In the univariate logistic regression analysis, age (> 60 vs. ≤ 60years), gender (male vs. female), CRP (> 90 vs. ≤ 90 mg/L), Serum Procalcitonin (0-0.5 ng/mL vs ≤ 0.5 ng/mL), D. Dimer (> 0.5 mg/L vs ≤ 0.5 mg/L), S. Creatinine (0.6-1.4 mg/dl vs out of range), and TLC (4000-11000/cu mm vs > out of range) were significantly associated with severity of COVID-19 at time of admission. On Day 3, we found that the risks of having more severe illness were 5.9 (95% CI: 5.00-9.4) times higher among patients belonging to the age group 60+ years older age. Patients with CRP > 5 mg/L had 4.52(2.1-5.45) * times greater risk of severe illness compared with patients with CRP 0-5 mg/L. The risk of having severity of illness was found to be significantly higher for patients with D-dimer > 0.5 mg/ L (OR = 2.02; 95% CI: 1.11-4.03), Neutrophil count >40 % and <75 % (OR = 1.9; 95% CI: 1.1-2.8) and N/L ratio >1 (OR = 1.8; 95% CI: 1.2-3.1). The risk of having severe illness at Day 7 was found significantly higher for older age patients (>60 years) with OR being 5.7 (95% CI: 4.12-9.31). COVID-19 patients with CRP >48.8 ng/ml had OR 2.38, (95% CI): 1.21-3.24 fold greater risk of having severe illness. The risk of having severe illness was found to be significantly higher for patients with D dimer > 0.5 (OR = 1.45; 95% CI: 1.2-3.62), S. Creatinine (OR = 1.65; 95% CI: 1.12-2.89) and N/L ratio (OR = 1.8; 95% CI: 1.2-3.1). Serum concentrations of inflammatory markers (TLC, neutrophil count, lymphocyte count, CRP, ferritin, IL 6, D-dimer, procalcitonin) were measured in all moderate, severe and critical patients. Out of these neutrophil count, CRP and IL 6 were found to found to be elevated in accordance with severity grading.

Discussion

Biomarkers are the quantitative measurement of relevant parameters which reflect the clinicopathological status of a disease. Numerous inflammatory biomarkers have been studied in various researches to see their role in the progression and severity of COVID-19 disease. These markers include White Blood Cell count, neutrophil count, lymphocyte count, neutrophil lymphocyte ratio, platelet count, C-Reactive Protein, Erythrocyte Sedimentation Rate, Interleukin-6, Interleukin-8, Interleukin-10, procalcitonin, Tumour Necrosis Factor α, ferritin, Lactate Dehydrogenase, D-dimer, cardiac troponin. The immune system plays an important role in the pathogenesis of the disease as it helps in the elimination of virus as part of host defense. But if this immune response becomes exaggerated, it leads to excessive release of inflammatory cytokines causing damage to own cells [4, 5]. Thus, COVID-19 infection does not only affect lungs but may also affect other organs in severe cases because of systemic inflammatory response. As cytokine analysis is not routinely available in laboratories and is costly, ferritin, C-reactive protein (CRP) can be used as surrogate markers of infection [6]. Derangement of these biomarkers would be a useful indicator of disease progression and timely treatment can be initiated before significant clinical deterioration of the patients affected by COVID-19 disease occur. Most of the biomarkers are not specific to COVID-19 disease as their levels are affected by many other factors apart from the disease itself. For example, total leucocyte count also increases in other bacterial and viral infections, corticosteroid therapy.

In the present study, age > 60years; male gender; raised levels of CRP, S. procalcitonin, S. creatinine, and TLC were significantly associated with severity of COVID-19 disease at the time of admission. Similarly, Pan Ji et al. [7] found elevated levels of white blood cell count, C-reactive protein, procalcitonin, erythrocyte sedimentation rate, interleukin-6, and interleukin-10 in patients with severe disease and in patients who died. Also, Kermali et al3 found similar results with CRP, serum amyloid A, IL 6, LDH, N/L ratio, D dimer, cardiac troponin, and renal biomarkers.

Age more than 60 years was associated with disease severity throughout the disease course. On the other hand, male gender had more severe disease than the female counterpart at the time of admission only and no significant gender-based difference in disease severity was found on later assessments. In an analysis of a large US cohort [8] and a study in China [9], it was found that males were more likely to test positive for COVID-19, more likely to have severe disease and fatal outcome than females, independent of age. CRP was significantly associated with disease severity at all time points and was more than two times elevated in critical patients than in moderate to severe patients. This corroborates with findings of multiple researchers such as Wang et al, Li et al, Liu et al, Ji et al [10, 11, 12, 13].

In our study, increased procalcitonin level was associated with more than two times risk of having severe symptoms at the time of presentation. But its serial measurements later during disease course did not significantly correlate with the severity. This may be because during viral infections concentration of interferon (INF)-γ increases which inhibits the synthesis of procalcitonin [14] Procalcitonin levels increase during bacterial infection and thus increase in procalcitonin in

disease timeline may suggest a bacterial coinfection. Hence it is prudent to expect normal procalcitonin value in patients with uncomplicated SARS-CoV-2 infection. Since we could not get bacterial cultures done in our present study, it was difficult to correlate serum procalcitonin levels with viral infection or bacterial coinfection. In contrast to our observation, Rui Hu et al. [15] and Francesco Del Sole et al. [16] found positive correlation of serum procalcitonin with disease severity and usefulness of serial measurements in predicting the disease prognosis.

D dimer levels correlated with the severity of COVID-19 disease and was found to be significantly higher in critical patients at all time points except on day of admission. This suggests more rise in D dimer levels in critical patients with increased disease duration which may be due to hyper fibrinolytic state and increased inflammatory burden [17]. Since not all patients with raised D dimer levels had evidence of thromboembolism, D dimer can be considered as a marker of disease severity.

In usual clinical practice, increased D dimer levels can be seen in thromboembolism, DIC, pregnancy, cancer, inflammation, and surgery [18, 19, 20]. Similar results were found in other studies [21] where patients with severe COVID-19 have a higher level of D-dimer than those with non-severe disease, and D-dimer greater than 0.5 mcg /ml is associated with severe infection in patients with COVID-19. In a meta-analysis, Haoting Zhan et al [22] found D-dimer to be moderately accurate in predicting severe and fatal cases of COVID-19. The study also showed D-dimer to exhibit high sensitivity but relatively low specificity for detecting COVID-19-related VTE events, indicating that it can be used to screen for patients with VTE.

NLR has also been proposed as prognostic marker for COVID-19 infection. It is an independent marker of systemic endothelial dysfunction and predictor of cardiovascular mortality [23]. It is proposed that NLR indicate endothelial dysfunction in COVID-19 infection due to endothelial thrombo-inflammatory syndrome following viral endothelial damage [24] It is noteworthy that since complete blood count is commonly performed, cheap and easily available parameter; NLR can be easily calculated and frequently monitored as compared to other tests. In our study, during assessments following admission day, NLR was found to be significantly raised in critical patients in comparison to patients with moderate and severe disease. This is similar to the findings of a study [25] where patients with worse outcomes had significantly higher NLR at admission ($P = .001$), greater increase in Peak NLR ($P < .001$) and higher increasing speed of NLR ($P = .003$). In contrast to this, another study cautioned against the use of NLR as independent markers for disease severity [26].

Limitations

Blood gas values as clinical marker of disease progression is not considered in the study. Post discharge status was also not taken in account. We did not include high risk patients who had CKD, CAD, Immunosuppressed disease, autoimmune disease, chronic lung disease and pregnant.

Conclusions

It is conclude that biomarkers' levels are affected by the severity of COVID-19 infection. Different biomarkers show different trends as the disease takes its course. Age more than 60 years is an independent risk factor determining the disease outcome and severity. Males are more likely to have severe COVID-19 illness compared to females. Single prognostic bio-inflammatory marker indicating the progression to disease severity early in disease timeline is the C - reactive protein. NLR with CRP together can have a good predictability of disease outcome. Since both CRP and NLR are easily available investigations, these can be done at centres with minimal facilities to improve disease outcome.

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Table 1:- WHO 10- point ordinal scale of clinical progression (Modified as per hospital treatment protocol)

Uninfected	No clinical/ virological evidence of disease	
Ambulatory	Asymptomatic; viral RNA detected	
	Symptomatic; independent	
Hospitalized (moderate disease SPO2<94-91% at room air)	Oxygen by nasal cannula /mask up to 5 ltrs.	Moderate
Hospitalized (moderate disease SPO2<94-91% at room air)	Oxygen by Venturi mask for rates 6–10 L/min	
Hospitalized (moderate disease SPO2<94-91% at room air)	Oxygen by high flow face mask with reservoir bag for flow rates 10–15 L/min)	
Hospitalized (severe disease, SPO2 <= 90% at room air)	Oxygen by NIV.	Severe
Hospitalized (severe disease, SPO2 <= 90% at room air)	Intubation and mechanical ventilation, pO2/FiO2 ≥150 or SpO2/FiO2 ≥200	
Hospitalized (severe disease, SPO2 <= 90% at room air)	Mechanical ventilation pO2/FIO2 <150 (SpO2/FiO2 <200) or vasopressors	Critical
Hospitalized (severe disease, SPO2 <= 90% at room air)	Mechanical ventilation pO2/FiO2 <150 and vasopressors, dialysis, or ECMO	
Dead	Death	

Table 2: Clinical features concerning the enrolled COVID-19 population.

Variables,	Total (N= 62)
Age, Years	63.24±20.12
Sex	
Male	44(70.96)
Female	18(29.03)
Days of symptomatology at admission	8.6±4.8
Diagnosis	
B/L Pneumonitis with T2-DM	36(58.06)
B/L Pneumonitis with HTN	24(38.70)
LFT	
BIL (0.1-1.2)mg/dl*	0.7±0.4
SGOT (15-37) IU/L*	57(22)
SGPT(30-65)IU/L*	94(48)
ALP (50-136) UL/L*	129(24)
Urea(13-45)mg/dl*	32(12)
S. Creatinine(0.6-1.4)mg/dl*	0.9±0.4
RBS (70-140)mg/dl*	189±28
CRP (0-5)mgm/L*	137±56
S. Ferritin (30-400)ng/ml	1245±489
S. PROCAL(0-0.5)ng/ml*	0.134±0.21
D DIMER(0.00-0.50)mg/L*	0.47±0.12
IL6 (0-35)pg/ml*	101.17±27.15
SPO2%	92%(26)
RR (12-16)/min*	21.77±1.45
CBC	
HB (12-16)gm%*	12.24±1.48
TLC(4000- 11000)/cumm*	7840±2512
Platelets	1.32±0.98

* Normal Ranges
B/L Pneumonitis with T2-DM (Bilateral Pneumonitis with Type 2 diabetes mellitus)
B/L Pneumonitis with HTN (Bilateral Pneumonitis with Hypertension)
LFT (liver Function test)
BIL (bilirubin)
SGOT (serum glutamic-oxaloacetic transaminase)
SGPT (serum glutamic-pyruvic transaminase)
ALP (Alkaline phosphatase)
S. Creatinine (Serum Creatinine)
RBS (Random Blood sugar)
CRP (c-reactive protein test)
S. Ferritin (Seum Ferritin)
S. PROCAL(Serum procalcitonin)
IL6 (Interleukin 6)
SPO2 (Oxygen saturation)
RR (Respiratory rate)
CBC (Complete blood Count)
HB (Hemoglobin)
TLC (Total Leukocyte Count)

Table 3:- Distribution of co morbidities and biomarkers according to severity of patients

	Day 0		
	Moderate	*Severe*	*Critical*
Comorbidity	*Number*		
Chronic Respiratory Disease	*4*	*7*	*9*
Hypertension	*7*	*8*	*11*
Coronary Artery Disease	*8*	*10*	*13*
Diabetes Mellitus	*12*	*15*	*19*
	Median (IQR)		
Age	*61*	*62*	*68*
	(58.0-69.0)	*(49.0-71.0)*	*(56.0-74.0)*
S. Ferritin (ng/ml)	*802*	*605*	*789*
	(472.0-1022.0)	*(351.0-1045.0)*	*(324.0-1105.0)*
Urea nitrogenmmol/L	*4.1 (3.2-5.4)*	*5.2 (3.6-8.5)*	*7.2 (3.9-8.9)*
IL6(PG/ML)	*69*	*74*	*78*
	(56.0-84.0)	*(66.0-91.2)*	*(67.0-92.0)*
Total Bilirubin(mg/dl)	*0.8*	*1.1*	*1.2*
	(0.4-0.12)	*(0.8-1.12)*	*(0.7-1.16)*
SGOT(IU/L)	*42 (36-53)*	*63 (49-78)*	*82 (63-98)*
SGPT(IU/L)	*48 (39-69)*	*78 (56-98)*	*102 (94-136)*
ALP(IU/L)	*51 (39-64)*	*115 (86-136)*	*104 84-139)*
RBS(mg/dl)	*152(102-259)*	*234(109-369)*	*489(321-547)*
CRP(mg/dl)	*42*	*66*	*92*
	(23.0-66.0)	*(46.0-82.0)*	*(84.0-106.0)*
S. PROCALCITOININ	*0.04*	*0.26*	*0.34*
(mg/ml)	*(0.03-0.17)*	*(0.02-0.12)*	*(0.03-0.12)*
S. Creatinine(mg/dl)	*0.8*	*0.9*	*1.2*
	(0.2-0.15)	*(0.4-1.2)*	*(0.8-1.6)*
D DIMER(mg/l)	*0.7*	*5.84*	*7.02*
	(0.2-0.13)	*(3.23-8.91)*	*(3.01-12.91)*
SPO2 %	*97(87-100)*	*98(94-100)*	*94(89-99)*
Neutrophil count × 10^9/L	*2.3(1.6-4.7)*	*3.5(2.3-5.6)*	*4.7(3.1-8.9)*
Lymphocyte count x 10^9/L	*0.6(0.5-0.8)*	*0.9(0.7-1.1)*	*0.8(0.5-1.2)*
N/L ratio	*1.9 (1.2–2.5)*	*2.3(1.5-4.9)*	*3.2(2.1-4.8)*
TLC (10^5)/cumm	*1.2(1.1-2.3)*	*1.3(1.2-2.9)*	*1.6(1.1-3.1)*
	Day 7		

	Moderate	*Severe*	*Critical*
Comorbidity		*Number*	
Chronic Respiratory Disease	*4*	*7*	*9*
Hypertension	*7*	*8*	*11*
Coronary Artery Disease	*8*	*10*	*13*
Diabetes Mellitus	*12*	*15*	*19*
		Median (IQR)	
Age	*61*	*62*	*68*
	(58.0-69.0)	*(49.0-71.0)*	*(56.0-74.0)*
S. Ferritin (ng/ml)	*1287*	*1145*	*1045*
	(874.0-1523.0)	*(745.0-1456.0)*	*(974.0-1365.0)*
Urea nitrogenmmol/L	*4.6 (3.2-5.8)*	*5.6 (3.9-7.2)*	*7.1 (2.1-8.5)*
IL6(PG/ML)	*72*	*76*	*79*
	(66.0-88.0)	*(68.0-84.0)*	*(67.0-91.0)*
Total Bilirubin(mg/dl)	*0.7*	*1.2*	*1.8*
	(0.3-1.12)	*(0.6-1.8)*	*(0.6-2.3)*
SGOT(IU/L)	*48 (39-57)*	*68 (57-82)*	*88 (72-102)*
SGPT(IU/L)	*54 (48-65)*	*89 (74-106)*	*116 (94-129)*
ALP(IU/L)	*69 58-82)*	*73 (46-86)*	*84 (62-109)*
RBS(mg/dl)	*197(165-369)*	*365(269-487)*	*489(368-523)*
CRP(mg/dl)	*48*	*62*	*88*
	(29.0-59.0)	*(44.0-73.0)*	*(63.0-99.0)*
S. PROCALCITOININ	*0.62*	*0.32*	*0.54*
(mg/ml)	*(0.42-0.73)*	*(0.25-0.49)*	*(0.26-0.45)*
S. Creatinine(mg/dl)	*0.7*	*1.3*	*1.4*
	(0.2-0.10)	*(0.9-1.12)*	*(0.2-1.9)*
D DIMER(mg/l)	*6.12*	*0.7*	*8.59*
	(3.21-8.09)	*(0.5-0.16)*	*(4.12-16.32)*
SPO2 %	*96(89-100)*	*98(88-100)*	*99(87-100)*
Neutrophil count × 10^9/L	*2.9(1.3-4.6)*	*4.6(2.3-6.9)*	*5.3(2.1-6.5)*
Lymphocyte count x 10^9/L	*0.7(0.4-0.9)*	*0.6(0.4-0.7)*	*0.5(0.2-0.8)*
N/L ratio	*1.8(1.2-2.9)*	*3.1(1.6-3.7)*	*3.9(1.9-5.4)*
TLC (10^5)/cumm	*1.1(1.1-1.8)*	*1.2(1.2-2.1)*	*1.3(0.9-1.12)*
		Final Outcome	
	Moderate	*Severe*	*Critical*
Comorbidity		*Number*	
Chronic Respiratory Disease	*4*	*7*	*9*
Hypertension	*7*	*8*	*11*

Coronary Artery Disease	*8*	*10*	*13*
Diabetes Mellitus	*12*	*15*	*19*
	Median (IQR)		
Age	*61*	*62*	*68*
	(58.0-69.0)	*(49.0-71.0)*	*(56.0-74.0)*
S. Ferritin (ng/ml)	*1340*	*1147*	*1078*
	(854.6-1658.0)	*(871.0-1478.0)*	*(914-1542)*
Urea nitrogenmmol/L	*4.4 (3.2-5.8)*	*5.8 (3.6-7.9)*	*7.9 (4.1-9.6)*
IL6(PG/ML)	*73*	*75*	*80*
	(66.0-86.0)	*(67.0-88.0)*	*(63.0-92.0)*
Total Bilirubin(mg/dl)	*0.4*	*0.9*	*1.9*
	(0.2-0.6)	*(0.4-0.13)*	*(0.9-2.9)*
SGOT(IU/L)	*58 (41-89)*	*64 (56-78)*	*93 (79-108)*
SGPT(IU/L)	*62 (54-78)*	*102 (86-142)*	*143 (120-159)*
ALP(IU/L)	*94 (78-132)*	*98 (73-121)*	*126 (91-156)*
RBS(mg/dl)	*234(136-488)*	*348(236-498)*	*547(321-602)*
CRP(mg/dl)	*56*	*67*	*94*
	(38.0-76.0)	*(59.0-78.0)*	*(79.0-109.0)*
S. PROCALCITOININ	*0.31*	*0.14*	*0.23*
(mg/ml)	*(0.23-0.46)*	*(0.06-0.23)*	*(0.05-0.26)*
S. Creatinine(mg/dl)	*0.9*	*0.6*	*1.1*
	(0.4-1.9)	*(0.1-1.3)*	*(0.6-1.6)*
D DIMER(mg/l)	*4.89*	*0.4*	*0.19*
	(3.21-9.12)	*(0.1-0.6)*	*(0.3-0.31)*
SPO2 %	*94(82-100)*	*97(82-100)*	*94(83-100)*
Neutrophil count × 10^9/L	*3.2(2.1-4.9)*	*4.8(2.6-5.8)*	*7.6(4.3-9.9)*
Lymphocyte count x 10^9/L	*0.4(0.1-0.6)*	*0.9(0.6-1.2)*	*0.8(0.6-1.2)*
N/L ratio	*2.9(2.1-3.9)*	*3.1(1.2-3.9)*	*4.8(2.9-5.7)*
TLC (10^5)/cumm	*1.4(0.2-1.9)*	*1.2(1.1-2.3)*	*1.1(0.8-1.12)*

Table 4:- Risk for Severity among COVID-19 patients using Logistic Regression

Variables	Day 1	Day -7	discharge / death
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
Age >60 Years	4.6 (3.10–9.4) *	5.9 (5.00–9.4) *	5.7 (4.12–9.31) *
Males	1.21(1.1-2.3) *	0.9(0.2-1.9)	1.8(0.7-2.31)
Laboratory Findings			
CRP	***3.71****(2.3-4.15)* *	4.52(2.1-5.45) *	2.38(1.21-3.24) *
S. PROCAL	2.02(1.12-3.59) *	1.30(0.54-2.65)	0.78(0.35-1.59)
D DIMER	1.21(0.58-2.14)	2.02(1.11-4.03) *	1.45(1.2-3.62) *
Il6	1.60(0.74-3.58)	1.02(0.69-3.05)	1.11(0.9-2.25)
S. creatinine	2.02(1.11-4.02) *	1.89(1.2-3.12)	1.65(1.12-2.89) *
Neutrophil count × 10^9/L	1.2(0.8-2.3)	1.9(1.1-2.8) *	2.2(1.7-3.9) *
N/L ratio	1.3(0.9-2.9)	1.8(1.2-3.1) *	2.1(1.3-4.1) *
Lymphocyte count,	1.12(0.9-1.89)	1.01(0.68-1.96)	0.98(0.86-1.19)
TLC (10^5)	1.48(1.02-2.12) *	1.12(0.89-1.56)	0.99(0.58-1.85)