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Correlation analysis between COVID-19 disease severity and clinical and biochemical parameters in a rural tertiary care hospital of central Maharashtra, India

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Original Article

Abstract

BACKGROUND: The novel coronavirus (COVID-19) infection continues to wreak havoc across the developed world and now seems to have gained a strong foothold in developing countries including India. The mortality rate in severe/critically ill patients with COVID-19 is high. The present study was conducted to analyze the clinical and laboratory markers that discriminate severe/critically ill patients from those with mild/moderate COVID infection early for better clinical management of the disease.

METHODS: This laboratory-based, cross-sectional study was conducted on 517 confirmed cases of COVID-19 disease. The patients were divided into mild/moderate and severe/critical groups. Correlation analysis between COVID-19 disease severity and clinical and biochemical parameters was performed on the confirmed COVID-19 infection patients admitted to Shri Vasantrao Naik Government Medical College, Yavatmal, from March 15, 2020, to July 20, 2020. The Pearson correlation coefficient was used for the variables with normal distribution. Cut-off values for critically ill patients were speculated through the receiver-operating characteristics (ROC) curve via SPSS software.

RESULTS: The study population included 517 confirmed cases of COVID-19 infection. The median age of the patients was 34 years (IQR: 22–47; range: 18-64 years), with a male to female ratio of 1.2:1. Moreover, 176 (34.04%) patients had one or more co-morbidities, and hypertension (11.5%) and diabetes mellitus (DM) (10.44%) were the most common coexisting co-morbidities. A significant difference was observed between the mild/moderate group and severe/critically ill patients group in the laboratory parameters of serum ferritin, D-dimer, CRP, LDH, prolactin, albumin, ionic calcium, cTnI, and IL6.

CONCLUSION: Clinicians should consider age, co-morbidities, and laboratory parameters like lymphopenia, elevated D-dimer levels, elevated CRP, IL6, serum ferritin, cTnI, and low levels of ionized calcium in risk stratification to predict the severity of COVID-19 in hospitalized patients.

KEYWORDS: COVID-19; Correlation Analysis; Laboratory Parameters; Prognosis

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Introduction

The novel coronavirus (COVID-19) infection is causing outbreaks of viral pneumonia throughout the world and now seems to have gained a strong foothold in developing countries including India, the second most populous country in the world.[1,5] As of now, more than 43147494 individuals have been infected and 1155553 people have succumbed

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to the infection across the globe. In India as of 27th of October 2020 nearly 7946429000 patients have been infected; Maharashtra state has reported the highest number of cases (1648665), followed by Karnataka (805947) and Tamil Nadu at (711713).[6]

The COVID-19 infection ranges in severity from asymptomatic or mild to moderate and severe. Most of the infected patients are asymptomatic or have mild to moderate severity of the diseases, with a better prognosis. However, a significant proportion of patients with clinically evident infection develop severe infection with remarkably high mortality.[5] The overall mortality rate is uncertain, as the total number of cases (including undiagnosed persons with milder illness) is unknown.[7] Therefore, the early recognition of critically ill patients with COVID-19 infections for timely triage of the cases to improve recovery rates and to reduce mortality has become a major challenge for intensivists.

Therefore, identification of clinical and laboratory parameters that define the severity of COVID-19 infection is necessary. Moreover, for the recognized risk factors, such as extremes of age, pregnancy, and underlying co-morbidities especially cardiovascular diseases, diabetes mellitus (DM), hypertension, chronic obstructive pulmonary diseases (COPD), and immunosuppression, various laboratory markers have been identified that modulate the severity of COVID-19 infection.[2]

Wang et al., in a study among 143 patients with COVID-19 infection, found that C-reactive protein of more than 64.79 mg/l, lactate dehydrogenase of more than 245 U/l, D-dimer of more than 0.96 µg/ml, serum amyloid A of more than 100.02 mg/l, or albumin of less than 36 g/l as the markers of the progress of COVID-19 to critical stage, which should be closely observed and possibly prevented. Lymphocyte count, serum potassium, high-density lipoprotein cholesterol, and procalcitonin (PCT) may also be prognostic indicators.[8]

Henry et al. conducted a meta-analysis of 21 studies on COVID-19 infection, on a total of 3377 patients and 33 laboratory parameters.[9] They concluded that patients with severe and fatal disease had significantly increased white blood cell (WBC) count, and decreased lymphocyte and platelet counts compared to patients with non-severe disease and disease survivors. Biomarkers of inflammation, cardiac and muscle injury, liver and kidney function measures, and coagulation measures were also significantly elevated in patients with both severe and fatal COVID-19. Interleukins 6 (IL-6) and 10 (IL-10) and serum ferritin were strong discriminators for severe disease.[9]

However, most of these studies were conducted in developed countries with ICU infrastructure and fully equipped clinical laboratories. In an economically developing country like India, understanding predictors of disease severity and outcome are crucial to providing early preventive measures for a better outcome especially in rural areas where intensive care setup might not match the increasing demand for the service.

Therefore, this study was conducted in a rural tertiary care hospital to analyze clinical and biochemical parameters that might be helpful in determining the severity of the COVID-19 infection for timely management of the patients.

Methods

This was a laboratory-based, cross-sectional study. All consecutive patients with confirmed COVID-19 infection admitted to Shri Vasantrao Naik Government Medical College, Yavatmal, (assigned by the government to the treatment for COVID-19) from March 15, 2020, to July 20, 2020, were included in the study. This study was approved by the Institutional Ethical Committee.

The clinical classification of severity and assessment parameters are as follows:[4]

a) Mild: minor symptoms of cough, nasal

congestion, and headache without symptoms of hypoxia, normal saturation, and no pneumonia in imaging

b) Moderate: fever, cough dyspnea, SpO2 of less than 94%, and pneumonia in imaging, but no signs of severe disease

c) Severe:

Adolescent or adult: clinical signs of pneumonia plus one of the following: 1) respiratory rate > 30 breaths/minute, 2) severe respiratory distress, 3]) SpO2 < 90% on room air;

Child: cough or difficulty in breathing plus at least one of the following: central cyanosis or SpO2 < 90%, severe respiratory distress signs of pneumonia with any of the danger signs of inability to breastfeed or drink, lethargy or unconsciousness, or convulsions

d) Critical: acute respiratory distress syndrome with mechanical support, sepsis with multiple organ dysfunctions, or septic shock using SOFA (Sequential Organ Failure Assessment Scale).

In the present study, cases with a mild/moderate symptom were classified as mild/moderate group, and those with severe or critical symptoms were classified as a severe/critical group. Laboratory tests and disease severity were assessed within 1-2 days of inpatient admission. The diagnosis and clinical classification of COVID-19 infection was based on the clinical management protocol, COVID-19 (Version 3) developed by the Indian Ministry of Health and Family Welfare.[3]

Data collection: From all suspected patients with clinical signs and symptoms of COVID-19 infection admitted to the emergency department, nasopharyngeal swab specimens were obtained for real-time or conventional RT-PCR test in a designated authorized laboratory. Tests on sputum and respiratory secretion for the detection of other respiratory infections (Viral, bacterial, and fungal) to rule out coinfections/dual infections were performed in the microbiology laboratory of the hospital.

Blood samples were also sent for complete blood count and coagulation studies. A comprehensive metabolic panel (CMP), including LFT, KFT, serum electrolyte, serum ferritin, and ionized calcium, was performed for all the participants using an automated biochemistry analyzer (Merilyzer AutoQuant 400, Meril Diagnostics Pvt. Ltd., Mumbai, India). D-dimer, CRP, and cardiac troponin I (cTnI) levels were assessed through the fluorescence immunoassay rapid quantitative test using a Fine Care analyzer.

Patients' clinical data related to epidemiological history, age, any type of co-morbidity, vital signs and symptoms, laboratory parameters, treatment, and clinical outcome were obtained from the patient's record in the hospital information system (HIS) and the medical record department (MRD) and were analyzed retrospectively.

Statistical analysis: Mean, median, and interquartile range (IQR) were calculated for continuous variables, and frequencies in rates and percentages were calculated for categorical variables. The Kolmogorov-Smirnov test was used to verify the normality of the distribution of continuous variables; our data follows a normal distribution. The chi-square test was used for categorical variables. The Pearson correlation coefficient was used for the variables with normal distribution. Receiver-operating characteristics (ROC) curve analysis was used to determine the positive correlation between disease severity and increased level of biochemical parameters. Statistical analyses were performed using SPSS software (version 20; IBM Corp., Armonk, NY, USA). A p-value of less than 0.05 was considered as statistically significant at a 95% confidence interval (CI).

Results

The study population included 517 confirmed cases of COVID-19 infection. Most of the patients (71.40%) had a history of travel from

the containment zone of Maharashtra State and these cases were not community-acquired. The median age was 34 years (IQR, 22–47; range, 18–64 years), and 286 participants were men and 231 were women with a man to woman ratio of 1.2:1. Of the 517 patients, 176 (34.04%) had one or more co-morbidities. Hypertension (60 [11.5%]), DM (54 [10.44%]), and chronic obstructive pulmonary diseases (45 [8.7%]) were the most common coexisting comorbid conditions. The most common symptoms at the initial stage of the disease were fever (469 [90.17%]), cough (307 [59.38%]), myalgia (267 [54.1%]), headache (171 [33.07%]), breathlessness (133 [25.7%]), chest tightness (149 [28.8%]), and dyspnea (97 [18.7%]). Less common symptoms included dysgeusia, nausea or vomiting, and diarrhea (Table 1).

X-ray and high-resolution computed tomography (HRCT) showed bilateral mid and lower zone multiple lung lobes consolidation or bilateral involvement in 290 mild to moderate cases and in 178 severe/critically ill cases. Figure 1 shows the X-ray images of a typical patient with early-stage bilateral consolidation.

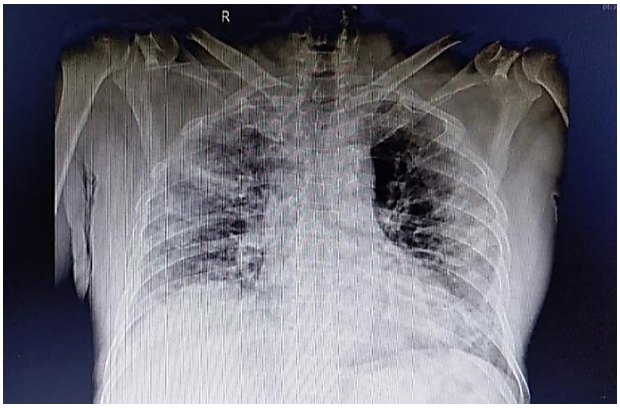

Figure 1. X-ray images of a typical patient with early-stage bilateral consolidation

Table 1. Demographic and baseline characteristics of COVID-19 disease

Characteristics	Total (N = 517)	Mild to moderate cases (N = 332)	Severe/ critically ill cases (N = 185)	P
Age Median (IQR) (Year)	34(22-47)	25(18-32)	50(45-60)	
Sex				0.46
Male	286(55.3)	188 (56.6)	98 (43.4)	
Female	231(44.7)	144 (42.3)	87 (37.66)	
CO-Morbidities				< 0.001
NO	341 (65.9)	247 (74.39)	66 (35.67)	
Hypertension	60 (11.60)	22 (6.6)	37 (20)	
Diabetes Mellitus	54 (10.44)	19(5.17)	36(19.45)	
Cardiovascular disease	8 (1.54)	1 (0.30)	7 (3.78)	
COPD	45 (8.70)	14 (4.21)	31 (16.75)	
CKD	9 (1.74)	1 (0.30)	7 (3.78)	
Signs and Symptoms				< 0.001
Fever	469 (90.17)	296 (89.1)	173 (93.51)	
Dry Cough	307 (59.38)	226 (68.07)	81 (43.71)	
Expectoration	73 (14.11)	9 (2.71)	64 (34.59)	
Myalgia	267 (54.1)	234 (70.48)	33 (17.83)	
Cold	255 (49.5)	202 (60.84)	53 (28.64)	
Headache	171 (33.07)	102 (30.03)	69 (37.29)	
Anorexia	235 (45.45))	157 (47.28)	72 (42.16)	
Breathlessness	133 (25.7)	30 (9.03)	103 (55.6)	
Dyspnea	97 (18.7)	11(3.3)	86(46.48)	
Chest pain	149 (28.8)	48 (14.4)	111 (60)	
Dysgeusia	103 (19.9)	19 (5.7)	84 (40.4)	
Nausea and vomiting	85 (16.44)	40 (12.04)	45 (24.32)	
Diarrhea	82 (15.86)	37 (11.74)	47 (25.40)	
HRCT Multiple lung lobe or bilateral involvement	468	290	178	

COPD: Chronic obstructive pulmonary disease; CKD: chronic kidney disease; HRCT: High-resolution computed tomography

The median age of the severe/critically ill cases was higher than the mild/moderate cases (50 years [IQR, 45–60] vs. 25 years [IQR, 18-32]; P = 0.085), but this difference was statistically insignificant. Similarly, we noticed that patients with severe infection were more likely to have underlying co-morbidities, including hypertension (37 [20%] vs. 22 [6.6%], DM (36 [19.45%] vs. 19 [5.7%]), and COPD (31 [16.75%] vs. 14 [4.2%]). Compared with the mild/moderate group, severely/critically ill patients commonly presented with dyspnea (3.3% vs. 46.48%), shortness of breath (9.03% vs. 55.6%), high grade fever (89.1% vs. 93.51), cough with expectoration (2.7% vs. 34.59%), and dysgeusia (5.7% vs. 40.4%).

There were significant differences between the mild/moderate and severe/critically ill patients in terms of the laboratory parameters, including hematological parameters. The absolute lymphocyte count was normal or marginally decreased in the mild/moderate group, but it was significantly lower normal lymphocyte range for age and sex in the severe/critically ill group. Moreover, 54/185 cases of severe/critically ill patients had thrombocytopenia (platelet count below one lac/cumm). Coagulation studies showed increased plasma level of D-dimer in severe/critically ill patients (0.7 ng/ml, IQR 0.50-1.00).

Besides, significant differences were seen between the mild/moderate and severe/critical groups in other biochemical findings, as serum ferritin, CRP, prolactin, albumin, vitamin D, calcium, ionic calcium, urea, creatinine, ALT, CKMB, and interleukin 6 (IL-6) (Table 2).

Table 2. Laboratory parameters of patients with mild/moderate disease and severe disease

Laboratory parameters	Normal range	Median Total		Mild/moderate		Severe /critically ill cases	
		(n = 517)	IQR	(n = 332)	IQR	(n = 185)	IQR
D-dimer	< 0.5	0.4	0.20-0.50	0.3	0.2-0.40	0.7	0.50-1.10
Sr. Ferritin	30-220	143	120-515	124	119-140	515	500-530
IL6	0-16.4	19	17-22	17	16-19	24	20-33
CRP	< 1	11	9-20	9	9-11	21	19-34
Total Bilirubin	< 1.2	0.5	0.30-0.90	0.3	0.30-0.50	0.9	0.90-1.0
Albumin	3.4-5.4	4.9	4.80-5.20	5.1	4.9-5.2	5.3	5.2-5.7
ALT	<40	20	10-50	11	10-20	35	30-35
AST	< 40	31	15-39	17	11--31	39	37-39
LDH	140-280	194	194-321	194	170-194	321	310-333
ALP	< 135	112	110-120	110	109-110	120	120-120
CKMB	< 5	4.5	4.1-4.7	4.7	3.1-4.7	4.4	4.4-4.5
Cardiac troponin	< 0.30	0.2	0.19-0.27	0.19	0.19-0.20	27	25-29
Calcium	8.5-10.5	9.1	8.4-10.5	9.5	9.1-10.6	8.3	8.3-8.4
Ionic calcium	4.4-5-4	4.7	4.3-5.7	4.9	4.5-5.5	4.3	4.2-4.3
Parathormone	11-51	49.27	20-49.27	35.15	14.47-40.15	49.27	49.27-50.13
Vitamin D	12-20	35	30-40	40	35-45	30	30-30
Urea	10-40	25	14-35	18	12-25	35	32-37
Creatinine	0.6-1.2	0.8	0.8-1.0	0.8	0.80-0.60	1	0.9-1.1
PT	9-14	12.16	11.32-12.23	12.16	11.20-12.23	12.16	12.13-13.21
APTT	21-37	33.12	31.14-35.17	33.12	31.14-32.15	38.11	33.12-40.11
Hemoglobin g/l	110-160	11.3	109-123	11.4	109-136	11.2	107-11.7
Total leucocyte count × 10^9/l	4.5-10.5	7	5-10	7	5-9	15	12-21
Neutrophil count × 10^9/l	1.4-6.5	5	3-7	5	2-6	14	11-20
Lymphocyte count × 10^9/l	1.2-3.4	1	0.8-1.4	1.2	1.2-1.8	0.6	0.5-0.9
Platelet count × 10^9/l	150-450	196	155-264	200	163-256	100	59-167

IL6: Interleukin-6; CRP: C-reactive protein; ALT: Alanine transaminase; AST: Aspartate Transaminase; LDH: Lactate dehydrogenase; ALP: Alkaline phosphatase; CKMB: Creatine Kinase-MB; PT: Prothrombin time; APTT: Activated partial thromboplastin time

Significant correlations were observed between the severity of COVID-19 and age, CRP, D-dimer, serum ferritin, urea, creatinine, albumin, AST, ALT, calcium, ionic calcium, LDH, PT, APTT, IL6, TBIL, ALP, vitamin D, and parathyroid hormone (Table 3).

Table 3. Correlation coefficient and p-value between laboratory parameters and severity of COVID-19 disease

Parameters	r	P
Age	0.053	0.085
D-dimer	0.666	0.031
Sr. Ferritin	0.588	0.089
IL6	-0.79	0.019
CRP	-0.97	0.003
BILU	0.331	0.070
ALBUMIN	0.726	0.025
ALT	-0.697	0.003
AST	0.459	0.059
LDH	0.327	0.071
ALP	0.244	0.084
CKMB	-0.719	0.026
Cardiac troponin	0.355	0.067
Prolactin	0.594	0.039
Calcium	-0.567	0.041
Ionic calcium	-0.846	0.014
Paratharmone	0.428	0.057
Vitamin D	-0.533	0.045
Urea	0.841	0.014
Creatinine	0.706	0.027
PT	0.348	0.068
APTT	0.408	0.060
Total WBCs count	0.320	0.070
Neutrophil count	0.350	0.066
Lymphocyte count	0.716	0.020

IL6: Interleukin-6; CRP: C-reactive protein; ALT: Alanine transaminase; AST: Aspartate transaminase; LDH: Lactate dehydrogenase; ALP: Alkaline phosphatase; CKMB: Creatine kinase-MB; PT: Prothrombin Time; APTT: Activated partial thromboplastin time

Figure 2 shows the area under the ROC curve of the study parameters in predicting the severity of COVID-19 disease. Age (AUC = 0.963; P < 0.001), D-dimer (AUC = 0.921; P = 0.00), LDH (AUC = 0.961; P < 0.01), CRP (AUC = 0.939; P < 0.001), and albumin (AUC = 0.791; P < 0.001) had a very good accuracy in predicting cases with severe COVID-19 disease.

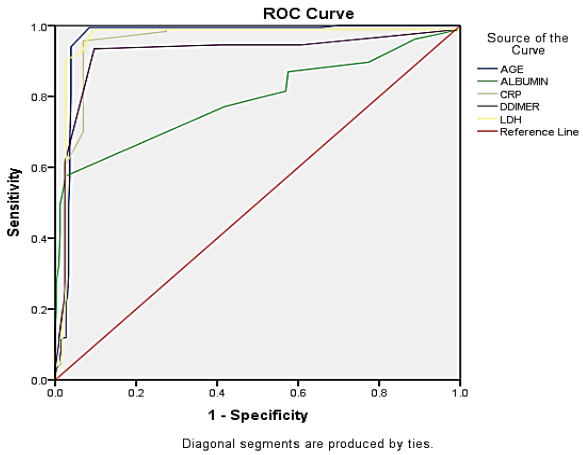

Figure 2. The area under the receiver-operating characteristics (ROC) of the study parameters in predicting the severity of COVID-19 disease

From among the 185 patients with severe COVID infection, 77 (41.61%) patients became critically ill and needed life support. From among these patients, 69 had a co-morbidity. The median age of the patients in this group was 61 years as compared to 36 years in those who did not require oxygen support. All 69 patients had lymphopenia, 57 patients had neutrophil leukocytosis, and 45 patients had thrombocytopenia during a hospital stay. Elevated D-dimer levels, serum ferritin levels, LDH levels, and reduced blood ionized calcium levels were observed in all these patients. In addition, 59 of these patients also suffered from deranged liver functions and elevation in serum bilirubin levels and liver enzymes. Moreover, 20 of these 77 individuals went into acute respiratory distress syndrome (ARDS) and multiple-organ failure (MOF) during treatment and succumbed to the disease. The mortality rate in our study was 3.86%.

Discussion

The novel coronavirus (Covid-19) infection continues to wreak havoc across the developed world and now seems to have gained a strong foothold in developing countries including India, the second most populous country in the world.[5]

Most of the infected patients are asymptomatic or have mild to moderate severity of the disease, with a better prognosis. However, a significant proportion of patients with clinically evident infection develop severe infection with a significantly high mortality rate.[5] Thus, identification of laboratory markers that have the potential to discriminate severe infection from non-severe COVID infection is necessary for better clinical management of the cases.

The present study included 517 COVID-19 infected patients with a median age of 34 years, which was almost one or two decades younger than that reported by Huang et al. (49.0 years) [10] and Wang et al. (58 years).[11] The primary reason for the higher rate of infection in the under 40 years age group is the demographic profile of India, as almost 35% of India's population is under 40 years of age and this working youth population has high mobility. Our findings were closest to the findings of Sharma et al. (35.1 years).[12] However, the median age of patients with severe COVID infection was 62 years, which was similar to that reported by Bhandari et al.,[5] Wang et al. (65 years),[11] and Chen et al.[13] Thus, elderly patients were more likely to have acute lung injury and require ICU monitoring and treatment.

We found a male preponderance, with a male to female ratio of 1.2:1. Gupta[14] and Bhandari et al.[5] also observed that women are half as likely to be infected with COVID-19 infection as men. This male predominance may be due to increased travel among men for educational and occupational purposes. Most of the COVID infected patients in our study had a history of foreign travel or travel to metro cities for education or jobs and business purposes, suggesting that these cases were not community-acquired.

The patients with severe COVID-19 disease were more likely to have underlying co-morbidities (93.8%) as compared with the mild to moderate group (25.60%) (P = 0.001). In our study, the most common co-morbidities seen in affected cases were hypertension, DM, and COPD.

Singh and Misra concluded that HT and DM were the most common co-morbidities associated with the severity of COVID-19 infection. [15]

The most common clinical symptoms include fever (90.17%), dry cough (59.38%), myalgia (54.1%), sputum production (14.4%), breathlessness (25.7%), chest tightness (28.9%), and non-respiratory symptoms including headache (33.7%), nausea or vomiting (16.4%), diarrhea (15.8%), and dysgeusia (19.9%). Similar clinical manifestations were reported by Gupta et al.[16] and Sharma et al.[17]

Among the hematological parameters, many differences were observed with the severity of the illness. We found a significant association between lymphopenia (P = 0.020) and the severity of COVID-19 infection. Patients who succumbed to illness had a significantly lower lymphocyte count, particularly CD4 lymphocytes. The lymphocyte count, specifically CD4 cells, may serve as an important hematological parameter for the determination of severity and clinical outcome in COVID patients.[18] Devanandan et al. also concluded that lymphopenia is an essential factor in predicting the outcome of the treatment and the course of hospitalization of COVID-19 patients.[19]

Other hematological parameters such as leukocytosis, neutrophilia, and thrombocytopenia were partial predictors of severity of disease, but were statistically insignificant.

A significant correlation was also observed between coagulation parameters and severity of the COVID-19 infection. Critically ill/severe COVID cases had significantly higher levels of plasma D-dimers, and increased prothrombin and activated partial thromboplastin times compared to the mild and moderate infection cases. The mean value of D-dimer in critically ill patients was 0.7 (IQR: 0.50-1.10) and in the

mild/moderate group was 0.3 (IQR: 0.2-0.40) (P = 0.031). Among the coagulation profile variables, a D-dimer level of > 1 µg /L was an independent predictor of disease outcome and mortality. Similar findings were also reported by Aggarwal et al.[20] and Velavan and Meyer.[21]

The frequency of liver dysfunction was higher among patients with severe COVID-19 disease compared to those with mild/moderate degree of infection. An increase was observed in serum bilirubin and alanine aminotransferase (ALT) and aspartate aminotransferase (AST) liver enzymes in severely ill patients. Immune-mediated inflammation and cytokine storm may lead to hepatic damage in severe COVID infected individuals.[2] In addition, a strong correlation was observed between C-reactive protein levels and severity and prognosis of COVID-19 disease.[21,22] The mean value of C-reactive protein in critically ill patients was 21 mg/dl (IQR: 19-34) as compared to 9 mg/dl (IQR: 9-11) in mild/moderate cases (P = 0.003). Sahu et al.[23] also reported CRP as a promising biomarker for assessing disease lethality.

Other prognostic parameters included serum ferritin and lactate dehydrogenase (LDH). The correlation between serum ferritin levels and severity of COVID-19 disease was found to be significant (P = 0.039). Our findings were in line with that of Velavan and Meyer.[21] Increased serum ferritin levels due to cytokine storm and hemophagocytic lymphohistiocytic syndromes (Excessive Immune Activation) have been noted with severe COVID-19 infection.[24]

Elevated cardiac troponin I (cTnI) levels, indicating myocardial injury, are observed in severe cases of COVID infection and act as a marker of clinical outcome.[21,25] The possible mechanisms of myocardial injury in COVID-19 infections include direct damage to the myocardium, systemic inflammation, interstitial fibrosis, interferon-mediated immune response, cytokine exaggerated response by Th1 and Th2 cells, oxygen supply-demand mismatch, micro embolic infarcts, hyperadrenergic state, and pulmonary embolism.[26] The value of cTnI was 27 in severely ill patients (IQR: 25-29) and 19 in mild/moderate cases (IQR: 0.19-0.20).

Renal abnormalities occurred in the majority of patients with severe COVID-19 infections.[27] Blood urea and creatinine levels were significantly higher in severely ill patients compared to those with mild/moderate COVID-19 infection (P = 0.014 and 0.027, respectively). Renal function impairment in COVID-19 infection was the result of intrinsic renal involvement, as the kidneys had varying degrees of acute tubular necrosis (ATN), luminal brush border sloughing, hyaline casts, microthrombi, and mild fibrosis in the interstitium, but severe glomerular injury and lymphocyte infiltration were not observed on the microscopic study of the kidney.[27]

We also analyzed the whole blood ionized calcium level and found that it was inversely correlated with the severity of the disease.[28] The mean value of ionized calcium was 4.9/dl and 4.3/dl in mild/moderate COVID-19 cases and severe cases, respectively, and this difference was statistically significant (P = 0.041). Decreased value of ionized calcium levels may be due to change in intestinal absorption, imbalance in the regulatory mechanism involving vitamin D and PTH, or a direct effect of COVID infection as calcium is essential for virus entry, structure formation, gene expression, virion maturation, and release.[29]

The clinical status (particularly SPO2) and underlying co-morbidities of COVID-19 infected patients significantly determine the course of the disease, and various laboratory parameters may facilitate the assessment of the severity of the disease and rational triaging. Wang et al.[11] found that the risk factors associated with the development of ARDS and progression of ARDS to death included older age, elevated D-dimer levels, elevated

C-reactive protein, serum ferritin, cTnI, and low levels of ionized calcium. These factors may be used in risk stratification and to predict severity and outcome in COVID-19 infected patients.

However, the present study has some limitations. First, the study cases were selected from a single center rather than multiple centers. Moreover, the study sample size was relatively small. In addition, it was not possible to assess inflammatory factors and immunological indexes due to the lack of facilities, as this study was performed in a rural tertiary care hospital. Therefore, further studies, including large datasheets, are needed to investigate the clinical significance of these parameters in COVID-19 patients.

Conclusion

The COVID-19 infections have shown a variable clinical presentation ranging from asymptomatic cases to critically ill cases requiring oxygen support. The clinical presentation depends on the age of the patients, underlying co-morbidities, and the strain of virus with which the patient was infected.

Laboratory parameters like lymphopenia, elevated D-dimer levels, elevated C-reactive protein, IL6, serum ferritin, cTnI, and low levels of ionized calcium were correlated with the severity of the disease. Thus, further investigation of these laboratory parameters is necessary and they should be considered for risk stratification, correct clinical management, and improved clinical outcome in COVID-19 infected cases.

Conflict of Interests

Authors have no conflict of interests.

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No.

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