Section: Biochemistry

Original Article

ISSN (O): 2347-3398; ISSN (P): 2277-7253

Serum Ferritin and C - Reactive Protein as Prognostic Factors in Patients with Novel Coronavirus 2019

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Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has resulted in Coronavirus disease 2019 (COVID-19) which has been widely spread in India and worldwide. We have aimed to investigate serum ferritin and CRP along with routine investigations and to correlate them amongst non- ARDS cases and ARDS cases which may help to predict severity and outcome of COVID-19. **Subjects and Methods:** Total number of 100 cases taken for study, admitted on priority basis. Consecutive blood tests that included ferritin and CRP in the study period were reviewed. Patients diagnosed with SARS-CoV-2 infection in whom, CBC, platelet count, RFT, LFT, RBS, serum ferritin and CRP had been analysed at the time of admission were selected. For assessment of severity and behaviour of the factors to be analysed the COVID-19 patients were grouped into Non-ARDS (mild) and ARDS (severely ill) cases, factors analysed in both groups and correlated. **Results:** For Non-ARDS patients, the median age was 48 years 72% were men. For ARDS patients, 60 years, and 74% were men. Out of 42 ARDS cases 28 are diabetic (66.7%) as compared to 11 cases being diabetic in total 58 Non-ARDS cases (19%) $p<0.001$. Out of 39 ARDS cases 35 had mild to severe dyspnea which accounts for 83.3% with p value <0.001. Lymhocyte count is drastically decreased in ARDS cases (Mean=10; 6-14 $p<0.001$). ESR is raised in most of the Covid cases, a significant increase in ARDS patients (Mean=36; 31.8-42.3 $p<0.05$). In LFT, T.Bilirubin and D.Bilirubin raised significantly (Mean=1.8 and 0.8 $p<0.001$ respectively) along with SGPT significantly increased (Mean=40.3 $p< 0.001$). Also, there is drastic decrease in platelet counts in these ARDS cases (Mean=$1.6X10^3$cells/cu.mm $p<0.001$) suggesting thrombotic storm and inflammatory signs in ARDS cases. In all ARDS cases there is significant increase in serum ferritin and CRP values (100%) whereas in Non-ARDS cases these values were raised in 84.5% of cases. we found that in COVID-19 patients the association between ferritin levels and CRP levels was stronger. **Conclusion:** Detailed investigation of 100 hospitalized COVID-19 cases suggests that the serum ferritin test and CRP test should be used for screening in patients with COVID-19 to evaluate the severity and to predict the prognosis and mortality in hospitalized COVID-19 patients. Lymphopenia, Thrombocytopenia, with more prominent laboratory abnormalities may be a potential indicator for diagnosis. Older age, high number of comorbidities were associated with severe patients.

Keywords: Covid-19, Non-ARDS cases, ARDS cases

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Received: 08 April 2021 **Revised: 22 June 2021** **Accepted: 01 June 2021** **Published: 21 June 2021**

Introduction

The outbreak of 2019 Novel coronavirus disease (COVID-19) has affected India and has become pandemic worldwide.Due to its rapid spread worldwide, COVID-19 was declared as a public health emergency by the World Health Organization.[1] In India 724 Local transmission of the disease was found by 25 March 2020 with first case of COVID-19 infection reported in Thrissur, Kerala, on January 27, 2020.[2]

By August 2020, A cumulative total of nearly 25 million cases and 8,00,000 deaths have been reported by WHO since the start of the outbreak. Countries of the South-East Asia reported the largest week-on-week increase. India has reported nearly 5,00,000 new cases in seven days in the middle of august, largely due to increased case detections in India, a 9% increase compared to the previous seven days and the highest numbers of new cases globally.[1]

Most Covid-19 cases in Karnataka were spread by a small fraction of infected patients, called “superspreaders”, showed by an analysis of contact tracing data between March 9 and July 21, 2020, of 17,008 Covid-19 patients who had tested

positive and were contact-traced by July 7. We faced total lockdown situation in Karnataka from March 24, 2020.[3]

The causative agent responsible for the pneumonia cases in Wuhan, in China, has been identified as a novel coronavirus, (of the same family of SARS-CoV and MERS-CoV) by next generation sequencing (NGS) from cultured virus or directly from samples received from patients suffering from pneumonia.[4] Even though majority of patients who were suffering from fever and cough, had good prognosis who recovered well, severe COVID-19 cases presented with acute respiratory distress syndrome (ARDS) and systemic inflammation. Despite the fact that COVID-19 rapidly spread in India the study data on various biomarkers to evaluate the prognosis remains limited.[5] Patient characteristics, disease course and patterns, resource utilization, mortality associated with COVID-19 have been characterized in only limited samples in India. Thus, it is urgent to evaluate and investigate possible biomarkers to assess disease severity so as to make fast and correct clinical decisions.

Several laboratory investigations have been associated with worse outcomes in patients with COVID-19, of them acute phase reactants or inflammatory biomarkers have important role such as Ferritin and C-Reactive Protein (CRP) which are known inflammatory biomarkers.

Ferritin is a blood protein that contains iron and releases in a controlled fashion. Its ability to sequester the iron gives ferritin the dual functions of iron detoxification and iron reserve keeping iron in soluble and non-toxic form. It is composed of a spherical protein shell called an apoferritin and a mineral core.[6] The evaluation of ferritin levels is important in diseases characterized by inflammatory and infectious processes and tissue damage and repair.[7]

CRP is an inflammatory marker and also an important factor that affects the development of inflammation. High serum levels of CRP are a result of an acute inflammatory condition; CRP measurement between 0.5 and 10.00 mg/L facilitates the detection of low-intensity chronic inflammatory processes.[8]

The literatures show that acute-phase proteins are of interest in the medical field in the context of the etiopathogenesis, severity and prognosis in diseases with chronic inflammatory processes. Hence in our setting, we aimed to identify serum ferritin and CRP along with routine investigations and to correlate them amongst non- ARDS (Mild cases; Non-Acute Respiratory Distress Syndrome) cases and ARDS (Cases with severe illness due to COVID infection) cases which may help to predict severity and outcome of COVID-19.

Subjects and Methods

This retrospective observational study was performed at teaching Hospital (District Hospital) attached to Belagavi Institute of Medical Sciences, (BIMS), Belagavi. It has total bed strength of 740 which serves the diverse population of Belagavi district and some places of neighbouring districts. A separate block in the hospital was dedicated with 300 beds including ICU for the treatment of COVID 19 patients. The laboratory-confirmed COVID-19 patient's laboratory data which was documented in medical records department of the hospital was collected. We performed ongoing retrospective manual data abstraction from the records of 100 patients with COVID-19 who received inpatient care at BIMS hospital from July 10, 2020 to December 20, 2020. Consent was taken by all COVID-19 hospitalized patients, included in the study, for use of data for research and education.

Inclusion Criteria

Patients with laboratory-confirmed SARS-CoV-2 infection according to World Health Organization guidance: a positive result of real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assay of a nasopharyngeal swab.[9] In our study 3 patients were diagnosed as COVID negative as their RT-PCR came negative but still they were included in the study because they were symptomatic and had a typical clinical presentation of COVID-19.

Exclusion Criteria

Patients who received monoclonal antibody, at any time during their hospital stay were excluded for the study because studies show that this agent has been associated with a decrease in CRP and ferritin levels.[10] Patients on repeated blood transfusion were also excluded because of iron overload.

Consecutive blood tests that included ferritin and CRP in the study period were reviewed. Patients diagnosed with COVID-19 in whom serum ferritin, CRP, CBC, platelet count, RFT, LFT, and RBS had been analysed at admission were selected. Serum ferritin was measured on an Diasorin chemiluminescence System (Diasorin Laboratories, IL) using a 2-step chemiluminescent microparticle immunoassay. CRP was determined in serum using Erba XL-640 Chemistry analyzer system (Transasia, MH), using a particle-enhanced immunoturbidimetric assay.

Total number of 100 cases taken for study, admitted in BIMS hospital on priority basis. The criteria for admission include positive RT-PCR test for COVID-19 with high grade fever with myalgia, SPo2 on pulse oximeter showing < 90%, Dyspnea on mild exertion and cases referred by Govt. officials from peripheries for isolation. All the cases who were subjected for CT- chest were showing CORAD 1-5, and CT severity scoring was done accordingly. All these RT-PCR positive cases were grouped into 3 groups.

Group 1 consists of mild fever, myalgia, no dyspnea, spo2> 90%.

2nd group consists of high-grade fever, myalgia, mild dyspnea, spo2< 85-90% requiring oxygen inhalation and CORAD<3. There hospital stay ranged from 7-10 days.

Group 3 consists of severe complications of COVID presenting with grade 4 dyspnea, SpO2<80% and CORAD>3, who were admitted in ICU.

Group 1 is named as Non-ARDS cases and Group 2 and 3 are named as ARDS cases.

Clinical and laboratory data extracted from medical records was evaluated till the discharge of the patient or death.

Results

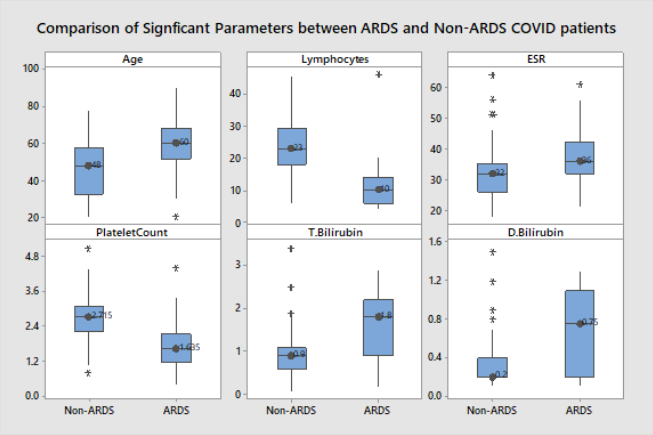
The study population included 100 hospitalized patients with COVID-19, in which 58 cases were Non-ARDS and 42 cases were ARDS. For Non-ARDS patients, the median age was 48 years (IQR 33-58), and 42 (72%) were men. For ARDS patients, the median age was 60 years (IQR 52-69), and 74% were men [Table 1]. Both of the COVID-19 Non-ARDS and ARDS patients had 1 or more coexisting medical conditions, and compared with Non-ARDS patients, ARDS patients were more likely to have existing co-morbidities, including Diabetes, CAD and Pulmonary diseases.

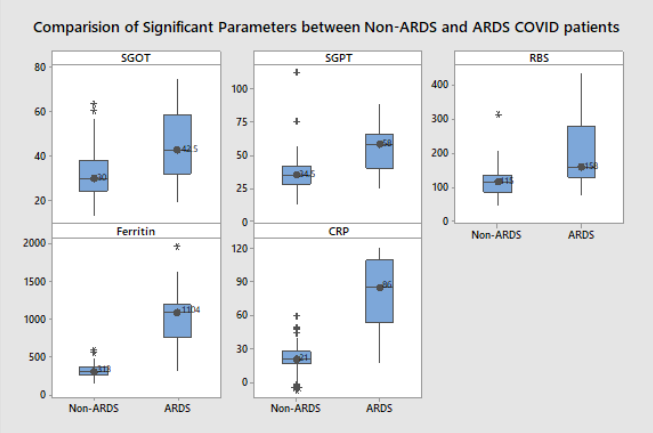
On admission most patients had fever, cough, mild to moderate dyspnea, myalgia, chest discomfort, and fatigue besides, numerous differences in laboratory findings [Table 2]. Compared with Non-ARDS patients, ARDS patients had higher neutrophil counts (N), Lymphocytopenia, as well as higher erythrocyte sedimentation rate (ESR), Thrombocytopenia and there were significant differences in other biomarkers levels as well between two groups, notifiable are increase in the Bilirubin and SGPT levels. There is also significant increase in RBS levels suggesting diabetics are more prone to get severe illness of COVID i.e., ARDS.

As shown in [Table 1] there is statistical significance between age, diabetes, dyspnea, ferritin and CRP with P value <0.05. There is positive association between age and ARDS cases and also there is significant increase in the number of ARDS cases with advanced age. ARDS cases are more between the age groups 40-59 and >60 years as compared to the age group of 20-39. There is total 39 cases of ARDS in >40 years age group to the total 42 ARDS cases. In the later age severity of COVID increased as compared to the earlier age group with probability p<0.001. There is positive association between diabetics and ARDS cases showing diabetics are more prone to get severe COVID infection. Out of 42 ARDS cases 28 are diabetic (66.7%) as compared to 11 cases being diabetic in total 58 Non-ARDS cases (19%) p<0.001. Out of 39 ARDS cases 35 had mild to severe dyspnea which accounts for 83.3% with p value <0.001.

There is significant probability between normal and high values of ferritin and CRP in ARDS and Non-ARDS cases with p value 0.009. In all ARDS cases there is significant increase in serum ferritin and CRP values (100%) whereas in Non-ARDS cases these values were raised in 84.5% of cases.

Lymhocyte count is drastically decreased in ARDS cases (Mean=10; 6-14 p<0.001) compared to Non-ARDS cases. ESR is raised in most of the covid cases, a significant increase in ARDS patients (Mean=36; 31.8-42.3 p<0.05). Both these show inflammatory condition in COVID patients. In LFT, T.Bilirubin and D.Bilirubin raised significantly (Mean=1.8 and 0.8 p<0.001 respectively) along with SGPT significantly increased (Mean=40.3 p< 0.001). Also, there is drastic decrease in platelet counts in these ARDS cases (Mean=1.6X10^{3}cells/cu.mm p<0.001) suggesting thrombotic storm in ARDS cases. RBS is significantly raised in ARDS cases proving that uncontrolled/poorly controlled diabetics are more prone to go for ARDS compared to non-diabetic patients.





In univariate and multivariate analysis of these parameters, all the parameters show significance in univariate analysis p<0.001, while ferritin shows significance in both univariate

Table 1: General characteristics of COVID19 patients with and without ARDS

Factors	Categories	ARDS (n=42)	Non ARDS (n=58)	Total (n=100)	P-value
Sex	Male	31 (73.8%)	42 (72.4%)	73 (73.0%)	0.877
	Female	11 (26.2%)	16 (27.6%)	27 (27.0%)	
Age	20-39	3 (7.1%)	20 (34.5%)	23 (23.0%)	<0.001
	40-59	16 (38.1%)	26 (44.8%)	42 (42.0%)	
	>=60	23 (54.8%)	12 (20.7%)	35 (35.0%)	
Diabetic	No	14 (33.3%)	47 (81.0%)	61 (61.0%)	<0.001
	Yes	28 (66.7%)	11 (19.0%)	39 (39.0%)	
Dyspnea	No	7 (16.7%)	54 (93.1%)	61 (61.0%)	<0.001
	Yes	35 (83.3%)	4 (6.9%)	39 (39.0%)	
Ferritin	Normal	0 (0.0%)	9 (15.5%)	9 (9.0%)	0.009
	High	42 (100.0%)	49 (84.5%)	91 (91.0%)	
CRP	<10mg/L	0 (0.0%)	9 (15.5%)	9 (9.0%)	0.009
	>=10mg/L	42 (100.0%)	49 (84.5%)	91 (91.0%)	

* P-values based on Chi-square test, Statistically significant P<0.05

Table 2: Comparison of Laboratory Investigations of COVID19 patients with and without ARDS

Parameters	ARDS (n=42)	Non ARDS (58)	Total (n=100)	P-value
Age	60.0 (51.5-67.8)	48.0 (32.5-57.5)	54.0 (40.0-62.8)	<0.001
TC	7800 (5800-12075)	9150 (6800-12850)	8550 (6325-12775)	0.296
Neutrophils	78.0 (68.0-85.0)	71.0 (66.8-82.0)	75.0 (67.0-82.8)	0.164
Lymphocytes	10.0 (6.0-14.0)	23.0 (17.8-29.3)	16.0 (10.0-25.0)	<0.001
HB	12.8 (11.1-13.7)	12.8 (11.6-14.0)	12.8 (11.5-13.9)	0.647
ESR	36.0 (31.8-42.3)	32.0 (26.0-35.3)	32.0 (27.3-40.0)	0.010
Platelet Count	1.6 (1.1-2.1)	2.7 (2.2-3.1)	2.3 (1.6-2.9)	<0.001
Blood Urea	36.0 (25.8-42.0)	30.0 (24.8-36.0)	32.0 (25.0-39.0)	0.072
Creatinine	1.2 (0.9-1.3)	1.1 (0.9-1.2)	1.1 (0.9-1.3)	0.670
T. Protein	6.8 (6.4-6.9)	6.8 (6.6-7.0)	6.8 (6.5-7.0)	0.436
Albumin	3.6 (3.3-3.9)	3.8 (3.5-4.1)	3.8 (3.5-4.0)	0.128
T. Bilirubin	1.8 (0.9-2.2)	0.9 (0.6-1.1)	1.0 (0.8-1.8)	<0.001
D. Bilirubin	0.8 (0.2-1.1)	0.2 (0.2-0.4)	0.3 (0.2-0.8)	<0.001
SGOT	42.5 (31.8-48.8)	30.0 (24.0-38.0)	35.0 (27.0-45.8)	0.052
SGPT	40.3 (40.3-66.0)	34.5 (28.0-42.0)	38.5 (30.0-57.0)	<0.001
ALP	95.0 (75.0-110.0)	90.5 (76.8-110.0)	92.0 (76.3-110.0)	0.886
RBS	158.0 (129.0-281.0)	115.0 (85.5-135.3)	128.0 (104.0-180.5)	<0.001
Ferritin ng/ml	1104.0 (773.2-1203.6)	313.0 (271.1-378.7)	419.0 (303.3-897.8)	<0.001
CRP mg/l	86.0 (53.7-110.5)	21.0 (16.9-28.0)	33.5 (20.0-79.8)	<0.001

* Data is presented with Median (Interquartile range), P-values based on Mann-Whitney U test, Statistically significant P<0.05

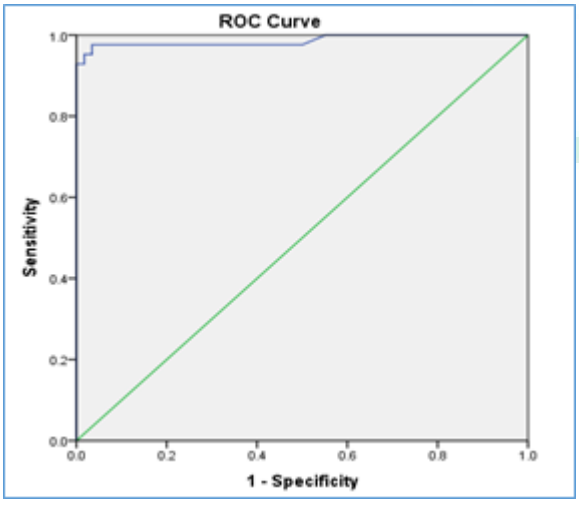
Table 3: Association of laboratory parameters in COVID patients with and without ARDS

Parameters	Univariate Analysis		Multivariate Analysis	
	P-value	OR (95% CI)	P-value	OR (95% CI)
Age	<0.001	1.06 (1.03-1.09)	-	-
Lymphocytes	<0.001	0.80 (0.74-0.87)	-	-
ESR	0.031	1.05 (1.00-1.10)	-	-
PlateletCount	<0.001	0.30 (0.15-0.50)	-	-
T.Bilirubin	<0.001	4.02 (1.96-8.22)	-	-
D.Bilirubin	<0.001	14.2 (3.84-52.73)	-	-
SGPT	<0.001	1.08 (1.04-1.11)	-	-
RBS	<0.001	1.02 (1.01-1.03)	-	-
Ferritin ngml	<0.001	1.02 (1.01-1.03)	<0.001	1.02 (1.01-1.03)
CRP mgl	<0.001	1.11 (1.06-1.17)	-	-

Table 4: Sensitivity analysis to predict ADRS using Serum Ferritin levels

Sensitivity	Specificity	AUC	Cut off score
0.98	0.97	0.98	531

as well as multivariate analysis showing high sensitivity and specificity, proving itself an ideal biomarker for assessment of severity and course of COVID-19 [Table 3&4].



In this regression analysis, in the ROC curve for ferritin values, the TPR/FPR>1 making it an ideal marker. AUC is more significant. There is 97% sensitivity and 100% specificity in the ferritin values making it an ideal biomarker for assessment of severity and outcome of the disease prognosis.

In addition, for ARDS patients, there were also positive correlations of ferritin and CRP levels at the time of admission (Mean=1104; p<0.001 and Mean=86; p<0.001 respectively).

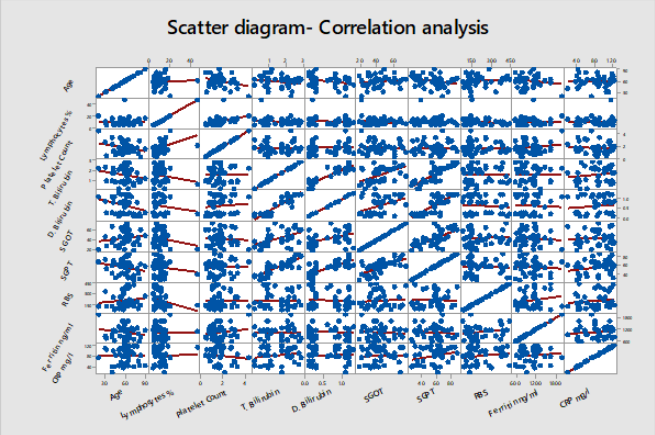
At the same time, we also analysed the association between these indicators after treatments in COVID-19 patients, and found that there were still great correlations between ferritin and CRP in ARDS patients. However, due to the absence of follow-up data, we couldn't study the relationships between biomarkers levels in the course of hospital stay of ARDS patients. More importantly, we could make out the association between ferritin and CRP levels before treatments was related to the levels of 0.05 significantly in COVID patients, especially when the levels of CRP was more than 10 mg/L, the correlation between ferritin and CRP was stronger.

We aimed to investigate whether ferritin and CRP levels is associated with infection related biomarkers levels in Non-ARDS and ARDS patients. As shown in Table 5, for Non-ARDS patients, ferritin and CRP levels were positively correlated with infection related biomarkers levels including Lymphocyte count, ESR, Total and Direct Bilirubin, SGOT, SGPT and RBS at the time of admission with significant correlation at 0.05 and 0.01 level. Thus, there is great correlations with inflammatory cells levels and thrombosis-related factors at the time of admission.

Table 5: Correlation analysis

Parameter	Age	Lymphoc	ESR	T. Bilirubin	D. Bilirubin	SGOT	SGPT	RBS	Ferritin ng/ml	CRP mg/l
Age		0.07	0.07	-0.21	-0.307*	0.15	-0.313*	0.27	-0.16	0.02
Lymphocy	0.07		0.11	-0.09	-0.03	0.00	-0.04	-0.21	-0.16	-0.05
ESR	0.07	0.11		0.11	0.07	0.26	-0.02	0.09	-0.12	-0.25
T. Bilirubin	-0.21	-0.09	0.11		0.847**	0.624**	0.796**	0.07	0.03	0.07
D. Bilirubin	-0.307*	-0.03	0.07	0.847**		0.490**	0.745**	-0.05	-0.05	0.04
SGOT	0.15	0.00	0.26	0.624**	0.490**		0.593**	0.08	-0.08	-0.03
SGPT	-0.313*	-0.04	-0.02	0.796**	0.745**	0.593**		-0.08	-0.03	0.22
RBS	0.27	-0.21	0.09	0.07	-0.05	0.08	-0.08		0.09	0.14
Ferritin ng/ml	-0.16	-0.16	-0.12	0.03	-0.05	-0.08	-0.03	0.09		0.05*
CRP mg/l	0.02	-0.05	-0.25	0.07	0.04	-0.03	0.22	0.14	0.05*	

*. Correlation is significant at the 0.05 level; **. Correlation is significant at the 0.01 level.



Discussion

Corona virus disease caused a rapid epidemic worldwide in less than three months. Although most patients with COVID-19 have suffered from mild symptoms without pneumonia, a large proportion of patients develop a severe conditions of respiratory distress or even caused death. This has led the researchers to explore effective predictors of disease severity that can help in assessing the severity of virus. The main purpose of this research was to establish the effectiveness of the biomarkers which can accurately predict the severity of coronavirus disease, thereby guiding clinicians in the clinical management of the patients and the disease outcome.

Our analysis showed that Serum ferritin and CRP are significantly elevated in severe cases of COVID-19 (ARDS cases) as compared to the mild course of the disease (Non-ARDS cases) and act as important predictors in the severity of the disease at the time of admission. Our results are consistent with the findings of review articles that concluded that ferritin and CRP, in patients infected with corona virus disease, are a crucial markers for predicting COVID-19 prognosis and mortality in these patients.[11–14]

The following variables showed significant positive association to the disease severity ($p < 0.01$): Advanced age, Lymphocyte count, ESR, Platelet count, Bilirubin (Total & Direct), SGOT, SGPT and RBS in known Diabetics, which is in accordance with the earlier studies.[11,14–16] Of these, CRP, and serum ferritin levels had particularly strong association in ARDS cases and to the above variables.

In severe COVID-19 infection, a deviation of the protective immune response into a dysfunctional program occurs, which results into cytokine storm with severe inflammation and, eventually, multisystemic failure. A better understanding of the mechanisms lying at the root of immune response failure which points towards the clinical spectrum of the COVID disease corresponding to variable spectrum of the immunity is needed; Due to cytokine storm serum levels of inflammatory markers are increased in COVID-19.[17] It shows an evidence

for the increase of serum levels of ferritin and CRP.

Ferritin is an iron-storing protein; serum ferritin level increases during viral infections and can act as marker for replication of the virus.[18,19] Increased levels of ferritin can contribute cytokine storm and same has been reported in severe COVID-19 patients. During the cytokine storm in COVID-19, many inflammatory cytokines are rapidly produced, including IL-6, TNF-α, IL-1β, IL-12, and IFN-γ, which stimulate hepatocytes, Kupffer cells, and macrophages to secrete ferritin.[20–22] The uncontrolled and dysfunctional immune response, hyper ferritinemic syndrome, and thrombotic storm finally leads to multiple organ damage. In the present study decreased platelet count and increased bilirubin levels can be explained by thrombotic storm.

Although ferritin is reported as an acute-phase protein, there is misunderstanding in reporting of ferritin levels due to lack of studies in the modifications of ferritin levels.[23] Zhou et al revealed that the increase in ferritin level is associated with the worsening of the COVID-19.[13] The cytokine storm and the exaggerated host immune response which results in development of ARDS, which is the leading cause of mortality if progresses to respiratory failure can result increase in acute phase reactants like ferritin. In our study, higher ferritin levels were found in groups of patients with severe respiratory distress conditions compared with the levels in less severe patients.[24] Moreover, our study also demonstrated that COVID-19 patients having one or more comorbidities, like Diabetes had a significantly higher level of ferritin compared to the patients without comorbidity, which suggests a poor prognosis. Wang et al firstly reported that COVID-19 patients with diabetes have more severe inflammation and higher mortality,[25] later other studies also supported that patients with diabetes had higher ferritin levels than non-diabetics.[26] The present study confirmed these results.

C-reactive protein is an acute-phase inflammatory protein, first isolated in the sera of patients suffering from the acute stage of Pneumococcus infection and it was named for its reaction with the capsular (C)-polysaccharide of Pneumococcus.[27] As an acute-phase protein, the plasma concentration of CRP increases by at least 25-30% during inflammatory disorders.[28] C-reactive protein is known to exhibit increased levels during inflammatory conditions such as rheumatoid arthritis, some cardiac and vascular diseases.[29] The main role of CRP in inflammation is opsonization of pathogens due to the activation of the C1q molecule in the complement pathway. CRP can also initiate cell-mediated pathways by activating complement as well as to binding to Fc receptors of IgG.[30]

Our analysis showed that CRP is significantly elevated in severe cases of COVID-19 as compared to the mild course of the disease and was an important predictor of severity of the disease. This result is consistent with the findings of review articles that conclude CRP a crucial marker for predicting COVID-19 prognosis and mortality.[31] Qin et al. and Gao et al also found a significant association between increased CRP, disease severity and prognosis.[32,33]

This study has several limitations, in particular, the number of patients enrolled were less mainly due to less testing and unavailability of the protocol in the initial period as well as retrospective nature of the study. Therefore, a wider analysis including a greater number of patients covering a large demographic area would be necessary in order to prove our outcomes.

Conclusion

This study revealed the association between the serum ferritin levels, CRP and other inflammatory and thrombotic parameters of COVID-19 patients including disease severity, mortality, comorbidities, and after treatment assessments. We strongly recommend that the serum ferritin test and CRP test should be used for screening in patients with COVID-19 to evaluate the severity and to predict the prognosis and mortality in hospitalized COVID-19 patients. Future clinical studies should be performed to further clarify its prognostic role in COVID-19, disease outcome and the potential therapeutic value in the inflammation control before end-organ damage.

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How to cite this article: Shekhanawar M, Sarala HT, Shaik RA. Serum Ferritin and C - Reactive Protein as Prognostic Factors in Patients with Novel Coronavirus 2019. Asian J. Med. Res. 2021; 10(2):9-17.

DOI: dx.doi.org/10.47009/ajmr.2021.10.2.BC2

Source of Support: Nil, **Conflict of Interest:** None declared.