Original Research Paper

Prognostic Biochemical Markers Predicting Severity Caused by COVID 19: A Retrospective Observational Study Conducted in a Small Health-care Set UP in Western U.P.

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Abstract

Background: For assessment of mild to severe outcome points of SARS COV-2 we need to observe patients with comorbidities along with basic laboratory markers like NLR, PLR, CRP, D-dimer, serum Ferritin etc. For the prediction of SARS COV-2 severity our study aims at basic available laboratory prognostic biomarkers.

Methods and Result: Our study included 46 patients with mild, moderate and severe outcomes which were categorised according to CRP, Serum Ferritin and D- dimer with p-Value < 0.001 for both outcomes which are significant as compared to outcome patients with p-Value = 0.01 which is slightly less significant.

Conclusion: A raised value of CRP, ferritin, D-dimer and involvement of male gender and old age patients were associated with severity of the disease.

Among these parameters, D-dimer was known to be the best predictor of the outcome.

Keywords: COVID-19, comorbidities, severe outcomes, CRP, D-dimer, Serum Ferritin

Introduction

A novel Coronavirus(SARS- COV-2) causing a cluster of respiratory infections was identified on 7th Jan 2020 in Wuhan, China[1]. An explosive increase in number of cases led WHO to declare this outbreak as a public health emergency of intestinal concern on 30th Jan 2020[2]. Since, being declared as a pandemic by WHO on March 2020, Covid 19 infection posed great threat to human health[3].

On 29th September 2022, there have been 61,39,42,561 confirmed cases of Covid 19 including 65,20,263 deaths globally reported to WHO. India recorded 528611 Coronavirus deaths since the epidemic began, according to WHO. In addition, India reported 4,45,79,088 Coronavirus cases[4]. In India, first confirmed case was reported on 27th Jan 2020 in Thrissur, Kerala in a female presented with a symptoms of sore throat and dry cough[5].

It was noticed that SARS-COV-2 infection, especially in older patients and those with pre-existing illness, can progress to severe disease with critical respiratory symptoms and significant

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pulmonary changes visible by imaging techniques[6]. It is well documented that inflammatory mechanisms and markers play a vital role in Covid-19 cases related outcomes of the disease[7].

Several studies showed low lymphocyte count, NLR with quick index of inflammation detection convinient in laboratory examination1. Clinicians should consider serum levels of CRP, D-dimer and Ferritin, which may be used in risk stratification to predict severe and fatal Covid-19 in hospitalised patients6. Our study used simple available laboratory markers of good predictive value for Covid-19 prognostic which summarises these markers that might be useful in indicating progression from mild to severe disease.

Material and Methods

We conducted a retrospective study in Western UP in a tertiary care hospital on 46 patients positive with COVID 19 antigen test. The study was conducted between the period April 2021 to June 2021.

Inclusion criteria- The study incorporated all the adult (>18 years) COVID 19 patients of both genders which are hospitalised with all disease severity levels.

Data Collection- Laboratory data and clinical records were considered in each study and then data will be collected on the basis of demographic and clinical data which includes age, gender, presenting symptoms, outcomes and comorbidities.

Various laboratory investigations were done like CRP, Neutrophill to Lymphocyte ratio, D-Dimer and Serum ferritin.

Clinical Outcome- Primary outcome of this study was placed on admission in ICU, if the patient had one or more of the following symptoms:

1. Respiratory rate >30 cycles / min.
2. SPO2 < 90% on room air or respiratory failure require mechanical ventilation.
3. Presence of shock or other organ failure requires monitoring or treatment in ICU.
4. Different prognostic biomarkers will be compared and the patients were divided into Mild, Moderate and Severe.

Furthermore, patients symptoms, such as shortness of breath, cough, sore throat, rhinorrhea, loss of smell etc were documented.

Statistical analysis:

The collected data was entered in Ms excel and was imported in IBM SPSS vs. 25.0. The collected data was analysed by appropriate statistical tools and techniques. A $p<0.05$ was taken as statistically significant.

Result

Screening of 46 patients record were conducted. Out of 46 patients, 7 were less than 30 years. The mean age of patients included in the study was 48, besides 54.35% were males (Table-1).

Table-1: Overall distribution of patients group according to age and gender (n=46)

Gender	No	Percent (%)
Male	25	54.35
Female	21	45.65

The patients with severe outcome complaint with the symptoms of fever, shortness of breath, cough, rhinorrhea, loss of smell and lower respiratory tract symptoms like dry cough predominantly. The comorbid conditions were observed more in poor prognostic patients whose age were >30 years.

The moderate and severe outcome patients showed highly significant p-value as 0.045 and 0.03 respectively as compared to mild outcome patients with p- value 0.669 which is not significant.

(Table 2 and 3).

Table-2: Distribution of age according to comorbidity (n=29)

S. No	Age group	Number
1	< 30 years	2
2	30 years	0
3	> 30 years	27

Table-3: Comparison of comorbidity p-Value in different outcomes (n=29)

S. No	Outcomes	No.	%	p- value
1	Mild	22	47.83	0.04
2	Moderate	16	34.78	–
3	Severe	8	17.39	–

In our study, Neutrophill Lymphocyte Ratio(NLR) was significantly higher in severe outcome patients. Patients with poor prognosis showed significant lymphopenia. There was not much difference between all the outcomes in the case of platelets. The moderate and severe outcome patients had raised levels of CRP, serum ferritin and D-dimer with p-values <0.001 for both outcomes which are significant as compared to mild outcome patients with p-value 0.01 which is slightly less significant (Table-4).

Table-4: Comparison of prognostic markers of COVID-19 patients in three outcomes alongwith their p-Values (n=46)

	Severity			
	Mild	**Moderate**	**Severe**	**p-Value**
NLR	2.22±1.49	4.35±4.34	8.95±3.88	0.10
CRP	7.69±6.03	44.10±20.66	62.26±7.04	<0.001
D-Dimer	162.70±174.77	238.95±202.80	512.62±245.89	<0.001
Ferritin	175.73±99.26	319.85±116.61	302.90±105.33	<0.001
p-Value	<0.001	<0.001	<0.001	

The comparison of various biochemical parameters of COVID-19 patients have been tabulated (Table-5).

	Age	**NLR**	**CRP**	**D-dimer**	**Ferritin**
No	46	46	46	46	46
Mean	48.00	4.1387	29.8513	250.0817	247.976
Std. Error of mean	2.350	.58231	3.80493	34.07182	18.5226
Median	46.50	2.2000	19.1200	186.0500	245.050
Std Deviation	15.936	3.94943	25.80630	231.08635	125.6262
Variance	253.956	15.598	665.965	53400.900	15781.935
Range	56	18.00	70.28	959.92	504.4
Minimum	22	.60	.40	.08	11.3
Maximum	78	18.60	70.68	960.00	515.7

Discussion

It has been shown that Covid-19 infection is associated with severe systemic immune response and extensive tissue damage by a cytokine release syndrome "Cytokine storm" resulting in capillary leak, thrombus formation and organ dysfunction[8].

Sustained cytokine production and hyper inflammation with severe Covid-19 cases is in association with distinctive form of immune dysregulation[9,10]. Several studies reminisce us that the prognostic markers does not play the sole role in severity of the disease but also we need to be in focus of cytokines and immune functions[1]. In Covid-19 patients, progression from mild to severe cases in dependable on inflammatory response[11].

In our study, we have focused an association between different prognostic parameters with outcome of the disease. Involvement of male gender was observed significantly higher as comparison to female gender which is in concordence with result of Sagar S Maddani et.al.[12].

In our study, old patients with COVID-19 were more prone to severe infection(Liu et al, 2020 a)[13]. One of the main reason for severe disease was observed in cases with underlying age related comorbidities. This was similar to Wang et al, Yang et al)[14,15 16].

CRP is an acute phase reacting inflammotory marker that is highly related with many severe complications and even death[17].

A useful relationship between severity of disease and values of CRP has been seen in many studies which is of clinical importance. It has been observed, that CRP was denoted as an early prognostic marker of disease severity in several studies.[18]

Several metaanalysis studies observed correlation between increased CRP with severe COVID 19 infection which is in concordance with our study.[3]

An essential inflammatory marker i.e. ferrtin is used to prognosticate the severity & mortality of the disease.[11] At the transcriptional and translational level ferritin expression is regulated by cytokines.[19]

In our study, we observed a significant level of ferritin. The raised levels may be due to cytokine storm which is released from lung parenchymal macrophages.[2]

It is also known as the inflammatory condition and the levels of inflammatory markers are directly proportional to one another helping in forecasting the outcome of the disease.[12] One of the main prognostic biomarker in our study is D-dimer which is a fibrin degradation product resulting from fibrin hydrolysis. D-dimer detects coagulation, clotting disorder, pulmonary embolism and myocardial infection in infectious disease alongwith severity of disease in long stay patients.[1]

In current study, few limitations were noticed, the study was based on laboratory reports obtained from outdoor patients due to limited medical resources. Limited number of patients were involved in our study. We investigated easy, effortless and economical biomarkers leaving behind IL-6, Lactate dehydrogenase, troponin etc in our study.

Conclusion

A raised value of CRP, ferritin, D-dimer and involvement of male gender and old age patients were associated with severity of the disease.

Among these parameters, D-dimer was known to be the best predictor of the outcome. For healthier outcome, we can use these parameters with limited medical resource so that high risk patients can be referred to higher centers.

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Ethical Clearance: Taken

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