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Correlation of Disease Severity with Biochemical Characteristic of Patients with COVID-19: A Single Centre Tertiary Care Covid Hospital Study

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ABSTRACT

The Severe Acute Respiratory Syndrome virus (SARS-CoV-2) that causes corona virus disease 2019 (COVID-19) was discovered in Wuhan, Hubei, China in December 2019, leading to a number of pneumonia cases. An epidemic was caused by the disease's quick spread and novelty combined with a lack of targeted action. The aims to determine the correlation of COVID-19 patients by systematically analyzing the baseline biochemical characteristic and laboratory indices. This is a hospital based; observational cross-sectional study was conducted in department of pathology medical college Kolkata in collaboration with department of chest medicine. The study period was One year. 382 patients were included in this study. In Mild, the mean LDH (mean±s.d.) of patients was 248.7961±79.7309. In Moderate, the mean LDH (mean±s.d.) of patients was 301.1972±93.0326. In Severe, the mean LDH (mean±s.d.) of patients was 463.5287±207.2682. Distribution of mean LDH with Severity was statistically significant (p<0.0001). In Mild, the mean Ferritin (mean±s.d.) of patients was 299.4790±225.5873. In Moderate, the mean Ferritin (mean±s.d.) of patients was 913.6915± 1365.3716. In Severe, the mean Ferritin (mean±s.d.) of patients was 1883.4747±2348.1545. Distribution of mean Ferritin with Severity was statistically significant (p<0.0001). In summary, the relationship between the severity of the disease and biochemical traits in COVID-19 patients provides important information on the pathogenesis of the virus. Higher levels of several biomarkers-like ferritin, D-dimer, C-reactive protein and liver enzymes-are closely linked to worsening illness outcomes. These biochemical measures can be useful markers for identifying high-risk individuals early on, which can help with prompt management and intervention plans.

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Key Words
COVID-19, biochemical characteristics, risk factors and disease severity

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INTRODUCTION

A cluster of pneumonia cases was caused by the Severe Acute Respiratory Syndrome virus (SARS-CoV-2) that caused the corona virus disease 2019 (COVID-19) to be discovered in Wuhan, Hubei, China in December 2019[1]. An epidemic was caused by the disease's quick spread and novelty combined with a lack of targeted treatment[2]. The World Health Organization (WHO) designated the illness as a Public Health Emergency of International Concern (PHEIC) as it started to spread over the world. The corona virus, an enveloped positive-sense RNA virus, grows in epithelial cells and is mostly responsible for respiratory infections in humans, such as acute exacerbation of chronic bronchitis (AECB) and severe acute respiratory syndrome (SARS)[3]. According to recent research, COVID-19 should be considered a multi-systemic illness that affects the immunological system, hematopoietic system, respiratory system, gastrointestinal system, and cardiovascular system[4]. When determining the severity and prognosis of an illness, a patient's metabolic profile is crucial. Numerous investigations have concentrated on several biochemical indicators in COVID-19 infections, including sodium levels, urea, alanine aminotransferases (ALT) and aspartate aminotransferases (AST). The cause of this illness is an infection with the Severe Acute Respiratory Syndrome Coronavirus 2 (SARSCoV-2), a newly discovered zoonotic virus[5]. These enclosed positive-strand RNA coronaviruses are all isolated from bats and may spread from one animal to another, from one person to another and from one animal to another[6]. Apart from certain notable distinctions that have been noted recently, they have comparable clinical signs. The disease's symptoms, which include fever, coughing, shortness of breath and weariness, might start to show up in the first five to six days and last up to fourteen days[7]. Afterward, critical symptoms may develop in some patients involving dyspnea and pneumonia that require patient's management in intensive care units to avoid the serious respiratory complications that may lead to death[8]. These parameters have not only been associated with the severity of COVID-19 infection but also with the worst outcomes in terms of in-hospital mortality. The aims to determine the correlation of COVID-19 patients by systematically analyzing the baseline biochemical characteristic and laboratory indices.

MATERIALS AND METHODS

Study Design/Experiment Design: Hospital based, observational cross sectional study.

Study Setting and Time Lines: The study was conducted in department of pathology Medical college Kolkata in collaboration with department of chest medicine.

Place of Study: Medical College, Kolkata.

Period of Study: One year.

Study Populations: Diagnosed patients with COVID-19 by RT-PCR (ICMR approved Centers).

Sample Size/Design: As it is a pandemic disease so we expect 382 cases to assess within the period of data collection fulfilling the inclusion and exclusion criterias.

Inclusion Criteria:

- Diagnosed patient with COVID 19 by real time polymerase chain reaction (ICMR approved centers).
- Admitted to the covid ward Medical College and hospital Kolkata.
- Admitted patient who has gone through all the laboratory test which are included to this study.

Exclusion Criteria:

- Patients with negative COVID-19 RT-PCR test.
- Previously critically ill patients.
- Vaccinated individuals.
- Foreign nationals.
- Travellers from foreign countries within l month of tier 4 lock down.
- Patients suspected of new/future strains of COVID-19.
- Those who do not give consent.

Study Tools: Questionnaire, Upper respiratory throat swab samples at admission to detect the COVID-19 by RT-PCR, c-reactive protein (CRP) by immuno turbidimetry method, (PCT) by electro chemilumine scence method. Erythrocyte sedimentation rate (ESR) by Westergren's international standard method. Other la6oratory techniques for complete hemogram (Hemoglobin, Total leucocyte count, platelet count, neutrophil count, lymphocyte count, NLR), coagulation profile (prothrombin time, D-dimer), inflammatory parameters (Procalcitonin, ferritin, LDH, IL6), biochemical parameters (Aspartate amino tranferase, alanine a minotranferase, total billirubin, Albumin).

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0., SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests, which compare the means of independent or unpaired samples, were used to assess differences between groups. Paired t-tests, which account for the correlation between paired observations, offer greater power than unpaired tests.

Chi-square tests (χ^2 tests) were employed to evaluate hypotheses where the sampling distribution of the test statistic follows a chi-squared distribution under the null hypothesis., Pearson's chi-squared test is often referred to simply as the chi-squared test. For comparisons of unpaired proportions, either the chi-square test or Fisher's exact test was used, depending on the context. To perform t-tests, the relevant formulae for test statistics, which either exactly follow or closely approximate a t-distribution under the null hypothesis, were applied, with specific degrees of freedom indicated for each test. P-values were determined from Student's t-distribution tables. A p-value #0.05 was considered statistically significant, leading to the rejection of the null hypothesis in favour of the alternative hypothesis.

RESULTS AND DISCUSSIONS

In Mild, the mean LDH (mean±s.d.) of patients was 248.7961±79.7309. In Moderate, the mean LDH (mean±s.d.) of patients was 301.1972±93.0326. In Severe, the mean LDH (mean±s.d.) of patients was 463.5287±207.2682. Distribution of mean LDH with Severity was statistically significant (p<0.0001). In Mild, the mean Ferritin (mean±s.d.) of patients was 299.4790±225.5873. In Moderate, the mean Ferritin (mean±s.d.) of patients was 913.6915±1365.3716. In Severe, the mean Ferritin (mean± s.d.) of patients was 1883.4747±2348.1545. Distribution of mean Ferritin with Severity was statistically significant (p<0.0001). In Mild, the mean Albumin (mean±s.d.) of patients was 3.8829±.4825. In Moderate, the mean Albumin (mean±s.d.) of patients was 3.4754±.5973. In Severe, the mean Albumin (mean±s.d.) of patients was 3.2966± .6829. Distribution of mean Albumin with Severity was statistically significant (p<0.0001). In Mild, the mean CRP (mean±s.d.) of patients was 28.1538±25.1832. In Moderate, the mean CRP (mean±s.d.) of patients was 77.5709±51.0397. In Severe, the mean CRP (mean± s.d.) of patients was 108.0000± 68.9692. Distribution of mean CRP with Severity was statistically significant (p<0.0001). In Mild, the mean PCT (mean±s.d.) of patients was .1655±.1560. In Moderate, the mean PCT (mean±s.d.) of patients was .5415±.3480. In Severe, the mean PCT (mean±s.d.) of patients was 4.2937± 9.7996. Distribution of mean PCT with Severity was statistically significant (p<0.0001). In Mild, the mean TBIL (mean±s.d.) of patients was .6268±.3402. In Moderate, the mean TBIL (mean±s.d.) of patients was .6900±.4888. In Severe, the mean TBIL (mean±s.d.) of patients was .8372±.5942. Distribution of mean TBIL with Severity was statistically significant (p=0.0036). In Mild, the mean SGPT (mean±s.d.) of patients was 44.7632±33.8046. In Moderate, the mean SGPT (mean±s.d.) of patients was 45.6831±48.8232. In Severe, the mean SGPT (mean±s.d.) of patients was 59.9080±96.1832. Distribution of mean SGPT with Severity was not statistically significant (p=0.1225). In Mild, the mean SGOT (mean±s.d.) of patients was 49.6382±29.3403. In Moderate, the mean SGOT (mean±s.d.) of patients was 54.7606±34.1064. In Severe, the mean SGOT (mean±s.d.) of patients was 76.6092±71.9867. Distribution of mean SGOT with Severity was statistically significant (p<0.0001). In Mild, the mean D-DIMER (mean±s.d.) of patients was .9207± .8093. In Moderate, the mean D-DIMER (mean±s.d.) of patients was 1.4409±1.5082. In Severe, the mean D-DIMER (mean±s.d.) of patients was 2.6352±3.2216. Distribution of mean D-DIMER with Severity was statistically significant (p<0.0001).

In Moderate cases, 5 (3.5%) patients were 31-40 years of age, 5 (3.5%) patients were 41-50 years of age, 21 (14.8%) patients were 51-60 years of age, 49 (34.5%) patients were 61-70 years of age, 48 (33.8%) patient were 71-80 years of age and 14 (9.9%) patients were 81-90 years of age. **Leulseged**[9] found that to find laboratory indicators for COVID-19 patients admitted to Ethiopia's Millennium COVID-19 Care Center that forecast illness severity and prognosis. Age group (p-value <0.0001, ARR =1.779, 95%CI =1.405–2.252).

The age group had the most significant correlation with the COVID-19 result (AOR =2.767, 95%CI =1.099-6.067, p-value =0.031). **Wang**[10] examined that corona virus disease 2019 (COVID-19) is a novel infectious disease caused by the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) emerged in Wuhan and has quickly spread across the world. Significantly, disease severity was associated with age (r=0.458, P<0.001). **Qiu**[11] found that currently, new corona virus disease 2019 (COVID-19) is a major public health concern on a worldwide scale. According to a meta-analysis, the median age of COVID-19 fatalities was 69.9 years and 66.6% of the deceased were men. **Li**[12] found that we studied admission and dynamic demographic, hematological and biochemical co-variates in 1449 hospitalized subjects with corona virus infectious disease-2019 (COVID-19) in five hospitals in Wuhan, Hubei province, China. They identified two admission co-variates: age (Odds Ratio [OR]=1.18, 95%. We found that, majority number of patients had Comorbidities in severe severity [78 (88.6%)] compared to moderate severity [117 (82.4%)] and mild severity [14 (9.2%)] though it was statistically significant (p<0.0001). In our study, mean TLC was significantly higher in severe cases [9706.2069± 9262.7828] compared to moderate [6866.9014± 2737.4659] and mild cases [6287.4934±2597.3056] (p<0.0001). **M Alroomi, R Rajan, AA Omar, A Alsaber**[13] study showed greater mortality rate in individuals with ferritin levels greater than 1000. Ferritin levels over 1000 were associated with 89% of patients who developed COVID-19 pneumonia. We found that, mean Ferritin was significantly higher severe severity [1883.4747±2348.1545] compared to

Table 1: Distribution of Mean LDH, Ferritin and Albumin: Severity (n=382)

		Number	Mean	SD	Minimum	Maximum	Median	p-value
LDH	Mild	152	248.7961	79.7309	120.0000	571.0000	231.5000	<0.0001
	Moderate	142	301.1972	93.0326	120.0000	919.0000	304.0000	
	Severe	88	463.5287	207.2682	185.0000	1894.0000	456.0000	
Ferritin	Mild	152	299.4790	225.5873	7.9900	968.0000	270.0000	<0.0001
	Moderate	142	913.6915	1365.3716	60.9000	9471.0000	669.2000	
	Severe	88	1883.4747	2348.1545	279.5000	9471.0000	1126.0000	
Albumin	Mild	152	3.8829	.4825	2.3000	5.1000	3.8000	<0.0001
	Moderate	142	3.4754	.5973	1.6000	4.6000	3.5500	
	Severe	88	3.2966	.6829	1.6000	4.6000	3.4000	

Table 2: Distribution of Mean CRP and PCT: Severity

		Number	Mean	SD	Minimum	Maximum	Median	p-value
CRP	Mild	152	28.1538	25.1832	1.0000	136.9000	25.2000	<0.0001
	Moderate	142	77.5709	51.0397	0.3800	236.1000	75.5000	
	Severe	88	108.0000	68.9692	10.3000	331.8000	105.7000	
PCT	Mild	152	.1655	.1560	0.1000	1.2000	0.1000	<0.0001
	Moderate	142	.5415	.3480	0.1000	1.9000	0.5600	
	Severe	88	4.2937	9.7996	1.0100	46.6000	1.4300	

Table 3: Distribution of Mean Total Bilirubin, SGPT, SGPT and D-DIMER: Severity

		Number	Mean	SD	Minimum	Maximum	Median	p-value
TBIL	Mild	152	.6268	.3402	0.3000	2.1000	0.5000	0.0036
	Moderate	142	.6900	.4888	0.3000	3.3000	0.5000	
	Severe	88	.8372	.5942	0.3000	3.1000	0.7000	
SGPT	Mild	152	44.7632	33.8046	10.0000	147.0000	37.0000	0.1225
	Moderate	142	45.6831	48.8232	10.0000	498.0000	34.5000	
	Severe	88	59.9080	96.1832	10.0000	812.0000	39.0000	
SGOT	Mild	152	49.6382	29.3403	12.0000	146.0000	44.0000	<0.0001
	Moderate	142	54.7606	34.1064	14.0000	231.0000	49.0000	
	Severe	88	76.6092	71.9867	22.0000	615.0000	61.0000	
D-DIMER	Mild	152	.9207	.8093	0.1900	4.5700	0.7700	<0.0001
	Moderate	142	1.4409	1.5082	0.1900	10.0700	0.9300	
	Severe	88	2.6352	3.2216	0.1900	25.0500	1.6400	

mild severity [299.4790±225.5873] moderate severity [913.6915± 1365.3716] (p<0.0001). **Pujani**[14] examined that COVID-19 is a systemic viral infection with a significant impact on the hematopoietic system, hemostasis as well as immune system. There were statistically significant differences in neutrophil-lymphocyte ratio (NLR) covid cases vs controls., among the clinical subgroups and among the survivors and non-survivors. There was a significant strong positive correlation between various parameters, that is, NLR and MLR (r: 0.852, P=0), NLR (AUC: 0.676, P=0) was the best single parameter. **Israfil**[15] examined that clinical characteristics are essential for the correct diagnosis of diseases. The prominent laboratory findings were LDH 40.8. The prominent laboratory findings were elevated levels of CRP 61.9. We found that, mean CRP was significantly higher in severe severity [108.0000± 68.9692] compared to moderate severity [77.5709± 51.0397] and mild severity [28.1538±25.1832] and statistically significant. (p<0.0001). We showed that, mean LDH was significantly higher in severe severity [463.5287±207.2682] compared to moderate severity [301.1972±93.0326] and mild severity [248.7961± 79.7309] (p<0.0001). **Israfil**[15] examined that clinical characteristics are essential for the correct diagnosis of diseases. The prominent laboratory findings were IL-6 52. We observed that, mean IL6 was significantly higher in severe severity [136.3001±57.4146] compared to mild severity [13.9713±12.1795] and moderate severity [54.8946± 38.5175] and (p<0.0001). In our study, mean SGPT was lower in mild severity [44.7632±33.8046] compared to moderate severity [45.6831±48.8232] and severe severity [59.9080± 96.1832] which was not statistically significant (p=0.1225). **Israfil**[16] examined that clinical characteristics are essential for the correct diagnosis of diseases. The prominent laboratory findings were SGOT 38.4%. We observed that, mean SGOT was significantly lower in mild severity [49.6382±29.3403] **Liang**[17] examined that or better understanding of the pathological changes of COVID-19, benefitting clinical management of the disease and the preparation for future waves of similar pandemics. Procalcitonin (PCT) was significantly higher in severely and critically ill patients than in moderately ill patients. In our study, mean PCT was significantly higher in severe severity [4.2937±9.7996] compared to moderate severity [.5415±.3480] and mild severity [.5415±.3480]. It is also significant (p<0.0001).

CONCLUSION

In conclusion, the correlation between disease severity and biochemical characteristics in patients with COVID-19 reveals critical insights into the pathophysiology of the virus. Elevated levels of certain biomarkers, such as C-reactive protein, D-dimer, ferritin and liver enzymes, are strongly associated with more severe disease outcomes. These biochemical parameters can serve as valuable indicators for early identification of high-risk patients, aiding in timely intervention and management strategies. Understanding these relationships not only helps in

prognostication but also offers potential therapeutic targets to mitigate the progression of severe COVID-19 cases.

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