

ORIGINAL RESEARCH

To determine the relationship between biochemical indicators and the severity of COVID-19

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ABSTRACT

Aim: To determine the relationship between biochemical indicators and the severity of COVID-19.

Methods: Blood samples were obtained by competent doctors and nurses in accordance with ICMR guidelines. The samples were then forwarded to the central biochemistry laboratory for additional analysis. The Access-2 completely automated chemical analyzer was used to test ferritin, quantitative CRP, and IL-6, while the AU 480 analyzer was used to assess LDH.

Results: We included 200 confirmed covid-19 patients in our trial. All of the patients were above the age of 18. The prevalence of HTN, diabetes, CKD, COPD, and Cardiac Disease in the study patients was 40%, 32%, and 15%, respectively. 20 and 30 percent, respectively. In the current research, the mean values of IL-6, ferritin, CRP, and LDH were shown to be higher in covid patients, with the rise being greater in patients on intubation. The mean and standard deviation of biochemical parameters in non-ICU, ICU, and intubation patients.

Conclusion: Serum CRP, LDH, IL-6, and ferritin levels that are increased may be employed as laboratory indicators for a bad prognosis in COVID-19.

Keywords: Serum CRP, LDH, IL-6, ferritin, COVID-19

Introduction

In late 2019, a pneumonia outbreak with an unknown source started in Wuhan, China's Hubei Province, and has since expanded dramatically globally. ¹ The virus that caused the illness was formerly known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) until the World Health Organization renamed it coronavirus disease-2019 (COVID-19). ² This condition often affects people between the ages of 30 and 79. About half of people infected with COVID-19 exhibit mild to moderate symptoms. Fatigue, fever, cough, muscular discomfort, and shortness of breath are all significant symptoms in symptomatic people. ^{2,3}

More serious illnesses, such as acute respiratory distress syndrome (ARDS) and multi-organ failure, may occur at times. Comorbid disorders, particularly hypertension (HT), diabetes mellitus (DM), and heart disease, are common in patients with these severe conditions. ³ The most prevalent laboratory values are neutrophilia and lymphopenia. Abnormal liver function test results have also been reported at various rates. Serum procalcitonin levels are typically normal, but C-reactive protein levels are slightly elevated. Furthermore, D-dimer values are elevated in 30% of individuals. ^{4,5} Coronaviruses are positively polarised encapsulated RNA viruses with a single chain. As a result, they lack RNA-dependent RNA polymerase enzymes, yet the enzyme code has been found in their genetic composition. Their surfaces are adorned with rod-like projections. ⁶

Previous research has linked specific haematological markers, such as haemoglobin and red cell distribution width (RDW), to both ICU admission and death in COVID-19. It has been found that in patients with severe disease, haemoglobin levels are much lower and RDW is significantly higher. Another study found that haemoglobin and RDW value were the most distinguishing predictors for the differential diagnosis of community-acquired pneumonia and COVID-19. ⁷

Lactate dehydrogenase (LDH) is an enzyme that converts lactate to pyruvate, a response that happens in many tissues after severe tissue loss caused by sepsis, malignancy, and severe infections. The researchers indicated in a study that LDH level was an indication for COVID-19 pneumonia, which rises with severe pneumonia and reduces when pneumonia was resolved, but no cutoff value could be offered. ⁸

Materials and procedure

The current research was conducted at the Department of Biochemistry among asymptomatic patients during the Corona pandemic. Blood samples were obtained by competent doctors and nurses in accordance with ICMR guidelines. The samples were then forwarded to the central biochemistry laboratory for additional analysis. After donning protective gear such as a facemask, PPE kit, and gloves, the sample was run and the results were recorded.

Inclusion Criteria: All diagnosed symptomatic Covid -19 patients were included.

The Access-2 completely automated chemical analyzer was used to test ferritin, quantitative CRP, and IL-6, while the AU 480 analyzer was used to assess LDH.

Statistical Analysis: SPSS version 25 was used to analyse the data. Because of the small sample size and the necessity for accurate indicators of illness severity, the continuous variables were converted to categorical variables.

Results

We included 200 confirmed covid-19 patients in our trial. All of the patients were above the age of 18. There were 130 men and 70 women among the 200 patients. The prevalence of HTN, diabetes, CKD, COPD, and Cardiac Disease in the study patients was 40%, 32%, and 15%, respectively. 20 and 30 percent, respectively (Table-2). Table no-2 depicts the severity distribution of patients in non-ICU, ICU, and intubation.

In the current research, the mean values of IL-6, ferritin, CRP, and LDH were shown to be higher in covid patients, with the rise being greater in patients on intubation. (See Table 3).

The mean and standard deviation of biochemical parameters in non-ICU, ICU, and intubation patients are shown in Table -3. Out of 200 participants, 135 were from non-ICU wards, 40 were from ICU wards, and 25 were on intubation.

Table 1 Gender and age distribution of patients

Gender	Number of patients	%
Male	130	65
Female	70	35
Age		
Below 25	20	10
25-35	47	23.5
35-45	102	51
45-55	23	11.5
Above 55	8	4

Table 2: Comorbidities

Parameter	No. patients	%
Hypertension	80	40
Diabetes	64	32
Cardiac Disease	60	30
COPD	40	20
Chronic Kidney Disease	30	15

Table 3: Biochemical parameter

Parameters	Mean \pm SD
IL-6 (<1.8 pg/ml)	12.74 \pm 3.10
Ferritin (10 to 250 ng/ml)	495.11 \pm 250.04
CRP (<5.0 mg/ml)	123.21 \pm 56.72
LDH (140-270 IU/L)	559.84 \pm 271.10

Table 4: Biomarkers in Non-ICU, ICU admitted and in Intubation Patients

Parameters	Non-ICU Patients(135)	Admitted ICU Patients(40)	Admitted Intubation Patients(25)
IL-6 (</1.8 pg/ml)	11.36 ± 2.59	14.74 ± 2.56	18.51 ± 2.16
Ferritin (10-250 ng/ml)	411.79 ± 170.52	631.09 ± 199.21	995.83 ± 206.98
CRP (<5.0 mg/ml)	106.31 ± 42.00	156.12 ± 45.22	217.05 ± 68.70
LDH (140-270 IU/L)	452.21 ± 161.51	812.03 ± 165.55	1095.55 ± 253.64

Discussion

Beginning in China in 2019, COVID-19 has spread throughout the world and has been declared a pandemic by the World Health Organization. This disease is caused by an RNA virus known as coronavirus 2 (SARS-CoV-2), which has caused a massive loss of life worldwide. The clinical signs are non-specific, but the disease typically manifests as a cough, fever, myalgia, weakness, and nausea. It may be more severe and cause multi-organ failure in patients with high levels of comorbidity. Patients are classified as mild, moderate, severe, or critical in the most recent Coronavirus Pneumonia Diagnosis and Treatment Program (7th Edition). Clinical findings such as blood values, respiratory counts, and blood pressures can help determine the severity of the disease.⁹The disease, which can range from asymptomatic to severe, causes acute respiratory failure. It is critical to collect data from patients in order to determine the patient's condition and predict complications in a timely manner.¹⁰ Inflammatory cytokines and biomarkers such as IL-2, IL-6, IL-7, granulocyte-colony stimulating factor, macrophage inflammatory protein 1, tumour necrosis factor- (TNF-), CRP, ferritin, PCT, and D-dimer are significantly elevated in the hyperinflammation phase of covid-19, which may lead to severe manifestations of cytokine storm. Hyperinflammation can lead to cardiopulmonary collapse and multi-organ failure.^{11,12} Estimation of biochemical parameters and biomarkers are quantitative measurements that represent disease pathophysiology and aid clinicians in determining disease severity. We enrolled 200 Covid patients in our study and discovered elevated levels of CRP and IL-6 in all Covid-19 patients admitted to the Covid hospital. These indicators increased higher in intubation patients than in non-ICU and ICU patients, indicating the severity of intubation patients and the establishment of lung lesions in the early stages of covid-19. Our findings are consistent with those of a previously published research. C-reactive protein (CRP) is a non-specific acute phase protein generated in the liver by IL-6. It is utilised as a biomarker for viral, inflammatory, and other diseases such as cardiovascular disease. CRP levels are strongly related to the amount of inflammation and illness severity. As a result, CRP is an essential biomarker in the diagnosis and severity assessment of infectious illnesses.¹³⁻¹⁶ CRP may be employed as a sensitive and effective biomarker for predicting covid-19 development. Many researchers discovered considerably higher levels of CRP and D-Dimer in COVID-19 participants in their study. Elevated D-dimer levels were linked to inflammatory indicators, particularly CRP.^{17,18} In our investigation, we found that all covid-19 patients had high LDH levels. The rise in LDH level was greater in patients on intubation. LDH is found in all tissues and catalyses the conversion of pyruvate to lactate through a NADH dependent process. Reduced oxygenation may cause changes in LDH levels, resulting in glycolysis upregulation and multi-organ damage. Lactate causes damage by activating metalloproteinases and increasing macrophage-mediated angiogenesis.¹⁹ A study of COVID-19 patients led to the conclusion that LDH may be a strong predictor of lung damage and severe COVID-19 cases.²⁰ Elevated LDH has also been linked to worse results in a number of studies.²¹⁻²³ Ferritin levels were also observed to be increased in covid patients. Ferritin has been linked to acute respiratory distress syndrome (ARDS), death, and severe covid-19 conditions. This might be because covid-19 patients have (secondary hemophagocytic lymphohistiocytosis) sHLH.²⁴ Hyperinflammation caused by cytokine storm may result in the development of sHLH, a disorder that causes catastrophic multi-organ failure.²⁵ Hyperinflammation is most typically caused by viral infections, which raises the possibility that SARS-CoV-2 is causing this hyperinflammatory illness. A recent comprehensive analysis by Veronese et al identified 542 individuals with contradictory findings from four trials and concluded that conventional corticosteroid medication in covid-19 is not indicated. Corticosteroids may lower mortality in COVID-19 individuals with ARDS, according to certain reports.

Conclusion

Serum CRP, LDH, IL-6, and ferritin levels that are increased may be employed as laboratory indicators for a bad prognosis in COVID-19. Serum CRP may be utilised not just as a prognostic measure, but also to track disease progression in COVID-19. All of these test indicators will aid clinicians in distinguishing critically unwell individuals.

References

1. He F, Deng Y, Li W. Coronavirus disease 2019: what we know? *J Med Virol*. 2020;92(7):719-725. doi:[10.1002/jmv.25766](https://doi.org/10.1002/jmv.25766)
2. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet*. 2020;395(10224):565-574. doi:[10.1016/S0140-6736\(20\)30251-8](https://doi.org/10.1016/S0140-6736(20)30251-8)
3. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. *JAMA*. 2020;323(13):1239. doi:[10.1001/jama.2020.2648](https://doi.org/10.1001/jama.2020.2648)
4. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020;382(13):1199-1207. doi:[10.1056/NEJMoa2001316](https://doi.org/10.1056/NEJMoa2001316)
5. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *J Am Med Assoc*. 2020;323(11):1061. doi:[10.1001/jama.2020.1585](https://doi.org/10.1001/jama.2020.1585)
6. Zhou Y, Yang Y, Huang J, Jiang S, Du L. Advances in MERS-CoV vaccines and therapeutics based on the receptor-binding domain. *Viruses*. 2019;11(1):60. doi:[10.3390/v11010060](https://doi.org/10.3390/v11010060)
7. Lu G, Wang J. Dynamic changes in routine blood parameters of a severe COVID-19 case. *ClinChimActa*. 2020;508:98-102.
8. Wu MY, Yao L, Wang Y, Zhu XY, Wang XF, Tang PJ, et al. Clinical evaluation of potential usefulness of serum lactate dehydrogenase (LDH) in 2019 novel coronavirus (COVID-19) pneumonia. *Respir Res*. 2020;21(1):171.
9. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*. 2020;395(10223):507-513. doi:[10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7)
10. Malik P, Patel U, Mehta D, Patel N, Kelkar R, Akrmah Mu, et al. Biomarkers and outcomes of COVID-19 hospitalisations: systematic review and meta-analysis. *BMJ Evidence-Based Medicine* 2021;26(3):107–108.
11. Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: a clinical therapeutic staging proposal. *J Heart Lung Transplant* 2020; 39: 405–407.
12. Zhang W, Zhao Y, Zhang F, Wang Q, Li T, Liu Z, et al. The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): the experience of clinical immunologists from China. *ClinImmunol* 2020; 214:108393.
13. Liu F, Li L, Xu M, Wu J, Luo D, Zhy Y, et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. *J ClinVirol* 2020;127:104370–70.
14. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. *Clin Infect Dis* 2020; 71:762–8.
15. Wang L. C-Reactive protein levels in the early stage of COVID-19. *Med Mal Infect* 2020;50:332–4.
16. Chalmers S, Khawaja A, Wieruszewski PM, Gazik O, Odeyemi Y. Diagnosis and treatment of acute pulmonary inflammation in critically ill patients: the role of inflammatory biomarkers. *WJCCM* 2019;8:74–96.
17. Yu B, Li X, Chen J, Ouyang M, Zhang H, Zhao X, et al. Evaluation of variation in D-dimer levels among COVID-19 and bacterial pneumonia: a retrospective analysis. *J Thromb Thrombolysis* 2020:1–10.
18. Ayanian S, Reyes J, Teufel K. The association between biomarkers and clinical outcomes in novel coronavirus pneumonia in a US cohort. *Biomark Med* 2020;14(12):1091-97.
19. Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: a pooled analysis. *Am J Emerg Med* 2020;38:1722–6.

20. Han Y, Zhang H, Mu S, Wei W, Jin C, Xue Y, et al. Lactate dehydrogenase, a risk factor of severe COVID-19 patients. *Med Rxiv* 2020:1
21. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. *J Clin Invest* 2020;130(5):2620–9.
22. Wu C, Chen X, Cai Y, Xia J, Zhou S, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med* 2020;180(7):934-47.
23. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult in patients with COVID- 19 in Wuhan, China: a retrospective cohort study. *The Lancet* 2020;395(10229):1054–62.
24. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020; 395(10229):1033–34.
25. Karakike E, Giamarellos-Bourboulis EJ. Macrophage activation-like syndrome: a distinct entity leading to early death in sepsis. *Front Immunol* 2019; 10: 55