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DIAGNOSTIC AND PROGNOSTIC MARKERS OF COVID-19 PATIENTS

Pathology

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ABSTRACT

The 2019 coronavirus disease (COVID-19) is caused by the coronavirus 2 of the severe acute respiratory syndrome (SARS-CoV-2), which spread rapidly all over the world and was declared by the World Health Organization (WHO) as a pandemic on 11 March 2020. Many laboratory parameters make it possible to assess the severity of the disease and predict the risk of it evolving toward more serious afflictions such as acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC) and multiple organ failure (MOF).This study included a total of 100 patients. All these cases were subjected to different maker studies which included C - reactive protein (CRP), D-dimer, Serum ferritin and Serum Lactate Dehydrogenase (LDH). Mean levels of all the markers were suggestively higher in severe cases with significant correlation. Majority of the patients from age group of ≥60 years were having severe disease. Level of biomarkers was significantly associated with the clinical stage of the disease.

KEYWORDS

CRP, D-dimer, Serum ferritin, Serum LDH.

INTRODUCTION

In December 2019, the city of Wuhan in China became the epicenter of unexplainable cases of pneumonia, which in January 2020 were identified as a new coronavirus, turning rapidly into a major problem of public health worldwide.[1] Laboratory tests validated for SARS-CoV-2 are crucial for the timely management of COVID-19 because they support the clinical decision-making process for controlling infections and detecting asymptomatic cases.[2] Some parameters for which an unfavorable course of the disease has been described are absolute neutrophilia, thrombocytopenia, hypoalbuminemia, the elevation of liver enzymes, creatinine and nonspecific inflammatory markers such as C-reactive protein (CRP) and Interleukin 6 (IL-6).[3]

Notwithstanding the above, the main progression predictors described are lymphopenia, elevated D-dimer and hyperferritinemia, although it is also necessary to consider LDH, CPK and troponin in the marker panel. [4]Following the outbreak of the COVID-19 pandemic, D-dimer has been identified as a potential indicator for its prognosis in COVID-19 patients. Admission day D-dimer has shown promise for predicting the disease severity in multiple studies. [5] Furthermore, it has been reported that the elevation of the lactate dehydrogenase enzyme (LDH) used as a marker of lung tissue damage, is one of the most frequent biochemical anomalies in COVID-19 patients on admission to the hospital. [6]

The present study is to predict prognosis and mortality in COVID-19 patients on the basis of their biomarker levels and to utilize various biomarkers for risk stratification and planning of a proper treatment protocol.

MATERIALS AND METHODS

This study was conducted at a tertiary care centre for a period of two years. Blood samples were collected from the patients under full aseptic conditions. Measurement of C-reactive protein (CRP) was done by CRP-Turbilatex which is a quantitative turbidimetric assay. D-dimer Quantitative test was performed using fully automated technique by STAGO- Satellite Max machine. Serum ferritin was determined by using Ferritin ELISA kit which acts on the principle of solid phase sandwich assay method. Serum LDH was determined by LDH reagent kit in which LDH catalyzes the oxidation of pyruvate to lactate accompanied by the simultaneous reduction of NADH to NAD. LDH activity in serum is proportional to the decrease in absorbance due to the reduction of NADH.

OBSERVATION AND RESULT

A total of 100 RT-PCR positive patients were studied. Clinical severity, CRP, D-dimer, Serum Ferritin and Serum LDH levels of these patients were taken into consideration. Majority (48.4%) from <60 years age group were having mild disease while 41.7% cases from ≥60 years age group were having severe disease.

Table 1: Association of Clinical stage of disease with age

Clinical stage	Age in years		
	<60	≥60	Total
Mild	31(48.4%)	5(13.9%)	36
Moderate	27(42.2%)	16(44.4%)	43
Severe	6(9.4%)	15(41.7%)	21
Total	64	36	100

CRP level of 24% cases were measuring >100mg/L from which majority (20 cases) were having severe disease. 42(42%) cases had D-dimer level of ≥1.5 µg/ml from which 15% of the patients were having severe disease with mean D-dimer level of 1.92µg/ml (±0.45µg/ml).

25 (25%) cases had serum ferritin level of >1000ng/ml from which 16% of the patients were having severe disease. 46 (46%) cases had serum LDH level of >350ng/ml from which 16% of the patients were having severe disease.

Table 2: Correlation of Level of Laboratory markers among COVID-19 patients on discharge with disease mortality

Laboratory marker	Reduced level on discharge	Elevated level on discharge/ death	Mortality among cases with reduced laboratory marker level	Mortality among cases with elevated laboratory marker level
CRP	82	18	2(2.4%)	17(94.4%)
D-dimer	84	16	6(7.1%)	13(81.2%)
Serum ferritin	78	22	3(3.8%)	16(72.7%)
Serum LDH	83	17	7(8.4%)	12(70.6%)

18 cases presented with elevated CRP level from which 17 patients died thus having mortality of 94.4%. D-dimer level of 84 patients were reduced on discharge while that of 16 cases were elevated from which 13 patients died hence with mortality of 81.2%.

Out of 22 patients who had elevated serum ferritin level, 16 patients died with mortality of 72.7%. 17 patients had elevated level of serum LDH from which 12 patients died having mortality of 70.6%.

Table 3: Laboratory biomarker related variables.

Variable	Covid-19 severity			p-value
	Mild	moderate	severe	
Mean Age (SD)	46.4±12.3	56.7±10.3	67.3±13.6	0.0000
Mean CRP (SD)	22.4±12.9	75.8±21.1	131.7±27.2	0.0000
Mean D-dimer (SD)	0.8±0.43	1.4±0.3	2.12±0.57	0.0010
Mean Serum ferritin (SD)	575.4±224.6	847.9±285.4	1212.4±445.2	0.0000
Mean Serum LDH (SD)	256.7±81	499.3±229.2	1219.3±518.5	0.0008

The mean age of the patients in mild, moderate and severe cases was 46.4±12.3, 56.7±10.3 and 67.3±13.6 respectively (p-value=0.00). Total mean CRP level in study population was 68.3±45.2 mg/L. Mean CRP level was suggestively higher in severe cases 131.7±27.2 mg/L as compared to mild and moderate cases 22.4±12.9 mg/L and175.8 ±21.1 mg/L respectively with significant *p-value*<0.000. Mean D-dimer level was 1.36±0.61µg/ml. Based on the cutoff value of 1.5µg/ml for D-dimer level, the mean admission D-dimer level among patients with D-dimer level of <1.5µg/ml was 0.95±0.33µg/ml, whereas that among patients with D-dimer level of ≥1.5µg/ml was 1.92±0.45µg/ml. Mean D-dimer level was higher in severe cases 2.12±0.57µg/ml as compared to mild and moderate cases 0.8±0.43 µg/ml and 1.4±0.3 µg/ml respectively with significant *p value of* 0.001. Out of 21 patients with severe disease, 16 patients had serum ferritin level of >1000 ng/ml. Mean serum ferritin level was suggestively higher in these severe cases 1212.4±445.2 ng/ml as compared to mild and moderate cases 575.4±224.6 ng/ml and 847.9 ±258.4 ng/ml respectively with significant *p-value*<0.000. A total of 46 patients presented with high LDH levels (>350 IU/L). Mean serum LDH level was higher in severe cases 1219.3±518.5 IU/L as compared to mild and moderate cases 256.7±81 IU/L and 499.3 ±229.2 IU/L respectively with significant *p-value* 0.0008.

DISCUSSION

According to Guo et al.2020[7] 65% of moderate cases, 25% of severe cases, 10% of critical cases and 0% of mild cases presented with age ≥75 years while 5.9% of mild cases fell in the age group of 60-75 years. Correlation of disease severity with increasing age was found in above mentioned studies along with the current study.

L. Wang, 2020[8] documented that mean (±SD) Age (years) among mild, moderate, severe and critical cases were 30.55 (±10.46), 33.29 (±14.97), 40.50 (±4.95) and 41.00 (±25.46) respectively and mean (±SD) CRP level (mg/L) were 1.52 (±1.56), 16.76 (±18.38), 54.15 (±1.06) and 105.00 (±12.73) respectively which shows that there is increasing values of mean CRP level with increasing age and disease severity. Similar findings have been found in the present study.

According to the study of Poudel et al.[9], 126 out of 182 patients had D-dimer on admission less than 1.5 µg/ml, out of which 10 patients (7.9%) died during hospital stay and 116 were discharged (including one discharge on patient request). The mean admission D-dimer among those having levels <1.5 µg/ml was 0.44 µg/ml (±0.36 µg/ml) and among those having levels ≥ 1.5 µg/ml was3.83 µg/ml (±2.42 µg/ml) while mean D-dimer value of all patients was 1.48 µg/ml (±2.08 µg/ml). The mean admission D-dimer among patients who survived was 1.067 µg/ml (±1.705 µg/ml), whereas that among patients who died was 3.208 µg/ml (±2.613 µg/ml). This was a highly statistically significant difference (p<0.001, independent samples T-test) which correlates with the present study.

A total of 595 patients were considered in the study of Alroomi et al. 2021[10], among whom 132 had ferritin levels > 1000ng/ml and 463 had ferritin levels ≤ 1000 ng/ml. Overall mortality was found to be 13.3% (79 cases), 29.5% mortality in cases having ferritin level of >1000 ng/ml and 8.64% mortality in cases having ferritin level of ≤1000 ng/ml which is found to be correlated with the current study.

According to Guan W et al. 2020[11], 44 (6.5%) cases out of total 675 cases had severe disease from which 31(70.5%) cases had elevated serum LDH level, 631(93.5%) cases had non-severe disease from which 246 (39.0%) cases had elevated serum LDH level. In the present study of total 100 cases, 16 (76.2%) cases had elevated serum LDH level from total 21 cases with severe disease and 30 (37.9%) cases had elevated LDH from total 79 cases with non-severe disease.

CONCLUSION

Laboratory markers in COVID-19 patients are useful for confirmation and classification of disease severity, play a crucial role in early suspicion, monitoring, recognition of complications, identification of high risk patients, predicting outcome and framing criteria for discharge.

REFERENCES

1. Abuelgasim E, Saw L J, Shirke M, Zeinah M, Harky A. *COVID19: Unique public health issues facing Black, Asian and minority ethnic communities.* Mosby Inc; 2020.
2. Kubina R, Dziedzić A. Molecular and serological tests for COVID19: A comparative review of SARS-CoV-2 corona virus laboratory and point-of-care diagnostics *Diagnostics.* 2020;10(6):1.
3. Ramírez-Truque M, Herrera-Morice M. Rol del laboratorioclínico ante la epidemia del COVID-19: Revisión de losmétodosdiagnósticosdisponibles y sus limitaciones *Revistamédica de Costa Rica.* 2020;85(629):73.
4. Sara F, Iván R C N, Andrés C M, Eduardo C A, Esteban L. Seguimiento y tratamiento del paciente con COVID-19 2020
5. Yao Y, Cao J, Wang Q, Shi Q, Liu K, Luo Z, et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. J Intensive Care. 2020;8: 49. pmid:32665858
6. Giuseppe L, Mario P. *Clinical Chemistry and Laboratory Medicine (CCLM)* De Gruyter; 2020. pp. 1–4.Laboratory abnormalities in patients with COVID-2019 infection
7. Gao, S., Jiang, F., Jin, W., Shi, Y., Yang, L., Xia, Y., Jia, L., Wang, B., Lin, H., Cai, Y., Xia, Z., Peng, J., 2020. Risk factors influencing the prognosis of elderly patients infected with COVID19: a clinical retrospective study in Wuhan, China. Aging 12, 12504–12516.
8. L. Wang,C-reactive protein levels in the early stage of COVID-19, Médecine et Maladies Infectieuses, Volume 50, Issue 4, 2020, Pages 332-334, I S S N 0399-077X.
9. Poudel A, Poudel Y, Adhikari A, Aryal BB, Dangol D, Bajracharya T, et al. (2021) D-dimer as a biomarker for assessment of COVID-19 prognosis: D-dimer levels on admission and its role in predicting disease outcome in hospitalized patients with COVID-19. PLoS ONE 16(8): e0256744.
10. MoudhiAlroomi, Rajesh Rajan, Abdulaziz A. Omar, Ahmad Alsaber, Jiazhu Pan, Mina Fatemi, Kobalava D. Zhanna, Wael Aboelhassan, Farah Almutairi, Naser Alotaibi, Mohammad A. Saleh, Noor AlNasrallah, Bader Al.Bader, Haya Malhas, Maryam Ramadhan, Mohammed Abdullah, Hassan Abdelnaby. Ferritin level: A predictor of severity and mortality in hospitalized COVID19 patients, Immunity, Inflammation and Disease, August 2021. DOI 10.1002/iid3.517 Pubmed ID 34438471
11. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708–20.