Open Access

Journal of Biomedical Sciences

ORIGINAL ARTICLE

DOI: https://doi.org/10.3126/jbs.v9i2.52048

D-Dimer as a biomarker for COVID-19 patients' illness severity and mortality: A hospital-based study from eastern Nepal

Mittal A[1]*, Farooqui MS[2]

Corresponding author:

Dr. Ankush Mittal, Associate Professor, Department of Biochemistry, Birat Medical College Teaching Hospital, Budhiganga, Morang, Nepal.

Email: drmittala@gmail.com ORCID

Information about the article:

Received: Aug. 18, 2022
Accepted: Dec. 20, 2022
Published online: Jan.12, 2023

Cite this article:

Mittal A, Farooqui MS. D-Dimer as a biomarker for COVID-19 patients' illness severity and mortality: A hospital-based study from eastern Nepal. Journal of Biomedical Sciences. 2022; 9(2):7-11

Publisher

Nepal Health Research Society, Bashundhara -6, Gokarnesowor Municipality, Kathmandu, Nepal
eISSN 2382-5545, ISSN 2676-1343 (Print)

ABSTRACT

Background

The biomarker D-dimer, produced when fibrin breaks down, is frequently used to diagnose thrombotic diseases. D-dimer has been recognized as a potential indication of the prognosis for COVID-19 patients since the inception of the COVID-19 pandemic. We collected and compared the demographic, clinical, and liver function data of patients with confirmed COVID-19 at admission between those with elevated and those with normal D- dimer levels in our hospital-based study.

Material and methods

A hospital-based study that used data from the biochemistry laboratory at Birat Medical College Teaching Hospital in Biratnagar, Nepal, was conducted between July 31 and December 31, 2021. Measurements included age, gender, D-Dimer, procalcitonin, C- Reactive Protein (CRP), aspartate transaminase, and alanine transaminase.

Results

In COVID-19 patients with normal D-dimer levels, the mean age was 55 years (CI, 43-67), while in those with increased levels, it was 66 years (CI, 52-80). In the increased group of the D- dimer, almost 20% had diabetes mellitus, and 8% had chronic obstructive pulmonary disease. Compared to the normal group, the mean values of D-Dimer, procalcitonin, C- Reactive Protein (CRP), aspartate transaminase, and alanine transaminase, alkaline phosphate in the raised group were noticeably higher.

Conclusion

In conclusion, SARS-CoV-2-infected individuals frequently have high D-dimer levels. Critically sick patients had much greater levels, which can be utilized as a predictive indicator for in-hospital mortality.

Keywords

COVID -19, C- Reactive Protein, D- Dimer, Nepal

Background

The illness caused by 2019-nCoV/SARS-CoV-2, a new coronavirus of group 2B, is referred to as Coronavirus Disease-19 (COVID-19). In December 2019, the sickness was initially discovered in Wuhan, the Chinese province of Hubei's capital. Human respiratory tract infections can range in severity from asymptomatic or moderate to severe, such as those observed in severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) [1]. The gastrointestinal, hepatic, cardiac, neurological, and renal systems can all be affected by COVID-19, even though the respiratory system is most commonly affected. Coagulation disorders and thrombotic conditions like Diffuse intravascular coagulopathy is common in COVID-19. Some symptoms that can appear include fever, coughing, dyspnea, watery diarrhea, myalgia, severe lymphopenia, delayed coagulation profiles, heart disease, and sudden death [2].

Clinical scientists conducted substantial and urgent research on accurate biochemical indicators of COVID-19 disease severity to identify high-risk groups and allocate resources in the already overburdened healthcare system in the most effective ways. The biomarkers studied in this context were procalcitonin, C-reactive protein, ferritin, D-dimer, interleukin-6, and lactate dehydrogenase [3]. A fibrin breakdown product known as D-dimer is frequently utilized as a biomarker for thrombotic diseases. Since the COVID-19 pandemic's emergence, D-dimer has been identified as a potential indicator of the prognosis for COVID-19 patients [4].

In numerous investigations, D-dimer showed promise for predicting the severity of the disease. Our hospital-based study gathered and analyzed patients' demographic, clinical, and liver function parameters with confirmed COVID-19 at admission between those with increased and those with normal D- dimer levels.

Material and methods

Study design and the participants

A hospital-based study that used data from the biochemistry laboratory at Birat Medical College Teaching Hospital in Biratnagar, Nepal, was conducted between July 31 and December 31, 2021.

Data collection

Gender, age, and information about pre-existing conditions such as diabetes mellitus, pulmonary illness, and chronic kidney disease were taken from the patient's medical records. Standard liver blood chemistry tests, procalcitonin, D-dimer, and C- reactive protein were performed both at admission and while the patient was in the hospital.

Inclusion criteria

Patients with verified Real-Time Polymerase Chain Reactions for SARS-CoV-2 were included in this study.

Exclusion Criteria

The study excluded patients with known hepatotoxic medications, alcoholics, hepatitis B or C, and pre-existing liver disease.

Measurement of total bilirubin

The total bilirubin in serum or plasma was determined using the method of Jendrassik and Gróf.

Measurement of AST and ALT

Test for estimation of AST&ALT activity in serum/plasma was done by using UV –Kinetic method.

Estimation of D- Dimer

Highly sensitive D-dimer was measured using chemiluminescent immunoassay [5].

Estimation of Procalcitonin

Chemiluminescent immunoassay was used for the measurement of highly sensitive procalcitonin [6].

Estimation of C Reactive Protein

Chemiluminescent immunoassay was used for measurement of highly sensitive C-reactive protein [7].

Sample Size Calculation

The results of the subsequent inquiry were used along with the hospital records of 200 COVID-19 patients who were admitted and received treatment there.

Sampling Technique

In our study, a convenience-based, non-probabilistic sampling technique was employed. To collect precise clinical and pathological information for the study subjects, we used the full enumeration technique.

Data management and statistical analysis

Once the acquired data was initially fed into the Microsoft Excel software, the initial data management tasks, including data cleaning, were completed (Microsoft Office 2013). Data entry in the SPSS (Statistical Package for Social Sciences) version 21 application came next (SPSS Inc; Chicago, IL, USA). To describe categorical and continuous data, the frequency with percentage and mean with standard deviation were utilized. The Chi-square test was applied to examine the relationship between the different variables. To determine whether there was a significant difference between the two variables, the t-test was utilized. Statistics were evaluated using a 0.05 (two-tailed) p-value.

Ethical committee approval

The Institutional Review Committee of Birat Medical College Teaching Hospital gave its clearance before the study was carried out.

Results

Table 1: Comparison of COVID-19 patients with normal and high D-dimer demographic and clinical traits

	Normal group (D -dimer)	Elevated group (D –dimer)	p-value
Number	50	150	--
Age (years)	55.0 ± 12	66 ± 14	<0.001*
Male gender (n%)	26 (51)	103 (68.6)	<0.001*
Hypertension	10 (20.0%)	60 (40%)	<0.001*
Diabetes mellitus	5 (11%)	30 (20.0%)	<0.001*
Chronic heart disease (CHD)	3 (4.8%)	9 (4.9%)	1.000
Chronic pulmonary disease (CPD)	2 (4%)	12 (8%)	<0.001*
Chronic kidney disease (CKD)	1(2%)	9 (6%)	<0.001*

*p <0.05, statistically significant

Table 1 shows that patients with normal D-dimer levels had an average age of 55 years (CI, 43–67) while those with increased levels had an average age of 66 years (CI, 52-80). In the increased group of D- dimer, almost 20% had diabetes mellitus and 8% had chronic obstructive pulmonary disease.

Table 2: Assessment of the liver function parameters based on the high D-dimer levels (N=200)

Liver parameters	Normal (50)	Elevated (150)	p-value
Total Bilirubin (μmol/L)	10.0 (6.7–13.0)	11.7 (8.6–15.5)	0.001*
Procalcitonin (ng/mL)	0.07 (0.05–0.10)	0.12 (0.07–0.21)	0.001*
Alanine Transaminase (U/L) 5-40	28.0 (20.0–45.0)	35 (26.0–57)	0.001*
Aspartate Transaminase (U/L) 8-40	29.0 (21.0–41)	38 (27.0–53.0)	0.001*
Serum creatinine (mg/dL)	0.8 (0.7.–1.2)	0.9 (0.8–1.4)	0.275
C-reactive protein(CRP) (mg/L)	7.5 (6–42.2)	53.4 (12.12–87.75)	0.001*
Random Blood glucose (mg/dl)	85 (70-110)	93 (75-125)	0.175
Prothrombin time (s)	11.7 (11.3–12.3)	12.1 (11.6–12.7)	0.001*
Alkaline phosphatase (25-140 U/L)	70.1 ± 15.4	87.7 ± 40.3	0.001*
Cardiac troponin I (μg/L)	0.01 (0.01–0.01)	0.01 (0.01–0.01)	0.000
D-dimer (mg/L)	0.40 (0.28–0.47	1.80 (0.81-5.60)	0.001*

*p <0.05, statistically significant

Table 2 indicates that the raised group's mean values for D-dimer, Prothombin time, ALT, AST, ALP, and total bilirubin were considerably greater than those of the normal group's. Blood glucose, serum creatinine, and cardiac troponin, on the other hand, were shown to be non-significant in the elevated group as compared to the normal group. The p values demonstrate whether there are differences between the enhanced and normal groups. Statistics were deemed significant at $p < 0.05$.

Discussion

We demonstrated that patients with COVID-19 frequently had D-dimer elevation at admission and that this elevation was associated with greater disease severity and in-hospital mortality. A D-dimer is one of the fragments formed when plasmin splits fibrin to disintegrate clots. The assays are frequently employed as a diagnostic process to rule out the presence of thrombosis [8].

In the current investigation, elevated group D-dimer values were shown to be higher at 1.80 (0.81-5.60) compared to normal group 0.40 (0.28-0.47). Another study found that individuals with a severe SARS-CoV2 infection requiring hospitalization had considerably higher D-dimer levels than patients with a milder illness [9].

Procalcitonin (PCT), a protein containing 116 amino acids, is the peptide precursor of calcitonin, a hormone generated by the parafollicular C cells of the thyroid that is important in calcium homeostasis. Endopeptidase breaks down preprocalcitonin to create procalcitonin.. However, it can also be produced after bacterial infection in numerous extrathyroid organs, which is mediated by elevated levels of interleukin and tumour necrosis factor-alpha (TNF-alpha) [10]. According to the current investigation results, mean serum PCT levels were substantially higher in raised patients, 0.12 (0.07-0.21) compared to normal patients, 0.07 (0.05-0.10). Recent studies have suggested that PCT may serve as a marker for disease severity and may help assess the severity of COVID-19 patients. Serial PCT readings may also aid in determining the prognosis [11].

Whenever there is an inflammatory reaction, serum CRP levels rise. Viral or bacterial illnesses may cause this biomarker to increase. In response to infections, the liver makes a significant number of acute-phase proteins (APPs), including CRP. This acute inflammatory protein is a highly sensitive biomarker for infection, inflammation, and tissue damage. It has been demonstrated that CRP levels and inflammation levels are related. CRP levels can stimulate phagocytosis and the complement system. CRP binds to germs and encourages phagocytosis, which helps remove them [12].

In the current investigation, we discovered that raised group 53.4 (12.12-87.75) had considerably higher CRP levels than the normal group 7.5 (6-42.2). Our study found that the liver function markers ALP, ALT, AST, and total bilirubin were significantly greater in the increased group than in the normal group. Cytokine storm and systemic inflammatory response are two more causes of COVID-19.

Conclusion

In conclusion, SARS-CoV-2-infected individuals frequently have high D-dimer levels. Critically sick patients had much

greater levels, which can be utilized as a predictive indicator for in-hospital mortality.

Limitation and future scope of the study

Because of how the study was designed, it was not possible to determine the cause-and-effect link between the various clinical symptoms observed in COVID-19 patients. The sample size of 200 in such a design also reduces the strength of the connections as shown. Despite these evident drawbacks, the results of the present study open the door to a more creative study design, like a longitudinal study, that would allow for a closer examination of the correlations between the many variables of interest.

Relevance of the study

The findings of this study may aid doctors in determining the best course of treatment for patients both now and in the future. As a result of the COVID-19 pandemic, the medical profession as a whole continues to face difficulties due to the emergence of new SARS-CoV-2 variants.

Abbreviations

Alanine Transaminase (ALT), Alkaline Phosphatase (ALP), Aspartate Transaminase (AST), C- reactive protein (CRP), Chronic Heart Disease (CHD), chronic kidney disease (CKD), chronic pulmonary disease (CPD), Corona Virus Disease 2019 (COVID-19), Severe Acute Respiratory Syndrome Corona Virus – 2 (SARS-CoV-2), total bilirubin (TBIL)

Acknowledgments

We really appreciate the assistance in locating the study's data provided by the department of biochemistry at Birat Medical College Teaching Hospital's Central Clinical Laboratory.

Authors' contribution

a. Study planning: AM, MSF
b. Data collection: AM, MSF
c. Data analysis/ interpretation: AM, MSF
d. Manuscript writing: AM, MSF
e. Manuscript revision: AM, MSF
f. Final approval: AM, MSF
g. Agreement to be accountable for all aspects of the work: AM, MSF

Funding

No funding has been obtained to conduct the study.

Availability of data and materials

All data and material of this study are a part of this article.

Competing interests

None declared.

Publisher's Note

NHRS remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

The publisher shall not be legally responsible for any types of loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Author information

[1]Dr. Ankush Mittal, Associate Professor, Department of Biochemistry, Birat Medical College Teaching Hospital, Nepal, ORCID

[2]Mohammad Shamim Farooqui, Department of Emergency Medicine, Paras HMRI Hospital, Patna ORCID

References

1. She J, Jiang J, Ye L, Hu L, Bai C, Song Y. 2019 novel coronavirus of pneumonia in Wuhan, China: emerging attack and management strategies. Clin Transl Med. 2020 Feb 20;9(1):19. https://doi.org/10.1186/s40169-020-00271-z
2. Asakura H, Ogawa H. COVID-19-associated coagulopathy and disseminated intravascular coagulation. Int J Hematol. 2021 Jan;113(1):45-57. https://doi.org/10.1007/s12185-020-03029-y
3. Blagojević A, Šušteršič T, Lorencin I, Šegota SB, Anđelić N, Milovanović D, et al. Artificial intelligence approach towards assessment of condition of COVID-19 patients - Identification of predictive biomarkers associated with severity of clinical condition and disease progression. Comput Biol Med. 2021 Nov;138:104869. https://doi.org/10.1016/j.compbiomed.2021.104869
4. Yu HH, Qin C, Chen M, Wang W, Tian DS. D-dimer level is associated with the severity of COVID-19. Thromb Res. 2020 Nov;195:219-225. https://doi.org/10.1016/j.thromres.2020.07.047
5. Cini M, Legnani C, Frascaro M, Cappelli C, Sartori M, Cosmi B. Evaluation of a chemiluminescent immunoassay, the HemosIL AcuStar D-Dimer, in outpatients with clinically suspected deep venous thrombosis. Int J Lab Hematol. 2015 Dec;37(6):e172-4. https://doi.org/10.1111/ijlh.12420
6. Wang G, Wan Y, Lin G, Li Z, Dong Z, Liu T. Development of a novel chemiluminescence immunoassay for the detection of procalcitonin. J Immunol Methods. 2020 Sep-Oct;484-485:112829. https://doi.org/10.1016/j.jim.2020.112829
7. Shiesh SC, Chou TC, Lin XZ, Kao PC. Determination of C-reactive protein with an ultra-sensitivity immunochemiluminometric assay. J

Immunol Methods. 2006 Apr 20;311(1-2):87-95. https://doi.org/10.1016/j.jim.2006.01.020
8. Chapin JC, Hajjar KA. Fibrinolysis and the control of blood coagulation. Blood Rev. 2015 Jan;29(1):17-24. https://doi.org/10.1016/j.blre.2014.09.003
9. Lehmann A, Prosch H, Zehetmayer S, Gysan MR, Bernitzky D, Vonbank K, Idzko M, Gompelmann D. Impact of persistent D-dimer elevation following recovery from COVID-19. PLoS One. 2021 Oct 28;16(10):e0258351. https://doi.org/10.1371/journal.pone.0258351
10. Davies J. Procalcitonin. J Clin Pathol. 2015 Sep;68(9):675-9. https://doi.org/10.1136/jclinpath-2014-202807
11. Hu R, Han C, Pei S, Yin M, Chen X. Procalcitonin levels in COVID-19 patients. Int J Antimicrob Agents. 2020 Aug;56(2):106051. https://doi.org/10.1016/j.ijantimicag.2020.106051
12. Sproston NR, Ashworth JJ. Role of C-Reactive Protein at Sites of Inflammation and Infection. Front Immunol. 2018 Apr 13;9:754. https://doi.org/10.3389/fimmu.2018.00754