



ROLE OF D-DIMER AND LYMPHOCYTE COUNT IN COVID-19 PATIENTS WITH POSITIVE RT-PCR

Pathology

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ABSTRACT

The first case of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was reported in Wuhan district, China in December 2019. It had caused a global outbreak of a novel disease. Lymphopenia ($<1000/\text{microlitre}$ of blood) is the prominent abnormality parameters occurring in the majority of Covid-19 patients. D-dimer is a by product of fibrin degradation. It is widely recognized as a biomarker for thromboembolism and as a prognostic marker for COVID-19 patients. It has been demonstrated that plasma D-dimer level has a prognostic indicator in COVID-19 patients. The aim of this study is to know the significance of D-dimer value and lymphocyte count in COVID-19 patients. This study included 100 COVID-19 patients diagnosed with RT-PCR between September 2020- December 2020 at NIMS hospital along with that 50 healthy controls were also taken. Majority of patients were males. Male and female ratio was 1:4. The mean $\pm$ SD of D-dimer in COVID positive patients was 1329.25 ± 611.02 ng/ml while the corresponding mean $\pm$ SD in controls was 230.7 ± 102.46 ng/ml. A higher mean $\pm$ SD of D-dimer was observed in COVID-19 patients. The mean $\pm$ SD of absolute lymphocytes count (ALC) in COVID-19 positive patients was 724.9 ± 520.75 while in control 1846.6 ± 542.9 . The decrease in mean $\pm$ SD in COVID-19 cases was observed. The mean difference was statically significant as p value was <0.0001 . This study showed the strong association between raised D-dimer and lymphopenia in COVID infection

KEYWORDS

COVID-19, Lymphopenia, D-Dimer, Absolute lymphocyte count

INTRODUCTION

The first case of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was reported in Wuhan district, China in December 2019. It had caused a global outbreak of a novel disease.¹ The disease had affected almost all countries and was declared as a pandemic by the World Health Organization on 11 Mar 2020. Different markers have been used for early identification and predicting patients with severe Covid-19 disease.²

Lymphopenia ($<1000/\text{microlitre}$ of blood) is the prominent abnormality parameters occurring in the majority of Covid-19 patients.³ Normal range of lymphocytes - 1,000 to 4,800 lymphocytes per microliter of blood². There are studies that explain the different mechanisms leading to the decrease in absolute lymphocyte count (ALC) during viral infection with COVID-19.

Angiotensin converting enzyme (ACE2) is a main receptor for Sars-CoV-2, this enzyme used by the virus to enter the host and cause damage in lymphoid organs.⁴ A study in Hong Kong, 2020 reported that lymphopenia was observed in 98% of patients with Sars-CoV-2 infection.⁵

D-dimer is a byproduct of fibrin degradation. It is widely recognized as a biomarker for thromboembolism and as a prognostic marker for COVID-19 patients. It has been demonstrated that plasma D-dimer level has the potential as a prognostic indicator in COVID-19 patients. Normal Value of D-dimer- $<500\text{ng/ml}$.⁵

The aim of this study is to know the significance of D-dimer value and lymphocyte count in COVID-19 patients.

MATERIAL AND METHOD

This retrospective study included 100 COVID-19 patients diagnosed with RT-PCR and 50 healthy controls who were admitted between September 2020 – December 2020 in NIMS hospital. All laboratory confirmed cases COVID-19 cases by RTPCR (Real Time Reverse Transcription Polymerase Chain Reaction) or RAT (Rapid Antigen test) were included in this study. Written informed consent was taken

from every patient.

Blood samples for evaluation were collected at patient's bedside by nurses or physicians and data of first blood drawn is included in this study. D-dimer values and absolute lymphocyte count in these patients were analyzed. D-Dimer test is done by Finecare™ D-Dimer Rapid Quantitative Test with Finecare™ FIA system. Absolute lymphocyte count (ALC) is done by Automated Hematology Analyzer Elite 580 (ERBA).

Data was collected and analyzed with SPSS version 25. The mean difference of cases and controls were compared by paired t test. P value <0.05 was taken as significant. This study was approved by institutional ethical committee.

RESULT

This study was done on 100 COVID-19 patients diagnosed with RT-PCR and 50 healthy controls. Majority of patients were males. Male and female ratio is 1:4. (Table 1)

The mean $\pm$ SD of D-dimer in COVID positive patients was 1329.25 ± 611.02 ng/ml while the corresponding mean $\pm$ SD in controls was 230.7 ± 102.46 ng/ml. A higher mean $\pm$ SD of D-dimer was observed in COVID-19 patients. (Figure 1 and 2)

The mean $\pm$ SD of absolute lymphocytes count (ALC) in COVID-19 positive patients was 724.9 ± 520.75 while in control 1846.6 ± 542.9 . The decrease in mean $\pm$ SD in COVID-19 cases was observed. (Table 2)

The mean difference was statically significant as p value was <0.0001 .

Table1- Distribution Of Participants Gender Wise Among Cases And Controls

	Cases	Control
Male	29	52
Female	21	48
Total	50	50

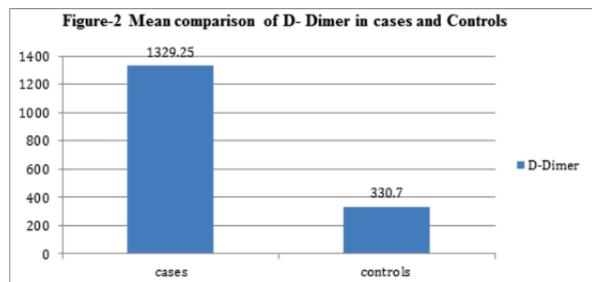
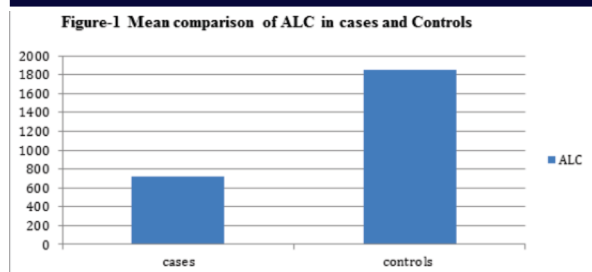


Table 2- Comparison Of Mean $\pm$ Sd Between Cases And Controls

	ALC	D-Dimer (ng/ml)	P value
Cases	724.9 $\pm$ 520.75	1329.25 $\pm$ 611.02	<0.0001
Control	1846.6 $\pm$ 542.9	230.7 $\pm$ 102.46	

P value is <0.0001 which is significant.

DISCUSSION

The rate limiting step in diagnosing COVID-19 is availability and turn-around-time for SARS-CoV-2 PCR testing. In this study we identified ALC cut-off values with corresponding sensitivities that may be used further as a surrogate marker to help identify patients who are unlikely to have COVID-19 upon hospital admission.

According to current CDC recommendations it is advised to avoid aerosol generating procedures (AGPs) in patients with COVID-19 as it may increase the risk of viral transmission.⁶ AGPs commonly performed in the ED include non-invasive positive pressure ventilation, airway suctioning, endotracheal intubation, nebulized medication administration and high-flow oxygen delivery. Knowing the sensitivity of ALC in patients with COVID-19 may help physicians identify those patients who are unlikely to have the disease, allowing patients who benefit from AGPs to receive timely treatment without exposing health care workers to infectious pathogens. In a study done by Illg zachary et al⁷ ALC values were compared among the various subgroups analyzed. It showed male patients had a lower ALC than female patients, with means of 0.90 K/uL and 1.06 K/uL, respectively ($p = 0.041$). And patients who required intubation had a lower ALC (0.91 K/uL) than those who did not (1.01 K/uL) ($p = 0.048$). This result is similar to our study.

Our study demonstrated a significant relation of D-dimer levels with COVID-19. D-dimer levels were significantly higher in the cases as compared to the controls. As per national guidelines all patients with moderate and severe COVID-19 received prophylactic or therapeutic anticoagulation.

In the study by Guan et al in Wuhan the primary composite endpoint of death, mechanical ventilation, and ICU admission was in 22% of the patients as compared to 6% in controls.⁸ D-dimer has been utilized in past as a marker of hypercoagulability. Studies done on COVID-19 patients revealed coagulation abnormalities with marked elevation in D-dimer levels in patients with severe disease. Recent studies concluded that D-dimer more than 2000 ng/mL was associated with increase fatality in COVID-19.⁹ Severe hypoxia in patients with ARDS (Acute respiratory distress syndrome) can lead to activation of extrinsic coagulation pathway and increase blood viscosity leading to hypercoagulable state in COVID-19 infection.¹⁰

In our study peak D-dimer levels were 1329.25 $\pm$ 611.02 ng/mL (Mean $\pm$ SD) in cases and 230.7 $\pm$ 102.46 ng/mL (Mean $\pm$ SD) in controls which is statistically significant. This shows that moderate disease has a statistically significant association with D-dimer levels. This could also be because the patients were triaged as per severity at admission, however peak D-dimer levels during entire course of hospital stay was

utilized in statistical analysis. Therefore it can be concluded that SARS CoV-2 infection is more likely to cause coagulopathy and result in poorer outcome.

CONCLUSION

This study showed the strong association between raised D-dimer and lymphopenia in COVID infection. Noting D-dimer trends and lymphocyte count early in a COVID-19 patient, regardless of patient's clinical condition, may allow opportunities for physicians to provide early intervention to prevent bad outcomes. As such, ALC may serve as a prognostic indicator in patients with COVID-19, allowing physicians to pursue more aggressive treatment regimens in patients at risk for severe disease.

Limitation

First is that all patients in our study required admission during study dates. It did not include patients who were discharged from hospitals with confirmed or suspected COVID-19. So further studies should be done to find ALC and D-dimer cutoff values which were found in our study extend to this population.

Second our study is limited to single center only so further studies should be done including multiple centers to see the significance.

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Conflict of Interest: None as stated by authors

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