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Original Article

Coagulopathy Spectrums in COVID-19 Patients at A Tertiary Care Diagnostic Center in Pakistan

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ABSTRACT

Objective: To determine the coagulopathy spectrums in patients with COVID-19 infection at a tertiary care diagnostic center in Pakistan.

Study Design: Cross-sectional study

Place and Duration of Study: Pathology Department, Armed Forces Institute of Pathology, Rawalpindi Pakistan, from Apr to Sep 2021.

Methodology: A total of 196 patients fulfilling the selection criteria were enrolled after taking written informed consent and investigations to assess coagulation parameters were carried out such as complete blood count, PT, APTT and D-Dimers and findings were subjected to statistical analysis.

Results: Mean age of the patients was 35.20±0.98 years. Platelet count was found to be normal in 152(77.6%) patients and low in 44(22.4%) patients, PT was normal in 182(92.9%) patients and prolonged in 14(7.1%) patients, APTT was normal in 152(77.6%) patients and prolonged in 44(22.4%) and D-Dimers was raised in 87(44.4%) patients and was raised in 109(55.6%) patients

Conclusion: The commonest coagulation pathology was D-Dimers i.e. in 52.6% patients, followed by APTT and platelet count in COVID-19 patients of varying severity.

Keywords: COVID-19, Coagulation, Respiratory Infection.

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INTRODUCTION

Almost 166 million people worldwide have experienced the new Coronavirus illness, an infectious respiratory tract infection.[1] There is strong evidence linking COVID-19 illness to other bodily systems. Severe cases have a greater incidence of COVID-19 linked coagulopathy, which may increase morbidity and death. COVID-19 infections have been reported to be associated with varying degrees of coagulopathy. In between 21 and 69% of ICU patients admitted with COVID-19, thromboembolic consequences have been documented.[2]

A robust inflammation and a hypercoagulable condition are both characteristics of severe COVID-19 disease. There is still a lack of knowledge regarding the pathophysiology underpinning the hypercoagulable state.[3] Current research, however, suggests that the early episodes take place in the lungs, causing a significant inflammatory response in the alveoli and an increase in acute phase proteins such fibrinogen. This process also involves neutrophil extracellular traps (NETs), which have just lately been identified as thrombosis mediators.[4] This hyperinflammatory response has the side effect of initiating a dysfunctional cascade of inflammatory thrombosis in the pulmonary vasculature. A stage of local coagulopathy results from this. In more severe individuals, a generalised hypercoagulable state occurs, which causes thrombosis in the macro- and micovasculature.[5] In COVID-19 individuals who are critically ill, the development of coagulopathy is one of the most important indicators of a bad prognosis and causes thrombotic events in both the arterial and venous circulation.[6]

Endothelial dysfunction, excessive platelet activation, excessive inflammation, and stasis have all been connected to this. Although the coagulation abnormalities seen in severe COVID-19 are similar to those seen in other systemic coagulopathies linked to severe infections, such as DIC or thrombotic microangiopathy, several distinctive characteristics, such as extremely high D-dimer levels and only moderately decreased platelet counts, have only been observed in COVID-19.[7] According to numerous

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research, dysregulation in multiple coagulation parameters has been observed in COVID-19 patients. Coagulation abnormalities are linked to a greater mortality rate. In SARS-CoV-2 patients, lower platelet counts were observed to be associated with increased risks of developing more severe disease and higher rates of hospital mortality.[8] Moreover, some individuals have shown mildly prolonged Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT), as well as mild thrombocytopenia, whereas many patients had markedly elevated levels of D-Dimer, which appear to have prognostic significance.[9] Patients with severe COVID-19 infections had larger amounts of D-dimers and fibrinogen degradation products (FDPs) than individuals with less severe illness.[10]

Coagulation parameters can be extremely helpful in predicting the severity of a disease early on and can serve as a better guide for prompt patient management, which can reduce morbidity and mortality from the disease. Numerous international studies have determined the coagulation spectrum in such patients, however, there is paucity of local data. Therefore, the current study aimed to determine the pattern of coagulopathies in individuals who had COVID-19 infection.

METHODOLOGY

It was a cross-sectional study. The study was carried out at the Armed Forces Institute of Pathology, Rawalpindi Pakistan, from Apr-Sep 2022, after taking approval from the Ethical Review Committee (IRB Number IRB/22/874). The sample size of 196 patients was calculated by keeping 95% confidence level, 7% margin of error, taking expected frequency of coagulopathies in COVID-19 infection in patients as 50%.[4] Non-probability consecutive sampling technique was used.

Inclusion Criteria: The study enrolled 196 patients of age 18 to 70 years, of both genders, with Covid-19 infection as confirmed by Real Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) test which was conducted on smear taken from the nasopharynx, were included in the study.

Exclusion Criteria: Patients who had chronic liver disease or any hematological disorder were excluded from the study.

After taking written informed consent from all patients who fulfilled the selection criteria, participants were enrolled in the study. A thorough history of the patients and clinical examination of all participants was done and findings were noted down on a proforma. Safety measures as given by the World Health Organization (WHO) were followed for assessing every patient with COVID-19 infection. Investigations to assess coagulation parameters were carried out such as complete blood count to see platelet count, PT, APTT and D-Dimers levels. The platelet count was categorized as normal ≥150x103 /ul and low <150x103 /ul. Similarly, the PT of ≥14 seconds was considered prolonged, PT of 14 was categorized as normal, APTT of ≥32 seconds was considered prolonged and D-Dimers of ≥0.5mg/L was labeled as raised. Findings were noted down on the proforma and were subjected to statistical analysis.

The data was analyzed through Statistical Package for social sciences (SPSS) version 25.0. Quantitative data such as age, platelet count, D-Dimer, PT, APTT values were presented as mean and standard deviation. Qualitative data such as gender, low platelet count, prolonged PT and APTT, raised D-Dimers were presented as frequency and percentages. Chi square test was applied and a *p*-value of ≤0.05 was considered significant.

RESULTS

A total of 196 patients were enrolled. The mean age (in year) of the patients was 35.20±0.98, the mean platelet count was 202.89±57.99 platelets per microliter, the mean PT was 14.18±0.69 seconds, the mean APTT was 32.54±1.23 seconds and the mean D-Dimers value was 0.56±0.22 (Table-I).

Table-I: Mean of Quantitative Variables (n=196)

Variables	Mean±SD
Age (in year)	35.0±0.98
Platelet count (platelets per microliter)	202.8±57.9
PT (in seconds)	14.18±0.69
APTT (in seconds)	32.4±1.2
D-Dimers (in mg/L)	0.56±0.22

There were 186(94.9%) males and 10(5.1%) females in the study. With respect to severity of COVID infection, 133(67.9%) patients had mild disease, 38(19.4%) patients had moderate infection, 20(10.2%) had severe infection and 5(2.6%) had critical infection. Platelet count was found to be normal in 152(77.6%) patients and low in 44(22.4%) patients, PT was normal in 182(92.9%) patients and prolonged in 14(7.1%) patients, APTT was normal in 152(77.6%) patients and prolonged in 44(22.4%) and D-Dimers was raised in 87(44.4%) patients and was raised in 109(55.6%) patients (Table-II).

Table-II: Frequency of Qualitative variables (n=196)

Variables	Frequency (percentage)
Gender:	
Male	186(94.9%)
Female	10(5.1%)
Disease severity:	
Mild	133(67.9%)
Moderate	38(19.4%)
Severe	20(10.2%)
Critical	5(2.6%)
Platelet count:	
Normal	152(77.6%)
Low	44(22.4%)
PT:	
Normal	182(92.9%)
Prolonged	14(7.1%)
APTT:	
Normal	152(77.6%)
Prolonged	44(22.4%)
D-Dimers:	
Normal	87(44.4%)
Raised	109(55.6%)

With respect to severity of disease, in mild disease, platelet count was normal in 104(53.1%) patients and low in 29(14.8%) patients, in moderate disease platelet count was normal in 30(15.3%) patients and low in 8(4.1%) patients, in severe disease platelet count was normal in 14(7.1%) patients and low in 6(3.1%) patients and in critical disease platelet count was normal in 4(2%) patients and low in 1(0.5%) patient and this association was statistically insignificant (p=0.862). In terms of PT, it was normal in 122(62.2%) patients with mild disease, in 36(18.4%) patients with moderate disease, in 19(9.7%) with severe disease and in 5(2.6%) with critical disease and was prolonged in 11(5.6%) patients with mild disease, 2(1%) patients with moderate disease and in 1(0.5%) patient with severe disease and this association between PT and severity of disease was insignificant (p=0.806). In terms of APTT, the values were normal in 97(49.5%) patients with mild disease, 32(16.3%) patients with moderate disease, 18(9.2%) patients with severe disease and 5(2.6%) patients with critical disease and was prolonged in 36(18.4%) patients with mild disease, 6(3.1%) patients with moderate disease, 2(1%) patients with severe disease and in none of the patients with critical disease and this association was statistically insignificant (p=0.120). In terms of D-Dimers, the values were normal in 61(31.1%) patients with mild disease, in 15(7.7%) patients with moderate disease, in 8(4.1%) patients with severe disease and in 3(1.5%) patients with critical disease and were raised in 72(36.7%) patients with mild disease, 23(11.7%) patients with moderate disease, 12(6.1%) patients with severe disease and 2(1%) patients with critical disease and this association was statistically insignificant i.e. p=0.768 (Table-III).

Table-III: Stratification of Coagulation Parameters with Respect to Severity of Disease

Coagulation parameters	Severity of Disease				*p*-value
	Mild disease n=133	Moderate disease n=38	Severe disease n=20	Critical disease n=5	
Platelet count:					
Normal	104(53.1%)	30(15.3%)	14(7.1%)	4(2%)	0.862
Low	29(14.8%)	8(4.1%)	6(3.1%)	1(0.5%)	
PT:					
Normal	122(62.2%)	36(18.4%)	19(9.7%)	5(2.6%)	0.806
Prolonged	11(5.6%)	2(1%)	1(0.5%)	0(0%)	
APTT:					
Normal	97(49.5%)	32(16.3%)	18(9.2%)	5(2.6%)	0.120
Prolonged	36(18.4%)	6(3.1%)	2(1%)	0(0%)	
D-Dimers:					
Normal	61(31.1%)	15(7.7%)	8(4.1%)	3(1.5%)	0.768
Raised	72(36.7%)	23(11.7%)	12(6.1%)	2(1%)	

DISCUSSION

The current study results showed that the commonest coagulation pathology seen in patients with COVID-19 was D-Dimers which was raised in 52.6% patients, followed by prolonged APTT i.e. and low platelet count in 22.4% patients each and prolonged PT in 7.1% patients. The majority of the patients in our study were males (94.9%) and had mild severity of infection i.e. 67.9%.

The severe acute respiratory syndrome coronavirus (SARS-CoV-2) that caused coronavirus disease 2019 (COVID-19) caused a systemic inflammatory reaction and an imbalance between the procoagulant and anticoagulant homeostatic

processes.[11] Moreover, it is compounded by thrombotic problems.[12] T cell activation and enormous cytokine generation and release in response to COVID-19 infection cause harm to internal organs, particularly the lungs.[13] Around 40% of COVID-19 hospital patients are at high risk of developing venous thromboembolism (VTE).[14] The incidence of pulmonary embolism and VTE were 22.5% and 10%, respectively, among COVID-19 French patients who were not in intensive care units (ICU) and were receiving thromboprophylaxis.[15] Poor prognosis was linked to abnormal coagulation factors in Chinese COVID-19 patients.[16] A high level of D-dimer (>1g/ml) at admission was associated with an increased risk of hospital death in certain trials (but not all).[17]

In a study conducted in Lahore, the authors revealed that in the survivors of COVID-19 infection, D-Dimers were raised in 50.5% patients, APTT was raised in 12.9%, PT was raised in 7.5% and platelet count was low in 3.2% patients.[2] In a study conducted in Wuhan, PT was prolonged in 6% patients, APTT was prolonged in 5% patients and D-Dimers were raised in 36% patients.[18] Levi *et al*., revealed that among patients with COVID 46% of patients had raised D-Dimers and patients had mildly deranged PT i.e. 15.6 seconds.[19] Sayed and Rahimi revealed that in COVID-19 patients, PT, APTT and D-Dimers were deranged in 77% patients who had COVID infection.[20] These findings support our study findings that coagulation parameters are deranged in COVID-19 infection with commonest being D-Dimers.

Levi *et al*., revealed that only about 5% of individuals with COVID-19 appear with a platelet count of less than 100x109 cells per L, according to studies. However in 70–95% of patients with severe COVID-19, modest thrombocytopenia (a platelet count of <150x109 cells per L) can be detected.[19] Sayed and Rahimi revealed that thrombocytopenia was seen in 30% of patients who had COVID-19 infection.[20] These findings support our study findings that thrombocytopenia can occur in patients with COVID-19 infection, however, the rates were lower in our study because majority of the patients had mild infection, whereas, in the study conducted by Levi *et al*., and Sayed and Rahimi majority of the patients had severe infection.

According to guidelines issued by the International Society on Thrombosis and Haemostasis, patients with significantly elevated D-dimers (three to fourfold rise) should be taken into consideration for hospital admission even in the absence of additional symptoms. Moreover, full therapeutic-intensity anticoagulation or thromboprophylaxis should be given to all hospitalized COVID-19 patients who have this increase. Our study supports this notion as in our study, D-Dimers were the commonest pathology found among other coagulation parameters.

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LIMITATIONS OF STUDY

There were certain limitations of the study. Results of this study cannot be generalized because it was a single center study with a small sample size. Secondly, the correlation of coagulation parameters in asymptomatic patients was not assessed and it cannot be commented if such parameters are also deranged in those without any symptoms.

CONCLUSIONS

The current study concluded that the commonest coagulation pathology was D-Dimers i.e. in 52.6% patients, followed by APTT and platelet count in COVID-19 patients of varying severity. In order to offer helpful predictive information, coagulation tests such as platelet count, PT, PTT and D-dimer should be conducted at the time of hospitalization in patients suspected or confirmed to have COVID-19 infection. A pharmacologic VTE prophylaxis should be administered to these patients unless there are specific contraindications.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

IA& HMR: Data acquisition, data analysis, critical review, approval of the final version to be published.

KA & NAR: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MBA & MS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Shukla S, Kamini K, Gupta B, Bahadur S, Kalhan S, Gupta M. Parameters of Coagulation in COVID-19 Patients: A Correlation with Clinical Severity. J Med Microbiol Infect Dis 2022; 10(4): 153-156.

2. Kashif A, Taj S, Moin S, Fatima SA, Lone A, Ahmed Q. Coagulation profile in COVID-19. Rawal Medical Journal 2022; 47(3): 523-526.
3. Nazir, I., Hamid, S.M., Shakoor, A., Khan, R.R., Farid, M.A., Imran, I. et al. Pattern of Coagulopathy and Their Association with Mortality in COVID-19 Patients in Makkah, KSA. Pak J Med Health Sci 2022: 16(06): 337-337.
4. Langer F, Kluge S, Klamroth R, Oldenburg J. Coagulopathy in COVID-19 and its implication for safe and efficacious thromboprophylaxis. Hämostaseol 2020; 40(3): 264-269.
5. Jandial A, Gupta A, Malviya A, Agastam S, Kumar D. Coagulation abnormalities & thromboprophylaxis in COVID-19. Ind J Med Res 2021; 153(6): 606-610.
6. Smirnova O, Matvienko O, Korsakova N, Lerner A, Shvedova T, Golovina O, et al. Correlation of coagulation parameters with prognosis of COVID-19. Res Pract Thromb Haemostasis 2021; 5(2): 34-39.
7. Zhang A, Leng Y, Zhang Y, Wu K, Ji Y, Lei S, et al. Meta-analysis of coagulation parameters associated with disease severity and poor prognosis of COVID-19. Int J Infect Dis 2020; 100: 441-448.
8. Pal S, Lahiri S, Bhattacharyya K, Ghosh A, Mukhopadhyay T. Coagulopathy biomarkers in mild to moderate CoVID-19 patients admitted in a tertiary care public hospital in eastern India. Al Ameen J Med Sci 2021; 14(3): 190-199.
9. Xu W, Fei L, Huang CL, Li WX, Xie XD, Li Q, et al. Dynamic changes in coagulation parameters and correlation with disease severity and mortality in patients with COVID-19. Aging 2021; 13(10): 13393-13396.
10. Srivastava S, Garg I, Dogra V, Bargotya M, Bhattar S, Gupta U,et al. Implications of COVID-19 on Thrombotic Profile of Severely Affected Patients. Pathobiol 2022; 89(6): 407-417.
11. Jamil SW, Ilyas M, Ahmad N, Bakri S, Hardjianti T, Parewangi ML, et al. Coagulation Profile and Outcomes of COVID-19 Patients at Wahidin Sudirohusodo Hospital, Makassar, Indonesia. Maced J Med Sci 2022; 10(2): 1097-1101.
12. Santasmita P, Subhayan L, Kuntal B, Amrita G, Tapan M. Coagulopathy biomarkers in mild to moderate COVID-19 patients admitted in a tertiary care public hospital in eastern India. Al Ameen J Med Sci 2021; 14(3): 184-192.
13. Abd El-Lateef AE, Alghamdi S, Ebid G, Khalil K, Kabrah S, Abdel Ghafar MT. Coagulation profile in COVID-19 patients and its relation to disease severity and overall survival: a single-center study. Bri J Biomed Sci 2022; 79: 10098.
14. Jin X, Duan Y, Bao T, Gu J, Chen Y, Li Y, et al. The values of coagulation function in COVID-19 patients. PLoS One 2020; 15(10): e0241329.
15. Lu H, Chen M, Tang S, Yu W. Association of coagulation disturbances with severity of COVID-19: a longitudinal study. Hematol 2021; 26(1): 656-662.
16. Sayyadi M, Khosravi M, Ghaznavi-Rad E. Contribution value of coagulation abnormalities in COVID-19 prognosis: a bright perspective on the laboratory pattern of patients with coronavirus disease 2019. Eur Rev Med Pharmacol Sci 2021; 25(1): 518-522.
17. AkhoundiMeybodi Z, Dehghan M, Mousavi SA, Vakili M, Foroghi Nasab N, Shahcheraghi SH, et al. Prevalence and impact of coagulation dysfunction in patients with COVID-19 in Yazd. Health Biotech Biopharm 2022; 6(1): 53-61.
18. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. New Engl J Med 2020; 382(18): 1708-1720.
19. Levi M, Thachil J, Iba T. and Levy J.H. 2020. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol 7(6): 438-440.
20. Sayad B, Rahimi Z. Blood coagulation parameters in patients with severe COVID-19 from Kermanshah Province, Islamic Republic of Iran. East Mediterr Health J 2020; 26(9): 999-1004.

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