

# The Impact of COVID-19 on Blood Coagulation Profile among Sudanese Hospitalized Adult Patients

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Received: 04 July 2022 / Received in revised form: 17 September 2022, Accepted: 17 September 2022, Published online: 20 September 2022

## Abstract

Covid-19 is a severe acute respiratory syndrome, the disease presents with a ranging from asymptomatic to severe symptomatic illness with multiple organ failure and death, and can cause a severe effect on the coagulation system. This study aimed to determine the effect of the covid 19 on the extrinsic and intrinsic pathway of coagulation [prothrombin time(PT), international normalized ratio (INR), and activated partial thromboplastin time (APTT)] and to determine the association of age and gender with the severity of COVID-19 in Sudan in order to improve the outcome. A cross-sectional study carried out among 487 COVID-19 patients attending Khartoum State. COVID-19 patients were confirmed by RT-PCR. For all patients, the prothrombin times (PT), International normalized ratio (INR), and Activated partial thromboplastin (APTT) were estimated by using a semi-automated coagulometer analyzer. Patients were divided into three subclass groups according to the Severity of COVID-19 (mild, severe in the emergency room (ER) and intensive care unit (ICU), and the clotting factors values were compared between the groups. The results were statically analyzed by spss version 21 for data analysis. These results showed statistically significant increased Levels of PT, INR, and APTT for all (P. value = 0.000), compared to the control group. Also, the levels of coagulation tests were higher in ICU COVID-19 patients (P. value = 0.000) compared to mild and severe subgroups. This study concluded that: coagulation clotting times were increased in COVID-19 patients, especially among patients in ICU which could be a marker for DIC and even death.

**Keywords:** Coagulation profile, COVID-19, PCR, INR.

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## Introduction

The Coronaviruses is severing acute respiratory syndrome (Lu *et al.*, 2020) emerged in Wuhan (China) at the end of 2019 with an unknown cause (Di Gennaro *et al.*, 2020), in January 2020, after a few weeks later, take a sample from the lower respiratory tract for analysis, identified a novel virus severe acute respiratory syndrome coronavirus as a causative agent for that observed pneumonia cluster (Huang *et al.*, 2020). the disease named SARS-CoV-2 “COVID-19” by Dr. Tedros Adhanom Ghebreyesus, in 2020 (March 11th) when there was an increased number of countries involved (114), with more than 118,000 cases and over 4000 deaths, then the WHO declared the pandemic status (Litijos *et al.*, 2020). The disease ranges from asymptomatic to severe symptomatic illness with multi-organ failure and death (World Health Organization Director-General’s Opening Remarks at the Media Briefing on COVID-19–11, 2020). Respiratory droplet transmission is the main route and it can also be transmitted through asymptomatic carriers by person-to-person contacts (Abou-Ismael *et al.*, 2020). COVID -19 can cause severe effects on coagulation systems. The complication of coagulation activation can be leading to the formation of disseminated intravascular coagulation (DIC) and death (Lupia *et al.*, 2020). The systemic inflammatory response by COVID -19 can cause severe effects in coagulation systems leading to endothelial damage, coagulation activation, and intravascular fibrin deposition (Yang *et al.*, 2020). the complication of coagulation activation can be leading to the formation of thrombus and even disseminated intravascular coagulation (DIC) (Qiu *et al.*, 2020). The coagulation blood cascade is start when the sub-endothelial tissue factor is exposed to the blood flow followed either by activation or damage of the endothelium. It may happen as a result of the activation of endothelium or perforation of the vessel wall by cytokines, chemicals, or inflammatory processes by extrinsic pathway (PT and INR) and extrinsic pathway (APTT) (Bikdeli *et al.*, 2020).

## Materials and Methods

This was a cross-sectional study, conducted among 487 COVID-19 patients. Information about gender, age, COVID -19 symptoms, Ethical permission was taken from Ethical Research Committee, faculty of Medical Laboratory Sciences, Alzim Alazhari University, certainly an informed consent was taken from selected subject before participation in the study The primary data was gathered using a self-administered questionnaire; this was particularly designed to obtain data that would support in the study. The isolation hospitals use a real-time polymerase chain reaction device AccuPower® COVID-19 RT-PCR kit to confirm the

diagnosis of COVID-19 patients (Bioneer Corporation, Daejeon, South Korea) following the manufacturer guidance; all cases were positive for COVID-19 by RT-PCR. PT, INR, and APTT clot analysis were performed for patients and 302 healthy individuals as a control group using Stago semi-automated analyzer. Patients were further subdivided into three subgroups [77 mild COVID-19, 137 severe COVID-19 (ER) and 273 patients in ICU], subject-categorized according to the following: the first group with or without clinical evidence of pneumonia but without oxygen requirements ("mild" group), the second group with oxygen requirements ("severe" group (ER) and the last group under mechanical ventilation (ICU group). The study was approved by the University of Alzaeim Alazhari committee (Van, 2022).

### Statistical Data Analysis

Statistical analysis was performed by Statistical Package for Social the Sciences (SPSS software version 16) for windows. P. values equal or less than 0.05 was considered statistically significant.

## Results and Discussion

This cross-sectional study was carried out on 487 COVID-19 patients (304 males and 183 females), aged between 20-88 years old in Sudan hospitals in Khartoum State during the period from April 2020 to December 2020. PT, INR, and APTT results were statically analyzed by SPSS version 21 to obtain descriptive statistics (mean ( $\pm$ ) SD, minimum and maximum results) also one-way ANOVA test was used for the comparison of more than two parameters, and an independent T-test used to compare between two parameters to obtain the P-value (P-value less than 0.05 was considered significant). These results showed statistically significant increased Levels of PT, INR, and APTT among patients with COVID-19 when compared with the control (for all P-value = 0.000) **Table 1**. Also, the levels of coagulation tests were higher in ICU COVID-19 patients compared to mild and severe subgroups **Table 2**. No statistical significant was revealed between PT, APTT, and INR among mild Covid-19 patients and control group (p value 0.987, 0.990, 0.137) respectively. Data were summarized in **Table 3** (Alizadeh *et al.*, 2022; Batarseh *et al.*, 2022; Halimah *et al.*, 2022; Kauser *et al.*, 2022; Nakagawa & Yamashita, 2022; Rohmani *et al.*, 2022; Sadeq *et al.*, 2022; Salama *et al.*, 2022; Yousefian *et al.*, 2022).

In this study (56% of a patient admitted into the ICU unit, 28.1% were admitted to ER unit, and 15.8% of covid 19 patients with mild symptoms), male was more affected by the disease than female; 303 versus 184, respectively. Also, males were mainly represented in the ICU unit (male 183 (67.3%) versus female 90 (32.7%) **Table 5**. This study showed that ages up to 60 years (97.5%) with COVID-19 and mainly represented in the ICU unit **Table 4**.

**Table 1.** Comparison of PT, APTT, and INR between Covid-19 patients and control group

Variables	Case (n=487)	Control (n=302)	P value
PT	15.2	13.9	0.000
INR	1.21	1.08	0.000
APTT	47.9	33.2	0.000

Mann-Whitney test was used to calculate the P-value

A p-value less than 0.05 is considered significant

**Table 2.** Comparison of PT, APTT, and INR between Covid-19 patients' subgroups and control group

Variables	ICU (n=273)	Sever (ER) (n=137)	Mild (n=77)	Control (n=302)	*P value	** Multiple P values
PT	19.6	14.3	13.9	13.9	0.000	AXB 0.000
						AXC 0.000
						AXD 0.000
						BXC 0.005
						BXD 0.000
INR	1.53	1.13	1.08	1.08	0.000	CXD 0.869
						AXB 0.000
						AXC 0.000
						AXD 0.000
						BXC 0.000
APTT	60	44.7	30.7	33.2	0.000	BXD 0.000
						CXD 0.957
						AXB 0.000
						AXC 0.000
						AXD 0.000

\* Kruskal Wallis Test was used to calculate the P-value

\*\* Mann-Whitney test was used to calculate the P-value

A p-value less than 0.05 is considered significant

**Table 3.** Comparison of PT, APTT, and INR between mild Covid-19 patients and control group

Variables	Mild(n=77)	Control (n=302)	P-value
PT	13.684 $\pm$ 1.0223	13.705 $\pm$ 1.0027	0.987
INR	1.063 $\pm$ 1.550	1.065 $\pm$ 1.546	0.990
APTT	30.807 $\pm$ 2.838	33.532 $\pm$ 4.087	0.137

**Table 4.** Distribution of age groups among COVID-19 subgroups

Study groups	COVID-19 Subgroup			Total
	ICU	Mild	Sever (ER)	
Age groups				
20-40	5 (5.8%)	72 (84.7%)	8 (9.4%)	85
41-60	72 (35.8%)	3 (1.4%)	126(62.6%)	201
More than 60	196 (97.5%)	2 (0.99%)	3 (1.4%)	201
<b>Total</b>	273 (56%)	77(15.8%)	137 (28.1%)	487

**Table 5.** Distribution of gender among COVID-19 subgroup

Study groups	COVID-19 Subgroup			Total
	ICU	Mild	Sever (ER)	
Gender				
Female	90 (48.9%)	49 (26.6%)	45 (24.4%)	184
Male	183 (60.3%)	28 (9.2%)	92 (30.3%)	303
<b>Total</b>	273 (56%)	77 (15.8%)	137 (28.1)	487

Recently the whole world affected by the pandemic COVID-19 which become rapidly spreading, and dangerous and may lead to death especially for the old aged, also with time there is wide heterogeneity regarding clinical remark for the disease, due to the virus diversity. The dangerous COVID-19 complications are to induce severe acute respiratory distress syndrome and multiple organ failure (MOF), which are at risk of DIC and death (Chang, 2019). Mortality of the covid 19 seems to be relatively low among patients with the critical disease or at high risk of developing acute respiratory distress syndrome and being admitted to ICU (Han *et al.*, 2020). This study was conducted to determine the effect of COVID-19 on the extrinsic and intrinsic pathway of coagulation

(PT, INR, and APTT) and to determine the severity of COVID-19 in Sudan regarding age and gender in order to improve the outcome. This study showed that significantly increased in PT, INR, and APTT among covid-19 patients when compared to control groups (P Value 0.000).

As mentioned in previous studies, COVID -19 can lead to disturbance in coagulation systems. The most dangerous outcome is the activation of coagulation which can be leading to the formation of disseminated intravascular coagulation (DIC) and death (Lupia *et al.*, 2020). PT and APTT are simple and first-line investigations for patients with coagulation disturbance and their results can predict the occurrence of DIC.

This study showed that there was no significant difference in PT, INR, and APTT results between patients in ER (severe) and mild subgroups (P.value < 0.05) but it was highly significantly increased among ICU patients (p.value 0.000). This current study agreed with the (Yongwei *et al.*, 2020) report that significantly increased PT, INR, and APTT among patients with COVID-19 than healthy controls (p-value < 0.05) (Sayad & Rahimi, 2020) and agreed with (Sayad & Rahimi, 2020) showed statistically significant in PT, INR and APTT result in ICU patient [pv<0.05] (Jin *et al.*, 2020) also this study was in concordance with (You *et al.*, 2020) showed a significant increase in PT (P.value 0.000, INR (P.value 0.000) in COVID-19 patient (Luo *et al.*, 2020), but This study was disagreed with (Micco *et al.*, 2020), showed statistically insignificant in PT, INR, and APTT (P.value > 0.05), this variation may relate to the low sample size of their study (67 patient). This recent study included (303) males and (184) females (56% of a patient admitted to the ICU unit, 28.1% were admitted to ER unit, and 15.8% of covid 19 patients with mild symptoms), this study revealed that males are more affected (60.3%) than female (48.9%) mainly represented in ICU unit, this study was similar to (Mahajan & Kaushal, 2020); the incidence in male =76%, and female =46% (Mahajan & Kaushal, 2020). This study showed that aged up to 60 years (97.5%) are more likely to get COVID-19 and represented in the ICU unit, the study was in agreement with (Pastor-Barriuso *et al.*, 2020); demonstrated that the old age individuals up to 60 years more likely to get COVID-19 infection with more complicated symptoms.

## Conclusion

This study concluded that significant increase in PT, INR, and APTT in covid 19 patients, especially among ICU covid 19 subgroups compared to mild and severe subgroups, which may indicate a risk of bleeding and or thrombosis that could lead to death (Adiga, 2019). Old age is more likely to increase the severity of covid 19 infection (Abd Elwahaab *et al.*, 2019).

**Acknowledgments:** This publication was supported by the Deanship of scientific research at Prince Sattam Bin Abdul Aziz University. Authors appreciated to Faculty of Medical Laboratory Sciences, Alzaeim Alazhari University, Sudan.

**Conflict of interest:** None

**Financial support:** None

**Ethics statement:** Ethical permission was taken from Ethical Research Committee, faculty of Medical Laboratory Sciences, Alzim Alazhari University, certainly an informed consent was taken from selected subject before participation in the study

## References

- Abd Elwahaab, H. A., Rahmy, A. F., Hagag, A. A., Fares, H. M., & Fouad, S. A. (2019). Effect of Aerobic exercises on Blood coagulation and Fibrinolysis factors in Elderly Hypertensive patients. *Journal of Advanced Pharmacy Education and Research*, 9(1), 44-48.
- Abou-Ismael, M. Y., Diamond, A., Kapoor, S., Arafah, Y., & Nayak, L. (2020). The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. *Thrombosis Research*, 194, 101-115. doi:10.1016/j.thromres.2020.06.029
- Adiga, U. (2019). Serum Indices—A tool to Measure Interfering Substances in Blood Samples. *International Journal of Pharmaceutical and Phytopharmacological Research*, 9(2), 43-46.
- Alizadeh, Y., Akbari, M., Soltanipour, S., Moghadam, R. S., Medghalchi, A., Dourandesh, M., & Alizadeh, H. (2022). Using oral Rifampin to treat acute central serous Choroidopathy: a randomized placebo-controlled clinical trial. *Journal of Advanced Pharmacy Education and Research*, 12(2), 11-18. doi:10.51847/dpPZJj2dvd
- Batarseh, N., Khalil, R., & Al-Domi, H. A. (2022). Hypothalamic neuroinflammation induced by obesity and the effect of Liraglutide. *Journal of Advanced Pharmacy Education and Research*, 12(1), 46-55. doi:10.51847/N1hvOB1anS
- Bikdeli, B., Madhavan, M. V., Jimenez, D., Chuich, T., Dreyfus, I., Driggin, E., Nigoghossian, C., Agno, W., Madjid, M., Guo, Y., et al. (2020). COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. *Journal of the American College of Cardiology*, 75(23), 2950-2973.
- Chang J. C. (2019). Acute Respiratory Distress Syndrome as an Organ Phenotype of Vascular Microthrombotic Disease: Based on Hemostatic Theory and Endothelial Molecular Pathogenesis. *Clinical and applied thrombosis/hemostasis: official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis*, 25, 1076029619887437.
- Di Gennaro, F., Pizzol, D., Marotta, C., Antunes, M., Racalbutto, V., Veronese, N., & Smith, L. (2020). Coronavirus Diseases (COVID-19) Current Status and Future Perspectives: A Narrative Review. *International Journal of Environmental Research and Public Health*, 17(8), 2690. doi:10.3390/ijerph17082690
- Di Micco, P., Russo, V., Carannante, N., Imparato, M., Rodolfi, S., Cardillo, G., & Lodigiani, C. (2020). Clotting Factors in COVID-19: Epidemiological Association and Prognostic Values in Different Clinical Presentations in an Italian Cohort. *Journal of Clinical Medicine*, 9(5), 1371. doi:10.3390/jcm9051371
- Halimah, E., Hendriani, R., Indradi, B., & Sofian, F. F. (2022). Cytotoxicity of ethanol extract and its fractions

- from *Acalypha wilkesiana* against breast cancer cell MCF-7. *Journal of Advanced Pharmacy Education and Research*, 12(1), 17-20. doi:10.51847/G2bMkvc6PO
- Han, H., Yang, L., Liu, R., Liu, F., Wu, K. L., Li, J., Liu, X. H., & Zhu, C. L. (2020). Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. *Clinical Chemistry and Laboratory Medicine*, 58(7), 1116-1120. doi:10.1515/ccm-2020-0188
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., et al. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*, 395(10223), 497-506.
- Jin, X., Duan, Y., Bao, T., Gu, J., Chen, Y., Li, Y., Mao, S., Chen, Y., & Xie, W. (2020). The values of coagulation function in COVID-19 patients. *PloS One*, 15(10), e0241329. doi:10.1371/journal.pone.0241329
- Kausar, S., Morrissey, H., & Ball, P. (2022). England local community pharmacists opinions on independent prescribing training. *Journal of Advanced Pharmacy Education and Research*, 12(1), 30-37. doi:10.51847/PaNZ94aVtA
- Llitjos, J. F., Leclerc, M., Chochois, C., Monsallier, J. M., Ramakers, M., Auvray, M., & Merouani, K. (2020). High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. *Journal of Thrombosis and Haemostasis: JTH*, 18(7), 1743-1746.
- Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., Wang, W., Song, H., Huang, B., Zhu, N., et al. (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet (London, England)*, 395(10224), 565-574.
- Luo, H. C., You, C. Y., Lu, S. W., & Fu, Y. Q. (2021). Characteristics of coagulation alteration in patients with COVID-19. *Annals of Hematology*, 100(1), 45-52. doi:10.1007/s00277-020-04305-x
- Lupia, T., Scabini, S., Mornese Pinna, S., Di Perri, G., De Rosa, F. G., & Corcione, S. (2020). 2019 novel coronavirus (2019-nCoV) outbreak: A new challenge. *Journal of Global Antimicrobial Resistance*, 21, 22-27.
- Mahajan, P., & Kaushal, J. (2020). Epidemic trend of COVID-19 transmission in India during lockdown-I phase. *Journal of Community Health*, 45(6), 1291-1300. doi:10.1007/s10900-020-00863-3
- Nakagawa, N., & Yamashita, T. (2022). Comparative study of traditional face-to-face teaching, audience response system, and a flipped classroom plus audience response. *Journal of Advanced Pharmacy Education and Research*, 12(1), 9-16. doi:10.51847/ODLhsGztZ9
- Pastor-Barriuso, R., Perez-Gomez, B., Hernan, M. A., Perez-Olmeda, M., Yotti, R., Oteo-Iglesias, J., Sanmartín, J. L., Leon-Gomez, I., Fernandez-Garcia, A., Fernández-Navarro, P., et al. (2020). Infection fatality risk for SARS-CoV-2 in community dwelling population of Spain: nationwide seroepidemiological study. *BMJ (Clinical research ed.)*, 371, m4509. doi:10.1136/bmj.m4509
- Qiu, H. J., Yuan, L. X., Huang, X. K., Zhou, Y. Q., Wu, Q. W., Zheng, R., & Yang, Q. T. (2020). Using the big data of internet to understand coronavirus disease 2019's symptom characteristics: a big data study. *Zhonghua er bi yan hou tou jing wai ke za zhi= Chinese journal of otorhinolaryngology head and neck surgery*, E004-E004.
- Rohmani, S., Desi, B. A., & Wardhani, W. D. (2022). Potassium-Azeloyl-Diglycinate BB-Cream formulation with Triethanolamine variation, and its effects on In-Vitro SPF stability and values. *Journal of Advanced Pharmacy Education and Research*, 12(1), 1-8. doi:10.51847/MUHp4ptold
- Sadeq, Z. A., Sabri, L. A., & Al-Kinani, K. K. (2022). Natural polymer Effect on gelation and rheology of ketotifen-loaded pH-sensitive in situ ocular gel (Carbapol). *Journal of Advanced Pharmacy Education and Research*, 12(2), 45-50. doi:10.51847/zOf4TcFeKT
- Salama, N. M., El-Rokh, E. M., Hashem, G., Mowafy, H. H., Elsisy, M. H., & Labib, D. A. A. (2022). Clopidogrel versus ticagrelor in elective percutaneous coronary intervention. *Journal of Advanced Pharmacy Education and Research*, 12(2), 30-37. doi:10.51847/nkVAYLdyKc
- Sayad, B., & Rahimi, Z. (2020). Blood coagulation parameters in patients with severe COVID-19 from Kermanshah Province, Islamic Republic of Iran. *Eastern Mediterranean health journal = La revue de sante de la Mediterranee orientale = al-Majallah al-sihhiyah li-sharq al-mutawassit*, 26(9), 999-1004. doi:10.26719/emhj.20.105
- Van, T. P. (2022). Relationship between well-being and social interaction of disabled people in Ho Chi Minh City, Vietnam. *Journal of Advanced Pharmacy Education and Research*, 12(2), 23-29. doi:10.51847/YNYliovLLq
- World Health Organization Director-General's Opening Remarks at the Media Briefing on COVID-19—11 March 2020. Available online: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020> (accessed on 11 March 2020)
- Yang, Y., Peng, F., Wang, R., Yange, M., Guan, K., Jiang, T., Xu, G., Sun, J., & Chang, C. (2020). The deadly coronaviruses: The 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China. *Journal of Autoimmunity*, 109, 102434.
- You, C. Y., Lu, S. W., Fu, Y. Q., & Xu, F. (2021). Relationship between admission coagulopathy and prognosis in children with traumatic brain injury: a retrospective study. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine*, 29(1), 67. doi:10.1186/s13049-021-00884-4
- Yousefian, M., Ghazi, A., Amani, F., & Movaffagh, B. (2022). Mortality rate in patients admitted to the ICU based on LODS, APACHE IV, TRIOS, SAPS II. *Journal of Advanced Pharmacy Education and Research*, 12(1), 56-62. doi:10.51847/CgHzosuz9x