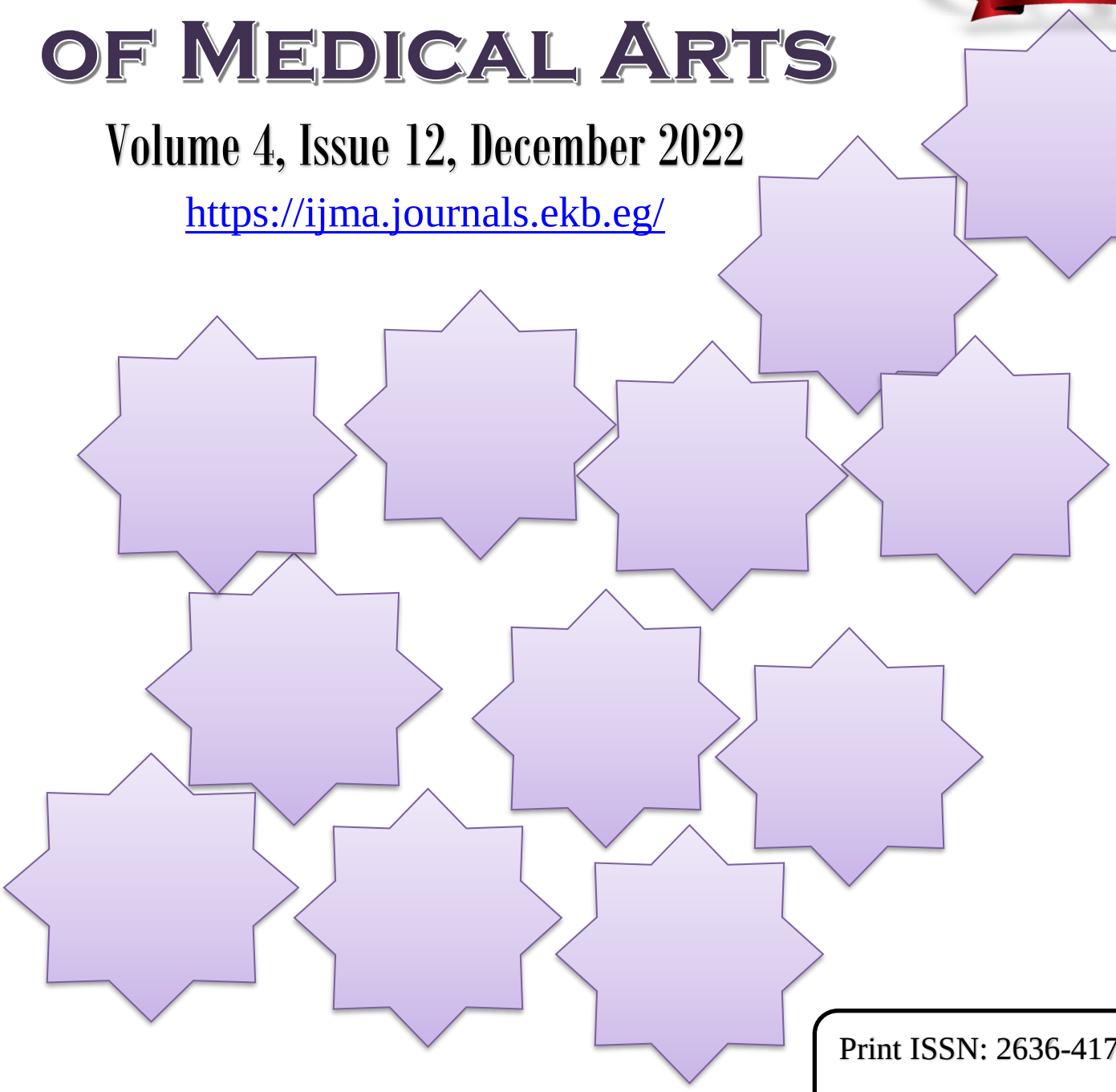
International Journal of Medical Arts

Volume 4, Issue 12, December 2022

https://ijma.journals.ekb.eg/



Print ISSN: 2636-4174

Online ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Internal Medicine]

Original Article

Prevalence of Thrombocytopenia in COVID-19 Isolated Patients

Hossam Hassan Saied Hassan [1]*, Yousef Khalil Ahmed [1], Youssef Abdallah Yousef Nassar [1], Mohammad Assayed Aboghabsha [2]

[1] Department of Internal Medicine, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[2] Department of Clinical Pathology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

Article information

Received: 06-01-2023

Accepted: 10-03-2023

DOI: 10.21608/IJMA.2023.185653.1592

*Corresponding author

Email: hoosaam2230@gmail.com

Citation: Hassan HHS, Ahmed YK, Nasser YAY, Aboghabsha MA. Prevalence of Thrombocytopenia in COVID-19 Isolated Patients. IJMA 2022 December; 4 [12]: 2885-2890. doi: 10.21608/IJMA.2023.185653.1592.

ABSTRACT

Background: Sever Acute Respiratory Syndrome Coronavirus [SARS-COV-2], a new highly transmittable coronavirus, with many variants recently appearing and spreading rapidly around the world.

Aim of the Work: To find out the prevalence of thrombocytopenia in COVID-19 patients, and the association between the severity of thrombocytopenia and severity of the disease in COVID-19 patients.

Patients and Methods: The current prospective study will include 300 patients with COVID-19 infection sector in Al Hussein University Hospital, Al-Azhar University, the inclusion Criteria included: Age between 18-60 years, positive nasopharyngeal swab PCR for COVID-19 RNA and isolated new-onset thrombocyte-penia, while the exclusion criteria included: history of liver cirrhosis or HCV, history of bone marrow disease or ITP, history of autoimmune disease or immunosuppressive therapy and previous treatment with platelet transfusion, danazol , or thrombopoietin receptor agonists, the eligible patients will be divided into 2 groups: group I: patients without thrombocytopenia, while group II: patients with thrombocytopenia.

Results: The studied patients who developed thrombocytopenia were 95/300 patients [31.7%], with variable degrees of thrombocyte-penia, half of those patients with moderate thrombocytopenia died from COVID, while 5/15 patients [33.3%] of those who developed severe thrombocytopenia, died from COVID, with statistically significant difference, P-value= 0.01.

Conclusion: Thrombocytopenia may be considered as a risk factor for mortality among patients who developed COVID infection.

Keywords: COVID; Thrombocytopenia; Platelet.

INTRODUCTION

Sever Acute Respiratory Syndrome Coronavirus [SARS-COV-2], a new highly transmittable coronavirus, with many variants recently appearing and spreading rapidly around the world [1]. The virus causes a spectrum of diseases, named novel coronavirus disease 2019 [COVID-19] by the World Health Organization [WHO] [2].

Thrombocytopenia is defined as low platelet count [less than 150 x 10^3 /L]. Viral infections can be associated with thrombocytopenia duo to a variety of causes [3], while hypo proliferative thrombocytopenia is observed at later stage of viral infection, the rapid development of thrombocytopenia in response to viral infection is generally mediated via enhanced platelet clearance/destruction [4].

Of the patients affected by the 2003 SARS epidemic, 20 – 25 % had thrombocytopenia, and these thrombocytopenic patients experienced greater morbidity/mortality [5]. As a coronavirus sharing 79% genomic sequence with SARS-CoV and the same cell entry receptor of angiotensin-converting enzyme II, it is possible that SARS-CoV 19 may cause thrombocyte-penia in a similar way [6].

The aim of the study is to find out the prevalence of thrombocytopenia in COVID-19 patients, and the association between the severity of thrombocytopenia and severity of the disease in COVID-19 patients.

PATIENTS AND METHODS

The current prospective study included 300 patients with COVID-19 infection sector in Al-Hussein University Hospital, Al-Azhar University.

Approval for this study will be obtained from Al-Azhar University Ethical Committee. Informed consent will be obtained from all included patients.

Inclusion criteria: age between 18-60 years and positive nasopharyngeal swab PCR for COVID-19 RNA,

Exclusion criteria: history of liver cirrhosis or HCV, history of Bone Marrow Disease or ITP, history of Autoimmune disease or immunosuppressive therapy and previous treatment with platelet transfusion, danazol, or thrombopoietin receptor agonists.

Eligible patients were divided into 2 groups: group I: patients without thrombocytopenia, while group II: patients with thrombocytopenia. All patients were subjected to detailed history taking including drug history that may be implicated in thrombocytopenia, weight loss, arthritis, skin changes, bleeding tendency and lymph node swelling; also, physical examination for demonstration of important signs as liver condition, bleeding disorders, pallor, lymphadenopathy, and/or splenomegaly.

The investigations included: nasopharyngeal swab PCR for COVID-19 RNA, platelet count, peripheral blood smear, CBC, CRP titer, reticulocyte count, anti-platelet Ab, Coombs's test [Direct & Indirect] for patients with hemolytic features, peripheral blood smear for any abnormalities & schistocytes, PT, PTT, INR.

The radiological investigations included: chest X-Ray [P/A], CT Chest without contrast, abdominal ultrasound [for presence of splenomegaly or evidence of liver cirrhosis].

Statistical analysis: The numerical variables will be expressed as the mean ± standard deviation [SD]. The COVID-19 severity and outcomes will be compared between all groups and statistically analyzed by the SPSS program. Categorical data were analyzed using the chi square test and the Fisher-exact test. Continuous data were analyzed by the t-test. A regression model was built for assessing various risk factors. P-value of 0.05 or less was considered as significant.

RESULTS

The mean age of studied patients was 39.4 [SD=10.8], ranging from [21 to 60 years]. Ninety-nine patients [33%] were females, while 201⁄300 patients [67%] were males.

We found that elderly patients and those who developed AKI and septic shock were among the most affected patients with thrombocytopenia [table 1].

Regarding mortality, the incidence was higher among elderly patients and those with AKI, septic shock and thrombocytopenia [table 2].

The studied patients who developed thrombocytopenia were 95⁄300 patients [31.7%], with variable degrees of thrombocytepenia. Half of those patients with moderate thrombocytopenia died from COVID, while 5⁄15 patients [33.3%] of those who developed severe thrombocytopenia, died from COVID, with statistically significant difference, [P-value= 0.01]. Worse degrees of thrombocytopenia were associated with higher incidence of mortality [p: < 0.05] as shown in table [3].

Table [1]: Factors affecting thrombocytopenia

Demographics and co-morbidities		Thrombocytopenia		P-value
		No thrombocytopenia	Yes thrombocytopenia	
		No. = 205	No. = 95	
Age Categories	Below 40 years	202 [98.5%]	45 [47.4%]	**0.001**
	Above 40 years	3 [1.5%]	50 [52.6%]	
Sex	Female	65 [31.7%]	34 [35.8%]	0.51
	Male	140 [68.3%]	61 [64.2%]	
Diabetic	No	143 [69.8%]	73 [76.8%]	0.21
	Yes	62 [30.2%]	22 [23.2%]	
Hypertension	No	127 [62.0%]	65 [68.4%]	0.3
	Yes	78 [38.0%]	30 [31.6%]	
Dyslipidemia	No	177 [86.3%]	81 [85.3%]	0.85
	Yes	28 [13.7%]	14 [14.7%]	
Acute kidney injury	No	205 [100.0%]	46 [48.4%]	**0.002**
	Yes	0	49 [51.6%]	
Septic Shock	No	205 [100.0%]	49 [51.6%]	**0.001**
	Yes	0	46 [48.4%]	

Table [2]: Factors affecting mortality among COVID infected patients

Demographics and co-morbidities		MORTALITY		OR [95% CI]	P – value
		Survivors	Non-survivors		
		No. = 254	No. = 46		
Age Categories	Below 40 years	227 89.4%	20 43.5%	0.3[5.3,22.1]	**0.001**
	Above 40 years	27 10.6%	26 56.5%		
Sex	Female	82 32.3%	17 37.0%	0.5 [0.4,1.5]	0.334
	Male	172 67.7%	29 63.0%		
Diabetic	No	181 71.3%	35 76.1%	0.5 [0.3,1.6]	0.372
	Yes	73 28.7%	11 23.9%		
Hypertension	No	158 62.2%	34 73.9%	0.1 [0.2,1.1]	0.360
	Yes	96 37.8%	12 26.1%		
Dyslipidemia	No	222 87.4%	36 78.3%	0.1 [0.8,4.2]	0.404
	Yes	32 12.6%	10 21.7%		
Acute kidney injury	No	228 89.8%	23 50.0%	0.3 [4.3,17.7]	**0.001**
	Yes	26 10.2%	23 50.0%		
Septic Shock	No	228 89.8%	26 56.5%	0.3 [3.3,13.7]	**0.002**
	Yes	26 10.2%	20 43.5%		
Thrombocytopenia	No	202 79.5%	3 6.5%	0.6 [16,18.6]	**0.004**
	Yes	52 20.5%	43 93.5%		

Table [3]: Relation between thrombocytopenia grades and mortality

Mortality				Total	P-Value
		Survivors	Non survivors		
No	Count	202	3	205	**0.01**
	% Within Mortality	79.5%	6.5%	68.3%	
Mild	Count	27	23	50	
	% Within Mortality	10.6%	50.0%	16.7%	
Moderate	Count	15	15	30	
	% Within Mortality	5.9%	32.6%	10.0%	
Severe	Count	10	5	15	
	% Within Mortality	3.9%	10.9%	5.0%	

DISCUSSION

COVID 19 was a major healthcare devastating issue as it affected most of human beings, caused more than 6 million deaths in the period between Jan 2020 until now. Thrombocytopenia was the most common manifestation of the early epidemic of viral infection. It was observed in 20–55% of the SARS epidemic [7].

Among COVID-19 patients, thrombotic complications become a major concern. These complications may cause thrombocytopenia which in turn may associate with disease severity [8]. Thrombocytopenia can prolong hospitalization, increase the need of ventilation, and increase patient mortality [9].

Studying the relationship between thrombocytepenia as a prognostic factor, and the severity of disease was the aim of this work.

Our study showed that [31.7%] of patients developed thrombocytopenia, with different degrees mild, moderate and severe. Similar findings were reported in Turkey [25.1%] [10], China [17.8%] [11], Iran [30%] [12], and USA [20%] [13].

Our results showed that there were 15% of cases associated with moderate or severe thrombocytopenia; 80% of them died from COVID-19 complications [p value 0.001].

APACHE trial showed that, a low platelet count correlates with higher disease severity scores such as Multiple Organ Dysfunction Score [MODS], Simplified Acute Physiology Score [SAPS] II, and Acute Physiology and Chronic Health Evaluation [APACHE] II [14].

Our results showed that those patients who had serious complications of COVID-19, like AKI and septic shock, were associated with significant incidence of thrombocytopenia [p value 0.002, 0.001], respectively. **Zou et al.** explained that, in the severe acute respiratory syndrome [SARS] outbreak, thrombocytopenia was reported to occur in up to 55% of patients and was identified as a significant risk factor for mortality Platelet count, with hypoxemia, were the only two variables used by **Zou et al.** for developing a SARS prognostic model which displayed 96.2% accuracy [5].

In our study, mortality from COVID-19, were prominent with elderly [OR: 0.3; P:0.001], thrombocytopenia [OR: 0.6; P: 0.004], AKI [OR: 0.3; P: 0.001], and septic shock [OR: 0.3; P: 0.002]. Other studies also supported this finding. **Jin et al.** [15] reported that platelets were correlated with COVID-19 disease severity. **Sayad et al.** [12] study was also reported that thrombocytopenia could be important indicator of severe COVID-19 which might associate with mortality. According to the systematic review and Meta-analysis reported by **Lippi et al.** [16], thrombocytopenia increased the risk of disease severity more than five times more likely.

Because platelets play a major role in thrombogenesis, an increased platelet activation will lead to platelet aggregation and platelet spreading, which will lead to thrombosis in COVID-19. It has been shown that the incidence of thromboembolic events in severe patients and non-survivors is much higher than non-severe patients and survivors [17].

Accumulating evidence has shown that thromboembolic complications emerging from COVID-19 are one of the main reasons for sudden deterioration and death [18]. **Helms et al.** [19] showed that compared with non-COVID-19 patients who suffered from acute respiratory distress syndrome [ARDS], COVID-19 patients with ARDS had significantly more thrombotic events [11.7%vs. 4.8%], mainly pulmonary embolism [11.7% vs. 2.1%].

Early detection and timely thromboprophylaxis can lower the incidence of thrombosis. **Zhang et al.** [20] demonstrated that thromboprophylaxis halved the incidence of deep-vein thrombosis in patients with COVID-19, with the Padua prediction scores being 4 or higher.

The explanation for thrombocytopenia in COVID-19, were enrolled in multi-centric trials, we can assume that thrombocytopenia may develop by platelets destruction, platelets consumption or bone marrow depression. In viral infection and inflammation which lead to lung damage. Damaged lung tissues and pulmonary endothelial cells may activate platelets in the lungs, resulting in aggregation and formation of microthrombi, which increases platelet consumption. Most patients with COVID-19 who have had thrombocytopenia, have elevated D-dimer levels and impaired coagulation time [21].

COVID-19 may increase levels of autoantibodies and immune complexes, resulting in specific destruction of platelets by the immune system. A study reported that the phenomenon of immune-mediated thrombocyte-penia in patients infected with HIV-1 is widespread [22]. Coronaviruses are also able to infect bone marrow cells, resulting in abnormal hematopoiesis [23].

The age factor was a dependent risk factor for thrombocytopenia incidence, as by using univariate and multi-variate analysis, there was a statistically significant difference as regard the age. We noticed that elderly have had a higher incidence of thrombocytopenia, [OR: 1.2; P: 0.001], it's not related to comorbidities as we found in this work, since there was no statistically significant difference as regards chronic comorbidities both groups who developed thrombocytopenia, or not developed.

Consideration of thrombocytopenia to be a prognostic factor for mortality related to COVID 19, not due to bleeding, as there was no history of bleeding, reported in COVID-19 patients during hospitalization. **Bikdeli et al.** [24] reported that the frequency of bleeding events was 0 in 35 COVID-19 patients who suffered from a prolonged activated partial-thrombo-plastin time [aPTT].

Our results also showed that elevated PDW was significantly associated with disease severity [P-value = 0.001]. Platelet distribution width reflects the variation in the size of platelets. It increases when platelets destruction increases and when the new large immature platelet production raises for compensation. A study conducted by **Bhandary et al.** [25] also showed that PDW was significantly associated with disease severity and it was higher in severe cases.

Tire et al. [26] also revealed that PDW had a statistical difference between outpatients, patients who received standard treatment in the hospital and patients who had to be connected to a mechanical ventilator [ICU patients].

Another COVID-19 related issue is emerging to be cause of thrombocytopenia in the patients, COVID vaccines, emerging data has suggested that thrombocytopenia events may likely occur unevenly across the three COVID-19 vaccines, with higher events among vaccinated persons with the Oxford-AstraZeneca vaccine relative to the Pfizer BioNTech vaccine, but further data is needed [27].

Conclusion: Thrombocytopenia is frequent among patients with COVID-19 and linked to increased mortality. Mortality is increased with the severity of thrombocytopenia.

Conflict of Interest and Financial Disclosure: None.

REFERENCES

1. World Health Organization. Situation Report – 84. Published April 13th, 2020. Accessed April 13th 2022.
2. World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it. Brazilian J Implantol Health Sci. 2020 Mar 24;2[3].
3. Chabert A, Hamzeh-Cognasse H, Pozzetto B, Cognasse F, Schattner M, Gomez RM, Garraud O. Human platelets and their capacity of binding viruses: meaning and challenges? BMC Immunol. 2015 Apr 28;16:26. doi: 10.1186/ s12865-015-0092-1.
4. Assinger A. Platelets and infection - an emerging role of platelets in viral infection. Front Immunol. 2014 Dec 18;5:649. doi: 10.3389/fimmu.2014. 00649.
5. Zou Z, Yang Y, Chen J, Xin S, Zhang W, Zhou X, *et al*. Prognostic factors for severe acute respiratory syndrome: a clinical analysis of 165 cases. Clin Infect Dis. 2004 Feb 15;38[4]:483-9. doi: 10.1086/380973.
6. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, *et al*. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020 Mar;579[7798]:270-273. doi: 10.1038/s41586-020-2012-7.
7. Wool GD, Miller JL. The Impact of COVID-19 Disease on Platelets and Coagulation. Pathobiology. 2021;88[1]:15-27. doi: 10.1159/ 000512007.
8. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, *et al.*; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr 30;382[18]:1708-1720. doi: 10.1056/NEJMoa2002032.
9. Breaux R, Dvorsky MR, Marsh NP, Green CD, Cash AR, Shroff DM, *et al.* Prospective impact of COVID-19 on mental health functioning in adolescents with and without ADHD: protective role of emotion regulation abilities. J Child Psychol Psychiatry. 2021 Sep;62[9]:1132-1139. doi: 10.1111/jcpp.13382.

10. Güçlü E, Kocayiğit H, Okan HD, Erkorkmaz U, Yürümez Y, Yaylacı S, *et al*. Effect of COVID-19 on platelet count and its indices. Rev Assoc Med Bras [1992]. 2020 Aug;66[8]:1122-1127. doi: 10.1590/1806-9282.66.8.1122.

11. Li Z, Liu T, Yang N, Han D, Mi X, Li Y, *et al*. Neurological manifestations of patients with COVID-19: potential routes of SARS-CoV-2 neuroinvasion from the periphery to the brain. Front Med. 2020 Oct;14[5]:533-541. doi: 10.1007/s11684-020-0786-5.

12. Sayad B, Sobhani M, Khodarahmi R. Sofosbuvir as Repurposed Antiviral Drug Against COVID-19: Why Were We Convinced to Evaluate the Drug in a Registered/Approved Clinical Trial? Arch Med Res. 2020 Aug;51[6]:577-581. doi: 10.1016/j.arcmed.2020.04.018.

13. Barrett TJ, Bilaloglu S, Cornwell M, Burgess HM, Virginio VW, Drenkova K, *et al*. Platelets contribute to disease severity in COVID-19. J Thromb Haemost. 2021 Dec;19[12]:3139-3153. doi: 10.1111/jth.15534.

14. Wu SC, Chou SE, Liu HT, Hsieh TM, Su WT, Chien PC, Hsieh CH. Performance of Prognostic Scoring Systems in Trauma Patients in the Intensive Care Unit of a Trauma Center. Int J Environ Res Public Health. 2020 Oct 2;17[19]: 7226. doi: 10.3390/ijerph17197226.

15. Jin Y, Yang H, Ji W, Wu W, Chen S, Zhang W, Duan G. Virology, Epidemiology, Pathogenesis, and Control of COVID-19. Viruses. 2020 Mar 27;12[4]:372. doi: 10.3390/v12040372.

16. Lippi G, Sanchis-Gomar F, Henry BM. Coronavirus disease 2019 [COVID-19]: the portrait of a perfect storm. Ann Transl Med. 2020 Apr;8[7]:497. doi: 10.21037/atm.2020.03.157.

17. Khave LJ, Zafari P, Pirsalehi A, Salari S, Baghestani A, Akbari ME, Bashash D. Association between thrombocytopenia and platelet profile with morbidity/mortality of severe and non-severe COVID-19 patients. Rev Assoc Med Bras [1992]. 2021 Nov;67[11]:1670-1675. doi: 10.1590/1806-9282.20210720.

18. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, *et al.*; Global COVID-19 Thrombosis Collaborative Group, Endorsed by the ISTH, NATF, ESVM, and the IUA, Supported by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020 Jun 16;75[23]:2950-2973. doi: 10.1016/j.jacc.2020.04.031.

19. Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, *et al*. Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med. 2020 Jun 4;382[23]:2268-2270. doi: 10.1056/NEJMc2008597.

20. Zhang Y, Ma ZF. Impact of the COVID-19 Pandemic on Mental Health and Quality of Life among Local Residents in Liaoning Province, China: A Cross-Sectional Study. Int J Environ Res Public Health. 2020 Mar 31;17[7]:2381. doi: 10.3390/ijerph17072381.

21. Ingraham NE, Barakat AG, Reilkoff R, Bezdicek T, Schacker T, Chipman JG, Tignanelli CJ, Puskarich MA. Understanding the renin-angiotensin-aldosterone-SARS-CoV axis: a comprehensive review. Eur Respir J. 2020 Jul 9;56[1]:2000912. doi: 10.1183/13993003.00912-2020.

22. Bing-Yuan, Zhang YH, Leung NHL, Cowling BJ, Yang ZF. Role of viral bioaerosols in nosocomial infections and measures for prevention and control. J Aerosol Sci. 2018;117: 200-211. doi: 10.1016/j.jaerosci.2017.11.011.

23. Liu K, Tan S, Niu S, Wang J, Wu L, Sun H, *et al*. Cross-species recognition of SARS-CoV-2 to bat ACE2. Proc Natl Acad Sci U S A. 2021 Jan 5;118[1]:e2020216118. doi: 10.1073/pnas.2020-216118.

24. Bikdeli B, Madhavan MV, Gupta A, Jimenez D, Burton JR, Der Nigoghossian C, *et al.*; Global COVID-19 Thrombosis Collaborative Group. Pharmacological Agents Targeting Thrombo-inflammation in COVID-19: Review and Implications for Future Research. Thromb Haemost. 2020 Jul;120[7]:1004-1024. doi: 10. 1055/s-0040-1713152.

25. Bhandari P, Subramaniam S, Bourke MJ, Alkandari A, Chiu PWY, Brown JF, *et al*. Recovery of endoscopy services in the era of COVID-19: recommendations from an international Delphi consensus. Gut. 2020 Nov; 69[11]:1915-1924. doi: 10.1136/gutjnl-2020-322329.

26. Tire Y, Yazar MA, Erdem SS. Can changes in platelet count, mean platelet volume, and platelet distribution width be used to determine the severity of COVID-19?. Medical Science and Discovery. 2021 Oct 14;8[10]:581-5. doi: 10. 36472/msd.v8i10.611

27. Cari L, Fiore P, Naghavi Alhosseini M, Sava G, Nocentini G. Blood clots and bleeding events following BNT162b2 and ChAdOx1 nCoV-19 vaccine: An analysis of European data. J Autoimmun. 2021 Aug;122:102685. doi: 10. 1016/j.jaut.2021.102685.

International Journal of Medical Arts

https://ijma.journals.ekb.eg/
Print ISSN: 2636-4174
Online ISSN: 2682-3780