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Cross-sectional Study

Association between thrombocytopenia and the severity of Covid-19 infection among hospitalized Egyptian patients

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ABSTRACT

Background: COVID-19, which is caused by the corona virus 2 that causes severe acute respiratory syndrome, causes a respiratory and systemic illness that in 10–15% of patients escalates to a severe form of pneumonia. Thrombocytopenia is frequent in patients with COVID-19. We aimed to evaluate the association between thrombocytopenia and the severity of COVID-19 infection in hospitalized patients.

Methods: A cross-sectional study was done on 800 Egyptian patients with confirmed covid-19 infection. They were divided into Group I (Mild): 200 symptomatic patients meeting the case definition for COVID-19 without radiological evidence of pneumonia or hypoxia. Group II (Moderate): 200 patients with clinical signs of non-severe pneumonia and radiological evidence of pneumonia. Group III (Severe): 200 patients with clinical signs of pneumonia plus: respiratory or lung dysfunction. Group IV: 200 critically ill patient in ICU: Acute respiratory distress syndrome (ARDS).

Results: there was a highly statistically significant difference between the studied groups regarding thrombocytopenia ($p < 0.001$). Thrombocytopenia was statistically higher in severe and critically ill patients. In addition, a statistically significant difference found in outcome among the studied groups ($p < 0.05$) {critically ill (40%), severe (17.5%)}. The most common cause of death was respiratory failure, which occurred in 28 severe patients (80%) and 65 critically ill patients (81.25%), followed by hemorrhage due to thrombocytopenia, which occurred in 7 severe patients (20%) and 15 critically ill patients, respectively (18.75%).

Conclusion: The Platelet count is a straightforward, inexpensive, as well as easily available laboratory parameter that is frequently linked to severe covid-19 infection and a significant death risk.

1. Introduction

Corona virus disease (COVID-19), which iscaused by severe acute respiratory syndrome corona virus 2 (SARSCoV-2), can lead to respiratory and lead also to systemic diseases that progress to sever pneumonia in 10–15% of patients [1]. Severe COVID-19 can lead to serious illness, with acute respiratory distress syndrome (ARDS) can result with severe covid-19 and multiorgan failure (MOF) as the primary complications, eventually followed by disseminated intravascular coagulopathy [2]. Clinical manifestations in COIVD-19 patients have been widely reported since the outbreak. [3] COVID-19 infected patients can present with pulmonary symptoms, abdominal symptoms, acute heart injury, liver injury and kidney injury, coagulation abnormalities, and major changes in whole blood cells characterized by lymphopenia and thrombocytopenia [4].

Thrombocytopenia is a common manifestation of infection with COVID-19 which is also an indicator of a poor prognosis of severe acute respiratory syndrome (SARS), middle east respiratory syndrome

Abbreviations: COVID-19, Corona virus disease; ARDS, Acute Respiratory Distress Syndrome; MOF, Multiorgan Failure; SARS, Severe Acute Respiratory Syndrome; MERS, Middle East Respiratory Syndrome; MODS, Multiple Organ Dysfunction Score; SAPS II, Simplified Acute Physiology Score; APACHEII, Acute Physiology and Chronic Health Assessment; MOHP, Ministry of Health Program; HB, hemoglobin; CRP, C-reactive protein; LDH, Lactate Dehydrogenase; RT-PCR, Real Time Polymearase chain reaction; HTN, hypertension; TLC, Total Leukocytic Count.

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(MERS), and COVID-19 [5]. Furthermore, low platelet counts are linked to an increase in the illness severity scores like Multiple Organ Dysfunction Score (MODS), Simplified Acute Physiology Score (SAPS II), and the Acute Physiology and Chronic Health Assessment (APACHEII) [6]. In chronic liver diseases like viral hepatitis B or C, COVID-19 infection can manifest as a serious infection (globally health burden particularly in Egypt) [7–12]. Little is known regarding the impact of COVID-19 infection among people suferring from cirrhosis in the liver [13–16].

Therefore, this study aimed to assess the relationship between thrombocytopenia and severity of COVID-19 infection in hospitalized patients.

2. Methods

Eight hundred patients with different demographic data were enrolled in a prospective study during the time span between April 2020 to March 2021. All included patients in this study who were suspected clinically and based on covid-19 imaging abnormalities, which were verified by + VE PCR (nasopharyngeal and oropharyngeal samples), divided according to the Ministry of Health Program (MOHP) in Egypt into 4 groups; Group I (Mild), included 200 symptomatic patients who met the COVID-19 case description without any radiological evidence of pneumonia or hypoxia. Group II (Moderate), included 200 patients with clinical signs of non-severe pneumonia and radiological evidence of pneumonia. Group III (Severe), included 200 patients with clinical signs of pneumonia plus one of the following: respiratory rate >30 breaths/min; severe respiratory distress; or SpO 2 < 93% on room air and radiological evidence of pneumonia; patients with more than 50% lesions progress within 24–48 h in lung imaging. Group IV, included 200 severly critically ill patients in intensive care unit: acute respiratory distress syndrome (ARDS) which met any of the following criteria as the occurance of respiratory failure requiring mechanical ventilation; the presence of shock; sepsis, other organ failures that require monitoring and treatment in the intensive care unit.

Ethical consideration including a written informed consent was given by every participant prior to the initiation of study in routine clinical practice at three specialized treatment centers especially concerned with COVID-19 management (Menoufia University Hospitals, National Liver Institute Hospital and Shebin El-Kom Teaching Hospital). The present study was conducted in compliance with the guidelines for Good Clinical Practice. The study methodology was reviewed and confirmed to be compliant with the ethical principles of 1975 Declaration of Helsinki's, as evidenced by prior approval by the institution's human research committee (Institutional Review Board of Faculty of Medicine, Menoufia University, Egypt). The research was established in the Academic Research Registry Department, number 9/2020TROP22. The work has been documented in line with the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) 2021 criteria [17].

Patients with history of thrombocytopenia or any other cases affecting platelets count such as immune thrombocytopenic purpura, chronic liver disease, sepsis, disseminated intravascular coagulation (DIC), acute liver failure, hypersplenism, heparin or other drug induced were excluded from the current study.

For all selected patients for this study, comprehensive history taking: a particular manifestation of respiratory symptoms (dyspnea, fever and cough) were recorded. A complete general examination (arterial blood pressure respiratory rate and body temperature), local chest examination was assessed. The laboratory research includes (full blood count) including: TLC, lymphocytes, platelet count & hemoglobin (HB) level. C-reactive protein (CRP), D-dimer, serum ferritine, Lactate Dehydrogenase (LDH); and arterial blood gases were done. Coagulation profile, Radiological examination including: pelvi-abdominal ultrasonography and computed tomography. Chest, serology including: RT-PCR for covid-19 was performed for the selected patients.

3. Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 23 was used to gather, tabulate, and statistically analyses data on an IBM compatible personal computer (Armonk, NY: IBM Corp, 2013). Percentage (percent), Median, Range, and IQR were descriptive statistics, whereas analytic statistics included the chi-square test, to compare different groups for categorical variables. Mann-Whitney test (U) to compare two studied groups for abnormally distributed quantitative variables. One-way ANOVA (F test), to compare more than two groups for normally distributed quantitative variables.Kruskal Wallis testto compare more than two studied groups for abnormally distributed quantitative variables, and Spearman's correlation (r)for correlation between two quantitative variables. Correlation coefficient test (Person test) results may be positive (+) correlation (reverse) or negative (−) correlation (inverse). A statistically significant P value of 0.05 was used.P-value<0.05 was considered statistically significant, P-value<0.01 was considered statistically moderately significant and P-value<0.001 was considered statistically highly significant.

4. Results

This study had a total of 800 Egyptians patients. The ages of the patients ranged from 21 to 81 years with mean of 53.15 ± 11.82 years old. Most of them were males (n = 478, 59.75%) and (n = 322, 40.25%) were females. There were statistically significant differences among the studied groups in terms of smoking, diabetes, asthma, fever, cough, dyspnea, abdominal pain and diarrhoea, and sore throat, with smoking being statistically significantly higher among severe patients'group, whereas, DM, hypertension, and dyspnea being statistically significantly higher among critically ill patients'group. While, abdominal pain, diarrhoea, and sore throat were more statistically significant higher in mild patients'group. In addition, moderate patients'group had a statistically significant greater of asthma and fever than the other groups ($p < 0.05$). However, no significant differences reported in age, gender, hypertension (HTN), or CKD among the studied groups ($p > 0.05$), (Table 1). Regarding, conscious level, crepitation, air entry, and wheezes were statistically significant variations among the studied groups ($p < 0.05$), where both crepitation and decrease air entry were higher in critically ill patients group and DLC was the most common with critically ill patients group (51.5%). Moderate group had a significant increase in the temperatures than the other studied groups. DBP, RR, and pulse were statistically significant higher in critically ill patients compared to other groups. So2 was also statistically higher in mild and moderate groups than other studied groups. As regards SBP there is no statistically significant difference between the studied groups ($p > 0.05$), (Table 2). As regard lab investigation, there was a significant difference among studied groups as regard TLC, creatinine, CRP, ferritin, LDH, Hb and D-Dimer where Critically ill patients had statistically significant increased levels of TLC, creatinine, CRP, ferritin, LDH, and D-Dimer than other groups. Hb and platelet count were also statistically significant higher in mild group than other groups ($p < 0.05$), lymphocytes showed no significant difference among the investigated groups ($p > 0.05$). In addition, as regard CT chest findings there was a highly statistically significant difference among the studied groups ($p < 0.001$) while CT findings increase in critically ill groups (Table 3).

There was a statistically significant positive correlation between platelet count with So2 where thrombocytopenia statistically significant related with hypoxia. While, we found a statistically significant negative correlation between platelet count with CRP, D-dimer, Serum ferritin, and LDH ($p < 0.05$) (Table 4).

As regards mortality rate, there was a statistically significant difference between the studied groups ($p < 0.05$). where the mortality rate in severily ill patients' group was (80) is (40%) Severe 35 (17.5%), Where the commonest cause of death was respiratory failure, which took place in 28 severe patients (80%) and 65 critical ill patients (81.25%),

Table 1
Demographic data, medical history, risk factors and complains & symptoms among the studied groups.

Variables	Studied groups (N = 800)								K	P-value
	Mild N = 200		Moderate N = 200		Severe N = 200		Critically ill N = 200			
Age/years	49.55 ± 11.44		53.46 ± 13.32		53.5 ± 10.9		56.07 ± 11.66		1.260	0.839
Mean ± SD	21.00–77.00		21.00–80.00		22.00–81.00		22.00–81.00			
Range										
Gender	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	X^2 =	0.914
Male	116	58.0	118	59.0	123	61.5	121	60.5	0.523	
Female	84	42.0	82	41.0	77	38.5	79	39.5		
Smoking	121	60.5	108	54.0	91	45.5	115	57.5	X^2 =	**0.015***
Non-smoker	79	39.5	92	46.0	109	54.5	85	42.5	10.46	
Smoker										
DM (mg/dL)	141	70.5	132	66.0	125	62.5	109	54.5	X^2 =	**0.007***
No	59	29.5	68	34.0	75	37.5	91	45.5	12.25	
Yes										
HTN (mg/dL)	123	61.5	116	58.0	112	56.0	98	49.0	X^2 =	0.071
No	77	38.5	84	42.0	88	44.0	102	51.0	7.02	
Yes										
CKD	187	93.5	182	91.0	184	92.0	191	95.5	X^2 =	0.286
No	13	6.5	18	9.0	16	8.0	9	4.5	3.78	
Yes										
Asthmatic	177	88.5	160	80.0	175	87.5	182	91.0	X^2 =	**0.007***
No	23	11.5	40	20.0	25	12.5	18	9.0	12.07	
Yes										
Fever	4	2.0	0	0.0	64	32.0	64	32.0	139.45	**<0.001***
No	196	98.0	200	100.0	136	68.0	136	68.0		
Yes										
Cough	110	55.0	131	65.5	91	45.5	91	45.5	24.70	**<0.001***
No	90	45.0	69	34.5	109	54.5	109	54.5		
Yes										
Dyspnea	193	96.5	7	3.5	1	0.5	0	0.0	729.56	**<0.001***
No	7	3.5	193	96.5	199	99.5	200	100.0		
Yes										
Abdominal pain and diarrhoea	164	82.0	194	97.0	176	88.0	178	89.0	22.28	**<0.001***
No	36	18.0	6	3.0	24	12.0	22	11.0		
Yes										
Sore throat	99	49.5	171	85.5	196	98.0	200	100.0	246.62	**<0.001***
No	101	50.5	29	14.5	0	0.0	0	0.0		
Yes										

K: Kruskal Wallis test, X^2: Chi-square test, * statistically significant, Group **I:** Mild covid-19, **Group II:** Moderate covid-19, **Group III:** Severe covid-19, **Group IV:** Critically ill covid-19, **DM**: Diabetes mellitus **HTN**: Hypertension**CKD**: Chronic kidney disease.

followed by thrombocytopenia associated hemorrhage (Table 5).

5. Discussion

SARS-CoV-2, a highly transmissible, novel respiratory pathogen infecting humans, caused the latest COVID-19 pandemic, which began in December 2019 [18]. Fever, dry cough, loss of taste or scent, weakness, shortness of breath, and acute respiratory manifestations are all common COVID-19 symptoms [19,20]. A total of 800 Egyptians patients were included in our study, the ages of the patients varied from 21 to 81 years with mean of 53.15 ± 11.82 years. Most of them were males (n = 478, 59.75%) and (n = 322, 40.25%) were females. Statistically, there were no significant differences among the studied groups as regard age and/or gender. These results agreed with the study by **Yameny,** performed on 504 patients their aged ranged from 20 years to 75 years with mean age 44.5 ± 30.5, male gender was more frequent than female gender with no statistically significant differences [21]. Also, the study by **Zhu et al.,** performed on 167 COVID-19 patients, and their age ranged from 29 to 93, female was frequent in 67.07% [22]. No statistically significant differences in age and gender between the studied groups. These results agreed with **Yang et al.,** who performed a study on 1476 patients, comprising of 1238 (83.9%) survivors and 238 (16.1%) non-survivors, were included. Their median (IQR) age was 57 (47–67) years and 776 (52.6%) patients were males [23].

According to our findings, fever was more frequent in moderate patients' group, while abdominal pain, diarrhoea, and sore throat were more common in mild patients. Dyspnea was more common in critically ill patients. Cough was more common in severe patients' group or critically ill. This result agreed with the study by **Yameny,** who found that, fever was higher among moderate patients'group while dyspnea and cough were statistically higher among critically ill patients'group [21]. Additionally, **World Health Organization,** [24] In severe cases, infection can cause pneumonia, severe acute respiratory syndrome and sometimes death, that were increased in critically ill patients.

Also, **Kim et al.,** summarized symptoms of 172 patients who were in community isolation facilities in South Korea for mild illness; the most common symptom was cough in 40.2%, and fever was mentioned in only 11.6% [25]. By contrast, **Blair et al.,** noted fever to be the most common initial symptom (reported by 55.8%) and cough a predominant symptom initially, increasing in the first and second weeks before decreasing to 37.4% and 15.1% in the third and fourth weeks of illness, respectively; these differences may reflect differences in the approach to referring for testing [26]. The present study showed that Hb was statistically significantly lower among critically ill patients group than in other groups.

The present study showed that, CRP, ferritin, D Dimer, LDH, TLC and creatinine levels were statistically significantly higher among critically ill patients' group than mild, moderate and severe patients' groups. While AST and ALT were statistically significantly increased among the severe group than in other groups ($p < 0.05$).

The study agrees with **Yameny,** found a significant value with critically ill infection as ferritin level which increased in 71.4% LDH has a high level in 67.7% and D-dimer has positive results in 36.4% [21]. Also, the study by **Wool and Miller,** reported that, temporally increasing

Table 2
General and chest examination among the studied groups.

Variable	Studied groups (N = 800)								K	P value
	Group I N = 200		Group II N = 200		Group III N = 200		Group IV N = 200			
Conscious level	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	X^2 =	<0.001*
Conscious	200	100.0	200	100.0	200	100.0	97	48.5	354.14	
DLC	0	0.0	0	0.0	0	0.0	103	51.5		
Crepitation	200	100.0	198	99.0	97	48.5	92	46.0	X2 =	<0.001*
No	0	0.0	2	1.0	103	51.5	108	54.0	279.27	
Yes										
Air entry	200	100.0	198	99.0	98	49.0	91	45.5	X2 =	<0.001*
Normal	0	0.0	2	1.0	102	51.0	109	54.5	279.58	
Decreased										
Wheezes	177	88.5	160	80.0	175	87.5	182	91.0	X2 =	0.007*
No	23	11.5	40	20.0	25	12.5	18	9.0	12.08	
Yes										
Temperature (C°)	38.81 ± 0.64		38.94 ± 0.58		38.60 ± 1.14		38.62 ± 1.13		6.285	<0.001*
Mean ± SD	35.80–40.00		37.90–40.00		36.90–40.00		36.90–40.00			
Range										
Post Hoc	p1 = 0.179, p2 = 0.018*, p3 = 0.036*, p4<0.001*, p5<0.001*p6 = 0.779									
SBP (mmHg)	126.23 ± 78.63		140.7 ± 134.2		130.2 ± 70.6		125.8 ± 11.58		1.31	0.269
Mean ± SD	100–1220		100–1220		100–1110		100–160			
Range										
DBP (mmHg)	80.64 ± 10.13		83.55 ± 8.56		83.65 ± 8.58		84.45 ± 8.43		6.94	<0.001*
Mean ± SD	8.00–110.00		70.00–110.00		60.00–100.00		60.00–110.00			
Range										
Post Hoc	p1<0.001, p2<0.001, p3 <0.001*, p4 = 0.911, p5 = 0.315, p6 = 0.372									
RR (BPM)	20.16 ± 1.67		20.02 ± 1.87		23.76 ± 5.14		36.45 ± 3.96		995.61	<0.001*
Mean ± SD	16.00–24.00		16.00–25.00		16.00–42.00		29.00–45.00			
Range										
Post Hoc	p1 = 0.697, p2<0.001*, p3<0.001*, p4<0.001*, p5<0.001*, p6<0.001*									
Pulse	82.25 ± 5.83		81.96 ± 5.07		82.18 ± 5.89		105.39 ± 9.59		580.20	<0.001*
Mean ± SD	66.00–91.00		68.00–90.00		66.00–91.00		85.00–120.00			
Range										
Post Hoc	p1 = 0.676, p2 = 0.923, p3<0.001*, p4 = 0.747, p5<0.001*, p6<0.001*									
SO_2	96.88 ± 1.12		96.88 ± 1.14		77.83 ± 5.14		76.99 ± 5.03		1858.053	<0.001*
Mean ± SD	95.00–99.00		95.00–99.00		70.00–98.00		65.00–88.00			
Range										
Post Hoc	p1 = 0.990, p2<0.001*, p3<0.001*, p4<0.001*, p5<0.001*, p6 = 0.025									

SBP: Systolic blood pressure,**DBP**: Diastolic blood pressure**RR:** Respiratory rate**X** [2]: Chi square test.
K: Kruskal Wallis test * statistically significant.
P1: mild compared moderate P2: mild compared severe.
P3: mild compared critically ill P4: moderate compared severe.
P5: moderate compared critically ill P6: severe compared critically ill.

D-dimer levels indicate the progressive severity of COVID-19 infection and can be used as a predictor that more aggressive critical care will be needed [27]. Also, the study by **Yang et al.,** found that, CRP, ferritin, TLC and creatinine levels were statistically significantly increased among critically ill group than other groups [23]. Another study by **Helms et al.,** revealed that, D-dimers are significantly increased in COVID-19 infection [28].

Also, **Wool and Miller,** reported that temporally increasing D-dimer levels indicate the progressive severity of COVID-19 infection and can be used as a predictor that more + aggressive critical care will be needed [27]. While, **Liu et al., [15]** reported that more severe cases infected with COVID19 expressed significantly higher CRP levels than non-severe patients suggesting that this biomarker can be monitored to evaluate disease progression [29]. The study by **Bayani et al.,** evaluated the association between CRP and COVID-19 infection, and the findings indicated that a patient with a CRP level >64.75 mg/L was more likely to develop the severe form of the disease [30].

In the present study, there was a statistically significant difference between the tested groups regarding thrombocytopenia. Thrombocytopenia was shown to be statistically significant higher in severe and critically ill patients. These findings agree with **Yang et al.,** findings that thrombocytopenia is prevalent in patients with severe COVID-19 and is linked to a higher risk of in-hospital mortality [23]. Also, **Lippi et al.,** found that, the rate of thrombocytopenia, a platelet count below the lower limit of the locally defined reference range was associated with an over 5-fold enhanced risk of severe COVID-19 [31]. The decreasing platelet count in patients in the intensive care unit usually indicates the dysfunction of organs or systems and leads to a disorder of homeostasis. Also, low platelet in the ICU tended to increase the risk of death [32]. It has also been reported that 2019-nCoV infection might affect the blood coagulation mechanism resulting in a disorder of blood coagulation [33].

In the present study, there was statistically significant positive correlation between platelet counts with So2. While, there was statistically significant negative correlation between platelet with CRP, D-dimer, Serum ferritin, and LDH ($p < 0.05$), These results are in agreement with **Draz et al,** who found that platelets were statistically significant associated with TLC among critically ill patients ($P < 0.05$) [32]. Also, the study by **Yang et al.,** that there is a statistically significant negative relationship between platelets with LDH among the studied critically ill patients ($P < 0.05$) [23]. Moreover, **Libby et al.,** indicated that the relationship between leukocyte count and increased platelet reactivity was observed in total leukocyte count, total neutrophil count, and total lymphocyte count [27]. Both neutrophil count and lymphocyte count showed a strong positive correlation with total leukocyte count ($p < 0.05$).The study by **Draz et al.,** found no significant correlations between platelet count and hemoglobin level and So2 [34].

In the present study, As regards mortality rate, there was a statistically significant difference between the studied groups ($p < 0.05$). Where the mortality rate in critically ill patients' group was (80) is

Table 3
Laboratory investigations and CT chest among the studied groups.

Variables	Studied groups (N = 800)				K	P value
	Group I N = 200	Group II N = 200	Group III N = 200	Group IV N = 200		
Hb (g/dl)	12.10 ± 1.15	11.89 ± 1.17	10.84 ± 1.13	9.62 ± 0.81	23.84	**<0.001***
Mean ± SD	9.50–15.00	10.00–14.10	8.00–14.00	6.00–12.00		
Range						
Post Hoc	p1 = 0.056, p2<0.001*, p3<0.001*, p4<0.001*, p5<0.001*, p6<0.001*					
TLC (10 [9]/per liter)	7.47 ± 1.87	7.60 ± 1.75	7.99 ± 1.85	8.08 ± 1.97	5.09	**0.002***
Mean ± SD	3.30–12.00	4.00–12.00	4.00–13.00	3.00–15.00		
Range						
Post Hoc	p1 = 0.941, p2<0.001*, p3<0.001*, p4<0.001*, p5<0.001*, p6 = 0.009					
Lymphocytes (10 [9]/liter)	0.74 ± 1.27	0.48 ± 0.59	0.59 ± 0.95	0.58 ± 1.00	2.30	0.076
Mean ± SD	0.10–6.00	0.10–3.80	0.10–6.00	0.10–5.50		
Range						
Platelet (10 [9]/L)	358.26 ± 37.11	315.8 ± 55.66	199.0 ± 48.2	185.9 ± 35.57	71.20	**<0.001***
Mean ± SD	250.0–440.0	166.0–428.0	100.0–315.0	99.00–295.00		
Range						
Post Hoc	p1<0.001, p2<0.001, p3<0.001, p4 = 0.033, p5 = 0.009, p6 = 0.638					
Creatinine (μmol/L)	0.96 ± 0.54	0.76 ± 0.28	1.07 ± 0.63	1.09 ± 0.55	18.064	**<0.001***
Mean ± SD	0.20–3.50	0.30–1.60	0.30–4.00	0.40–3.80		
Range						
Post Hoc	p1<0.001*, p2 = 0.025, p3 = 0.008, p4<0.001*, p5<0.001*, p6 = 0.693					
CRP (mg/L)	17.30 ± 8.36	27.72 ± 17.91	83.17 ± 27.3	129.8 ± 32.78	984.657	**<0.001***
Mean ± SD	6.00–48.00	10.00–84.00	48.0–194.0	69.00–198.00		
Range						
Post Hoc	p1<0.001*, p2<0.001*, p3<0.001*, p4<0.001*, p5<0.001*, p6<0.001*					
Ferritin (μg/L)	190.28 ± 64.88	242.35 ± 55.8	344.2 ± 58.5	433.4 ± 48.34	714.255	**<0.001***
Mean ± SD	52.00–270.00	110.0–310.0	170.0–520.0	280.0–546.0		
Range						
Post Hoc	p1<0.001*, p2<0.001*, p3<0.001*, p4<0.001*, p5<0.001*p6<0.001*					
LDH (U/L)	213.75 ± 40.15	228.04 ± 35.6	237.1 ± 40.1	276.3 ± 42.98	90.564	**<0.001***
Mean ± SD	135.0–290.00	135.0–290.0	136.0–310.0	175.0–395.0		
Range						
Post Hoc	p1<0.001*, p2<0.001*, p3<0.001*, p4 = 0.023, p5<0.001*, p6=<0.001*					
D Dimer	0.36 ± 0.12	0.64 ± 0.16	1.85 ± 0.84	1.98 ± 0.93	337.120	**<0.001***
Mean ± SD	0.10–0.60	0.30–1.20	0.50–4.00	0.50–5.00		
Range						
Post Hoc	p1<0.001*, p2<0.001*, p3<0.001*, p4<0.001*, p5<0.001*p6 = 0.042					
CT chest	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**X^2**	**P value**
Corad.1	93	46.5	0	0.0	0	0.0	0	0.0	28.973	**<0.001***
Corad.2	107	53.5	0	0.0	0	0.0	0	0.0		
Corad.3	0	0.0	176	88.0	8	4.0	0	0.0		
Corad.4	0	0.0	24	12.0	42	21.0	0	0.0		
Corad.5	0	0.0	0	0.0	150	75.0	200	100.0		

Hb: Haemoglobin, TLC: Total Leukocyte Count, AST: Aspartate aminotransferase, ALT: Alanine transaminase, CRP: C - reactive protein test, **LDH**: lactate dehydrogenase.
K: Kruskal Wallis test X^2: chi-square test *statistically significant.
P1: mild compared moderate, P2: mild compared severe P3: mild compared Critically ill.
P4: moderate compared severe, P5: moderate compared Critically ill, P6: severe compared Critically ill.

Table 4
Correlation between platelet count with studied parameters with laboratory investigations among the studied patients.

Variables	PLT							
	Mild		Moderate		Severe		Critically ill	
	r	p value	r	p value	r	p value	r	p value
CRP	−0.004	0.953	−0.221	**0.002***	−0.036	0.616	−0.029	0.688
Ferritin	−0.029	0.681	−0.016	0.825	−0.168	**0.018***	−0.006	0.933
LDH	−0.108	0.127	−0.072	0.309	−0.130	0.066	−0.200	**0.005***
D-dimer	−0.150	0.206	−0.298	**0.001***	−0.019	0.785	−0.103	0.825
So2	0.124	0.081	0.088	0.213	0.200	**0.004***	0.210	**0.039***

DM: Diabetes mellitus **HTN**: Hypertension**CKD**: Chronic kidney disease**RR:** Respiratory rate**Hb:** hemoglobin**, TLC**: Total Leukocyte Count, **CRP**: c-reactive protein test, **Cr**: Computed tomography, **LDH**: lactate dehydrogenase.
r: correlation coefficient *Significant.

(40%) Severe 35 (17.5%), where the most common cause of death was respiratory failure, which occurred in 28 severe patients (80%) and 65 critical ill patients (81.25%), followed by thrombocytopenia associated hemorrhage. These findings matched those of **Zhu et al.,** [22]**; Yang et al.,** [23]**;** and **Lippi et al.,** [31]. Also, **Helms et al.,** found that, outcome of the COVID-19 was statistically significant difference among the studied patients and the rate of mortality was statistically significantly higher among severe and critically ill patients [28].

It was established that mortality increases when platelet count decreases. Abnormal platelet count is quite common in patients in the

Table 5
Outcome among the studied groups.

Variables	Studied groups (N = 800)								X [2]	P value
	Group I N = 200		Group II N = 200		Group III N = 200		Group IV N = 200			
	N	%	N	%	N	%	N	%		
Outcomes	200	100.00	200	100.0	165	82.50	120	60.00	6.13	**0.024***
Survivor	0.00	0.00	0.00	0.00	35	17.50	80	40.00		
Non- survivor										
Couse of death	0	0.00	0	0.00	28	80.0	65	81.25	——	
Respiratory failure	0	0.00	0	0.00	7	20.0	15	18.75		
Hemorrhage and hemorrhagic shock										
Thrombocytopenia	0	0.00	0	0.00	40	20.0	50	25.0	94.06	**<0.001***
Yes	0	0.00	0	0.00	160	80.0	150	75.0		
No										
Death due to Hge/Thrombocytopenia	0	0.00	0	0.00	7/40	17.5	15/50	30.0	——	

X^2: chi-square test *statistically significant.

intensive care unit [35]. In this concern, **Lippi et al.,** found that the rate of thrombocytopenia below the lower limit of the locally defined reference range was associated with an over fivefold enhanced risk of severe COVID-19 [28].

6. Conclusion

Platelet count is a simple, inexpensive, and readily available laboratory parameter that is frequently linked to severe covid-19 infection and a significant death risk. From this work, we recommended that: special consideration should be given to platelet count as a simple indicator for severe COVID-19 infection. Also, close follow-up of critically ill patients with thrombocytopenia is required to avoid a bad outcome to occur. Wheeze, the Platelet count should be closely observed before and during anticoagulant therapy. Finally, further studies on a wide scale of patients should be done to confirm our results.

Ethical approval

The study methodology was reviewed and found to be compliant with the 1975 Declaration of Helsinki's ethical principles, as evidenced by prior approval by the institution's human research committee (Institutional Review Board of Faculty of Medicine, Menoufia University, Egypt).

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This study did not receive any specific fund.

Author contribution

•All authors contributed to the conceptualization, design, data curation, resource identification, formal analysis, and data interpretation. Validation and technique, as well as revision of new software used in the work. All authors shared writing of this work. All authors reviewed the Manuscript.

Registration of research studies

1. Name of the registry: the Academic Research Registry Department
2. Unique Identifying number or registration ID: 9/2020TROP22
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

Guarantor

•All data are available upon request from the last author: Dr Ahmed Abozaid Ahmed Teima.

Consent

A written informed consent was given by every participant prior to the initiation of study in routine clinical practice at three specialized treatment centers especially concerned with COVID-19 management (Menoufia University Hospitals, National Liver Institute Hospital and Shebin El-Kom Teaching Hospital).

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The following information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories then this should be stated.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Conflicts of interest

No conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103973.

References

[1] C. Sohrabi, Z. Alsafi, N. O'neill, M. Khan, A. Kerwan, A. Al-Jabir, et al., World Health Organization declares global emergency: a review of the 2019 novel coronavirus (COVID-19), Int. J. Surg. 76 (2020) 71–76.
[2] C. Gomes, Report of the WHO-China joint mission on coronavirus disease 2019 (COVID-19), Brazilian Journal of Implantology and Health Sciences 2 (3) (2020).
[3] C. Mattiuzzi, G. Lippi, Which lessons shall we learn from the 2019 novel coronavirus outbreak? Ann. Transl. Med. 8 (3) (2020).
[4] D. Khurana, S.A. Deoke, Thrombocytopenia in critically ill patients: clinical and laboratorial behavior and its correlation with short-term outcome during hospitalization, Indian J. Crit. Care Med.: peer-reviewed 21 (12) (2017) 861, official publication of Indian Society of Critical Care Medicine.
[5] P. Schuff-Werner, J. Mansour, A. Gropp, Pseudo-thrombocytopenia (PTCP). A challenge in the daily laboratory routine? J. Lab. Med. 44 (5) (2020) 295–304.
[6] N. Chen, M. Zhou, X. Dong, J. Qu, F. Gong, Y. Han, et al., Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, Lancet 395 (10223) (2020) 507–513.

[7] T.E.S.A. Helal, N.A. Ehsan, N.A. Radwan, E. Abdelsameea, Relationship between hepatic progenitor cells and stellate cells in chronic hepatitis C genotype 4, APMIS 126 (1) (2018 Jan) 14–20, https://doi.org/10.1111/apm.12787.Epub.2017.Nov.20.

[8] S.F. Abdelwahab, Z. Zakaria, W.R. Allam, S. Hamdy, M.A. Mahmoud, M. Sobhy, E. Rewisha, I. Waked, Interleukin 28B.rs12979860 genotype does not affect hepatitis C viral load in Egyptians with genotype 4 chronic infection, Arch. Virol. 160 (11) (2015 Nov) 2833–2837, https://doi.org/10.1007/s00705-015-2555-3. Epub 2015 Aug 18.

[9] Khaled Metwally, Maha Elsabaawy, Mohamed Abdel-Samiee, WessamMorad, NermineEhsan, EmanAbdelsameea, FIB-5 versus FIB-4 index for assessment of hepatic fibrosis in chronic hepatitis B affected patients, Clin. Exp. Hepatol. 6 (4) (2020 Dec) 335–338, https://doi.org/10.5114/ceh.2020.102157.Epub.2020.Dec.30.

[10] S.F. Abdelwahab, Z. Zakaria, M. Sobhy, S. Hamdy, M.A. Mahmoud, N. Mikhail, W. R. Allam, E. Rewisha, I. Waked, Differential distribution of IL28B.rs12979860 single-nucleotide polymorphism among Egyptian healthcare workers with and without a hepatitis C virus-specific cellular immune response, Arch. Virol. 160 (7) (2015 Jul) 1741–1750, https://doi.org/10.1007/s00705-015-2446-7. Epub 2015 May 15.

[11] M.A. El Samiee, E.S. Tharwa, M.A. Obada, A.K.A. Gabal, M. Salama, Gamma-glutamyltranspeptidase and α-fetoprotein: are they predictors of treatment response in patients with chronic hepatitis C? Egyptian Liver Journal 1 (1) (2011) 18–24.

[12] El-Sayed Ibrahim, Mohamed Abdel-Samiee, Mohamed I. Youssef, Helmy El-Shazly, Abd-ElAleem A. El-Gendy, Ayman Ahmed Sakr, Doaa Elwazzan, AmrAlyElshormilisy MervatRagabNassar, Madkour Ahmad, Mostafa Kamal, Yasmine M Amrousy, Sally WaheedElkhadry, EmanAbdelsameea, Variceal recurrence 4 years post endoscopic band ligation in hepatitis C patients who achieved sustained virological response with oral direct-acting antiviral therapy, J. Viral Hepat. 28 (2) (2021 Feb) 279–287, https://doi.org/10.1111/jvh.13426.Epub.2020.Nov.9.

[13] M. Essa, A. Sabry, E. Abdelsameea, E.S. Tharwa, M. Salama, Impact of new direct-acting antiviral drugs on hepatitis C virus-related decompensated liver cirrhosis, Eur. J. Gastroenterol. Hepatol. 31 (1) (2019) 53–58.

[14] M. Abozeid, A. Alsebaey, E. Abdelsameea, W. Othman, M. Elhelbawy, A. Rgab, M. Elfayomy, T.S. Abdel-Ghafar, M. Abdelkareem, A. Sabry, M. Fekry, N. Shebl, E. Rewisha, I. Waked, High efficacy of generic and brand direct acting antivirals in treatment of chronic hepatitis C, Int. J. Infect. Dis. 75 (2018 Oct) 109–114, https://doi.org/10.1016/j.ijid.2018.07.025. Epub 2018 Aug 2.

[15] T. Elbaz, M. Abdo, H. Omar, E.A. Hassan, A.M. Zaghloul, M. Abdel-Samiee, A. Moustafa, A. Qawzae, M. Gamil, G. Esmat, Efficacy and safety of sofosbuvir and daclatasvir with or without ribavirin in elderly patients with chronic hepatitis C virus infection, J. Med. Virol. 91 (2) (2019 Feb) 272–277, https://doi.org/10.1002/jmv.25287.Epub.2018.Nov.8.

[16] Eman Abdelsameea, AymanAlsebaey, Mohamed Abdel-Samiee, Wael Abdel-Razek, Mohsen Salama, Waked Imam, Direct acting antivirals are associated with more liver stiffness regression than pegylated interferon therapy in chronic hepatitis C patients, Expert Rev Anti Infect. Ther. 29 (2020 Dec) 1–7, https://doi.org/10.1080/14787210.2021.1864326.

[17] G. Mathew, Agha R for the STROCSS Group, STROCSS: Strengthening the Reporting of cohort, cross-sectional and case-control studies in Surgery, Int. J. Surg. 96 (2021), 106165.

[18] S.H. Wong, R.N.S. Lui, J.J.Y. Sung, Covid-19 and the digestive system, J. Gastroenterol. Hepatol. 35 (5) (2020) 744–748.

[19] Y. Tian, L. Rong, W. Nian, Y. He, Gastrointestinal features in COVID-19 and the possibility of faecal transmission, Aliment. Pharmacol. Ther. 51 (9) (2020) 843–851.

[20] Ahmed Abozaid Ahmed Teima, Amany Abas Amer, Lamiaa I. Mohammed, Zeinab A. Kasemy, Samar Ha Aloshari, Mohamed Meligy Ahmed, Abuamer Ahmed, Shabaan Ahmed, Hassan Ahmed Elzohry, Sayed F. Abdelwahab, Heba Mohamed Abdallah, Sabry Moawad Abdelmageed, Mohamed A. Sakr, Mohamed Abdel-Samiee, A cross-sectional study of gastrointestinal manifestations in COVID-19 Egyptian patients, Ann. Med. Surg. (London) Jan 11 (2022), 103234, https://doi.org/10.1016/j.amsu.2021.103234.

[21] A.A. Yameny, Association between thrombocytopenia and mild infection of COVID-19 patients, Journal of Bioscience and Applied Research 7 (3) (2021) 130–134.

[22] Y. Zhu, J. Zhang, Y. Li, F. Liu, Q. Zhou, Z. Peng, Association between thrombocytopenia and 180-day prognosis of COVID-19 patients in intensive care units: a two-center observational study, PLoS One 16 (3) (2021), e0248671.

[23] X. Yang, Q. Yang, Y. Wang, Y. Wu, J. Xu, Y. Yu, et al., Thrombocytopenia and its association with mortality in patients with COVID-19, J. Thromb. Haemostasis 18 (6) (2020) 1469–1472.

[24] World Health Organization, Coronavirus Disease (COVID-19) Outbreak: Rights, Roles and Responsibilities of Health Workers, Including Key Considerations for Occupational Safety and Health: Interim Guidance, 19 March 2020, World Health Organization, 2020.

[25] N. Kim, K.H. Kim, S.J. Lee, S.H. Park, I.S. Kim, E.Y. Lee, J. Yi, Bone marrow findings in severe fever with thrombocytopenia syndrome: prominent haemophagocytosis and its implication in hemophagocytic lymph histiocytosis, J. Clin. Pathol. 69 (6) (2016 Jun 1) 537–541.

[26] J.E. Blair, A. Gotimukul, F. Wang, S.A. Mina, H.C. Bartels, M.W. Burns, A.E. Kole, H.R. Vikram, J.C. Gea-Banacloche, M.T. Seville, S.A.B. Petty, A. Vikram, R. Orenstein, Mild to moderate COVID-19 illness in adult outpatients: characteristics, symptoms, and outcomes in the first 4 weeks of illness, Medicine (Baltim.) 100 (24) (2021), 26371.

[27] G.D. Wool, J.L. Miller, The impact of COVID-19 disease on platelets and coagulation, Pathobiology 88 (1) (2021) 15–27.

[28] J. Helms, C. Tacquard, F. Severac, I. Leonard-Lorant, M. Ohana, X. Delabranche, et al., High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study, Intensive Care Med. 46 (6) (2020) 1089–1098.

[29] Z. Liu, X. Xiao, X. Wei, J. Li, J. Yang, H. Tan, J. Zhu, Q. Zhang, J. Wu, L. Liu, Composition and divergence of coronavirus spike proteins and host ACE2 receptors predict potential intermediate hosts of SARS-CoV-2, J. Med. Virol. 92 (6) (2020 Jun) 595–601.

[30] M. Bayani, M. Sadeghi-Haddad-Zavareh, M. Shokri, S. Ebrahimpour, A. Babazadeh, R. Mehraeen, E. Moudi, A. Rostami, M. Barary, A. Hosseini, A. Bijani, C-reactive protein as a prognostic indicator in COVID-19 patients, Interdisciplinary Perspectives on Infectious Diseases 2021 (2021) 1–5, https://doi.org/10.1155/2021/5557582, 5557582.

[31] G. Lippi, M. Plebani, B.M. Henry, Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis, Clinical chemical acta 506 (2020) 145–148.

[32] D. Moreau, J.F. Timsit, A. Vesin, M. Garrouste-Orgeas, A. de Lassence, J.R. Zahar, Platelet count decline: an early prognostic marker in critically ill patients with prolonged ICU stays, Chest 131 (2007) 1735–1741.

[33] M. Xiong, X. Liang, Y.D. Wei, Changes in blood coagulation in patients with severe corona virus disease 2019 (COVID-19): a meta-analysis, Br. J. Haematol. 189 (6) (2020. Jun) 1050–1052.

[34] I.H. Draz, I.A. Shaheen, E.A. Youssef, Platelets count and platelets indices; mean platelet volume and platelet-crit in chronic lung disease, Egyptian Association Gazette 68 (1) (2020 Dec) 1–5.

[35] J. Pluta, J. Trzebicki, Thrombocytopenia: the most frequent haemostatic disorder in the ICU, Anaesthesiol. Intensive Ther. 51 (1) (2019 Jan 1) 56–63.