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Post-intensive care complications and mortality in severe and critically ill COVID-19 patients

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Abstract

Introduction: COVID-19 presents a wide spectrum of illnesses, ranging from asymptomatic to critical disease and multi-organ dysfunction.

Aim of the study: Detection and following up on early and remote complications and cause of mortality in severe and critically ill COVID-19 patients post their ICU discharge.

Subjects and Methods: 120 COVID-19 patients, who were admitted to the intensive care unit (ICU) of Fayoum University Hospitals, were recruited from October 2021 to October 2022. For each patient, the full clinical history, clinical examination, d-dimer level evaluation, and different body imaging according to the patient's clinical situation. That included ECG, echo, vascular duplex, CT chest, CT brain, MRI brain, and abdominal ultrasonography.

Results: The results showed that 32.11% of post-COVID-19 patients suffered from palpitation, dyspnea, chest pain and hypertension. 38.3 % of patients had different types of shocks. CO-RADS 4, 5, and 6 scores were diagnosed for 33%, 23.9%, and 37.6% of patients, respectively. 52.5% of patients had neuropsychiatric disorders. 35.8% of patients had renal complications, while 25.8% had gastrointestinal issues and 32.4% had endocrinal issues. Thrombocytopenia was diagnosed in 22.0% of cases. The mortality percentage was about 90%, where the most abundant causes were cardiac issues, sepsis, and renal failure.

Conclusion: Severe and critical COVID-19 with prolonged ICU stay is considered a multi-organ disease affecting both functional and biological status which needs close follow-up of COVID-19 survivors from their families and their health care team for early screening and adequate treatment of fatal complications with physical and mental rehabilitation.

Keywords: Complications; Intensive Care; Multi-organ Dysfunction; COVID-19.

1. Introduction

Coronavirus disease (COVID-19) is caused by severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2). COVID-19 primarily affects the respiratory system ranging from none or mild symptoms to fatal viral pneumonia, causing severe acute respiratory distress syndrome (ARDS). Recent data indicates that COVID-19 is a systemic disease affecting multiple systems including respiratory,

cardiovascular, neurological, gastrointestinal, immune, and hematopoietic systems leading to critical illness and multi-organ failure. Advanced age and comorbid medical conditions, such as hypertension and diabetes, have been shown to predispose individuals to severe illness due to COVID-19 [1]. Roughly, 5% of patients are admitted to the intensive care unit (ICU) and

it was reported that they have high in-hospital mortality [2].

The mortality rate ranges from 1% to 4% in all patients, and up to 20% of patients admitted to the intensive care unit (ICU) with severe or critical COVID-19. This high mortality is not associated with pulmonary affection alone

2. Subjects and methods

2.1. Subjects

In the current prospective and observational study, 120 patients who were previously admitted to the ICU of Fayoum University Hospitals with severe and critical COVID-19 after their discharge from October 2021 to October 2022, were recruited.

2.2. Inclusion criteria

Patients recovered and were discharged after the previous admission to the ICU of Fayoum University Hospitals with severe and critical COVID-19 after their discharge.

2.3. Exclusion criteria

Mild-severity COVID-19 patients, uncooperative patients, and children ≤ 14 years old were excluded.

2.4. Experimental design

All patients were subjected to the following: full clinical history, full clinical

3. Results

Our study showed that the mean age of the patients was 58.13 ± 15.5 with 62 (51.7%) females and 58 (48%) males having a previous

but may be caused by other organ involvement especially the kidneys and heart [3].

The current study aimed to assess the detection and following up for early and remote complications, besides the causes of mortality in severe and critically ill COVID-19 patients post their ICU discharge.

examination, and D-dimer levels measurement. Besides, different body imaging according to the patient's clinical situation such as ECG, Echo, vascular duplex, CT chest, CT brain, MRI brain, abdominal ultrasonography, were performed.

2.5. Statistical analysis

Descriptive statistics are presented in the form of mean with standard deviation for numerical variables, while numbers and percentages were used for categorical variables. The association between different types of complications and categorical variables was studied using the Chi-Square test or Fisher's exact test, while the independent samples t-test was used for the association between age and different types of complications. IBM SPSS 28 was used for the statistical analysis and a *P-value* < 0.05 was considered statistically significant.

medical history of different diseases, as shown in Table 1.

Table 1: Clinical History of the study population.

Variables		Frequency (n = 120)
Gender	Male	58 (48.3%)
	Female	62 (51.7%)
Age (years)		58.13 ± 15.5
Chronic chest disease		50 (41.6%)
Hypertension (HTN)		46 (38.3%)
Diabetes (DM)		44 (36.6%)
Ischemic heart disease (IHD)		25 (20.8%)
Chronic kidney disease (CKD)		15 (12.5%)

In the current study, several post-COVID-19 complications were reported. Clinically, 35 (32.11%) patients complained of recurrent attacks of palpitation, dyspnea, chest pain, and uncontrolled hypertension. New ECG

changes, not present previously, were observed in 74 (61.66) patients. New Echo findings were detected in 86 (71.6%) patients, as shown in Table 2.

Table 2: New findings of ECG and Echo measurements of the studied population.

Variables	Frequency	Variables	Frequency
<i>ECG</i>		<i>Echo</i>	
Sinus Tacky	50 (41.6%)	Cardiomyopathy	30 (25%)
Extrasystoles (Atrial, Ventricle)	46 (38.3%)	Pulmonary hypertension (PHTN)	14 (11.66%)
Atrial Fibrillations (AF)	44 (36.6%)	Moderate to severe Mitral resurge	10 (8.33%)
Pathological Q waves	25 (20.8%)	Dilated right heart side	9 (7.5%)
Tacky-Brady syndrome	15 (12.5%)	Left ventricular hypertrophy (LVH)	8 (6.66%)
Inverted t waves	15 (12.5%)	Mass on mitral or tricuspid valves	8 (6.66%)
Depressed ST segment	15 (12.5%)	Moderate Pericardial effusion	7 (5.83%)

Post-COVID-19 patients developed many fatal vascular complications with a higher incidence of thrombosis in abnormal sites as shown in Table 4. 46 (38.3 %) patients presented with shock as follow:

septic in 17 (14.16) patients, neurogenic in 9 (7.5%) cardiogenic in 9 (7.5%) patients, mixed in 6(5%) patients, and obstructive in 5 (4.16%) patients, as shown in Table 3.

Table 3: The vascular Complications reported in the studied population.

Vascular Complications	Frequency
Pulmonary embolism (PE)	22 (18.33%)

Deep venous thrombosis (DVT)	Lower limb	25 (20.83%)
	Left Internal Jugular Vein	17 (14.16%)
	Upper limb	13 (10.83%)
Acute myocardial infarction		10 (8.33%)
Abdominal Aortic Aneurysm		5 (4.16%)
Cavernous sinus thrombosis		5 (4.16%)
Shock	Septic	17 (14.16%)
	Neurogenic	9 (7.5%)
	Cardiogenic	9 (7.5%)
	Mixed	6 (5%)
	Obstructive	5 (4.16%)

Diagnosis of respiratory complications showed that 71 (59%) patients were dependent on different types of home oxygen therapy post-ICU discharge from low-flow oxygen up to home CPAP. 29 (24.16%) of them were

readmitted with type I respiratory failure (RFI), 18 (15%) patients with type II respiratory failure (RFII), and 2 patients (1.66%) with lung malignancy, as shown in Table 4.

Table 4: Home oxygen therapy results of the study population.

Variables	Frequency
Nebulizer	20 (16.66%)
Low-flow oxygen	17 (14.16%)
Continuous positive airway pressure (CPAP)	14 (11.66%)
High flow from 10-15 L	12 (10%)
Venturi mask	8 (6.66%)

The mean CO-RADS score in the studied patients was 4.92 ± 1.00 (ranging from 1.0 to 6.0). Only 1 (0.9%) patient had CO-RADS 1, 5 (4.6%) patients had CO-RADS 3, 36

(33.0%) patients had CO-RADS 4, 26 (23.9%) patients had CO-RADS 5 and 41 (37.6%) patients had CO-RADS 6, as shown in Figure 1.

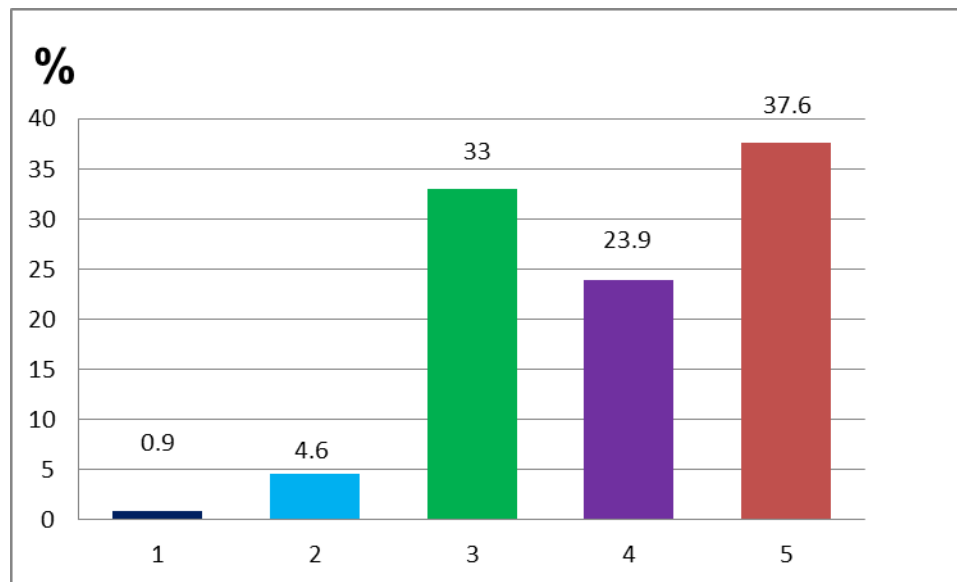


Figure 1: CO-RADS score of the studied population.

Reporting of the neuropsychiatric complications showed that 63 (52.5%) of the patients had neuropsychiatric disorders in the form of thrombotic, autoimmune, infectious, and other events. as shown in Table 5.

The reported renal complications showed that 43 patients had newly developed renal impairment ranging from elevated baseline renal functions up to hemodialysis. Renal ultrasonography in those patients revealed grade II- III nephropathy in 9 (7.5%) patients, borderline echogenicity in 9 (7.5%), and mild back pressure with no renal stone in 4 (3.33%) patients. Furthermore, two renal biopsies were examined and revealed focal segmental glomerulonephritis in one of them and microangiopathic renal vein thrombosis in the other, as shown in Table 5.

The abdominal ultrasound findings of the studied population showed that 31 (25.8%) patients presented with elevated liver enzymes, total Bilirubin, and direct or impaired coagulation profile, where most of patients had ultrasonographic findings, as shown in Table 5.

The endocrinal complications were reported in 10 (8.3%) patients, who developed hyperglycemia and maintained on anti-diabetic drugs, 8 (15%) patients with hypothyroidism, recurrent attacks of hypoglycemia occurred in 6 (5%) patients, 5 (4.1%) patients with hyperthyroidism, and pancreatitis in 3 (2.5%) patients. Furthermore, the results showed that 2 (1.8%) patients presented with gas gangrene and 3 (2.7%) patients with mucormycosis, as shown in Table 5.

Also, Thrombocytopenia occurred in 24 (22.0%) patients. The serum D-dimer levels ranged from 0.5–1.5 $\mu\text{g/ml}$ observed in 35 (32.1%) patients and were not associated with evidence of thrombi. The serum D-dimer levels ranged from 1.5-3.5 $\mu\text{g/ml}$ and were found in 12 (11%) patients and were associated with different vascular thromboses-like minor cerebral stroke and DVT. The serum D-dimer levels ranged from 3.5-5 $\mu\text{g/ml}$ and were found in 2 (1.8%) patients who developed serious infections (mucormycotic and gas gangrene). Marked elevation ≥ 5 $\mu\text{g/ml}$ was detected in 8 patients with complete middle cerebral occlusion (MCA), 8 (7.33%) patients with multi-organ

dysfunction (MODS), 3 (2.7%) patients with main trunk pulmonary embolism, and 3 (2.7%) with GBS. Orthopedic complications reports showed that Femoral head avascular necrosis

(AVN) was detected in 12 (10%) of patients mostly complications of steroid therapy during ICU admission and some of them underwent a hip replacement.

Table 5: The post-COVID-19 complications reported in the study population.

Variables	Frequency
Neuropsychiatric complications	
Encephalopathy	20 (16.66%)
Psychiatry Disorders	15 (12.5%)
Cerebrovascular Stroke	12 (10%)
Intracerebral Hemorrhage	7 (5.8%)
Guillain Barre Syndrome	6 (5%)
Encephalitis	3 (2.5%)
Renal Complications	
Elevated base line creatinine	23 (19.1%)
Acute kidney injury (AKI)	12 (10%)
Dialysis	8 (6.66%)
Gastrointestinal complications	
Portal vein thrombosis	18 (15%)
Subtle courses texture	7 (5.83%)
Cirrhotic liver	2 (1.66%)
Focal lesion	2 (1.66%)
Fatty liver	5 (4.16%)
Splenomegaly	2 (1.66%)
Gall bladder stones	2 (1.66%)
Endocrinal complications	
Hyperglycemia	10 (8.3%)
Hypothyroidism	8 (15%)
Hypoglycemia	6 (5%)
Hyperthyroidism	5 (4.1%)

The most common cause of death was cardiac events in 34 (31.1%) patients followed

by sepsis in 21 (19.2%) patients and renal failure in 12 (11%) patients (Figure 2).

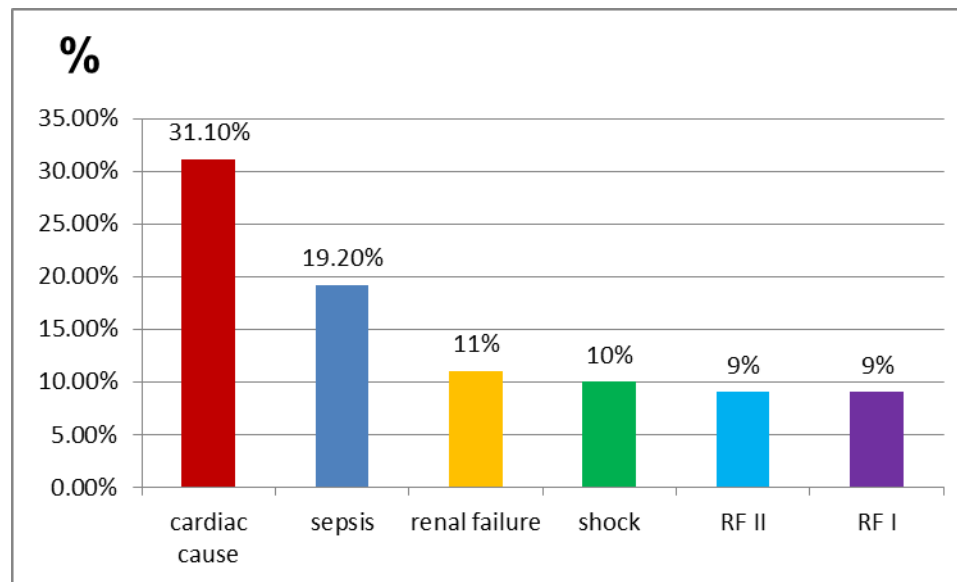


Figure 2: Percentages of mortality among the studied population.

Shocks were reported in 11 (10%) patients as follows; 3 (2.75%) had a cardiogenic shock, 2 (1.8%) had a septic shock, 4 (3.6%) had mixed shock, and obstructive shock in 2 (1.8%)

The Chi-square test, Fisher's exact test, and independent samples t-test were used to study the association of different types of complications with patients' past medical history. The history of hypertension was associated with higher cardiovascular complications ($P=0.013$), higher endocrinal complications ($P=0.035$), and higher liver complications ($P=0.028$). The history of diabetes was associated with higher hematological

4. Discussion

In the current study, COVID-19 had a broad spectrum of complications post-ICU discharge that affects the functions of multiple systems, such as cardiovascular, respiratory, neuropsychiatric, renal, gastrointestinal, endocrinal, and hematological systems. That might be the leading reason for chronic critical illness and multi-organ failure with high mortality.

In agreement with our findings, in the study conducted by Ng *et al.*, (2020), COVID-19 patients were observed for 56 days post-

patients. Type II respiratory failure was detected in 10 (9%) patients and type I respiratory failure was detected in 10 (9%) patients.

complications ($P=0.044$). The history of IHD was associated with higher cardiovascular complications and vascular complications ($P=0.024$). The history of CKD was associated with higher neuropsychiatric disorders ($P=0.032$). Finally, none of the complications was associated with age ($P=0.18$), sex ($P=0.85$), or chronic chest disease ($P=0.15$).

recovery by CMR, where some of them progressed to a myocardial inflammation (myocarditis) [4].

Mandal *et al.*, (2021), reported many post-COVID-19 complications, where 53% of patients had shortness of breath, 34% had a persistent cough, 69% had persistent fatigue, 15% had depression, and 30.1% had increased D- dimer levels [5].

Kumar *et al.*, (2021), reported the development of DVT and lower GI bleeding post-discharge [6].

Furthermore, the study conducted by Lim *et al.*, (2020), revealed that psychiatric symptoms continued for 40 days post-discharge, which included delusion, delirium, auditory, and visual hallucinations [7]. Also, Ayoubkhani *et al.*, (2021), showed that one-third of the recovered patients were re-admitted because of arising complications including pulmonary (33%), cardiac (32%), renal (12%), and hepatic (10%) complications [8]. Parpas *et al.*, (2021), found that acute kidney injury leading to renal failure and impaired diastolic function along with severe hyponatremia were common complications, as well [9].

Another study showed that 33.62% of COVID-19 patients had neuropsychiatric disorders, 17.39% had anxiety disorders, 0.11% had Parkinson's disease, and 0.56% had intracranial bleeding [10]. In the study conducted by Weng *et al.*, (2021), 44.0% of patients had gastrointestinal manifestations after 90 days of recovery including anorexia, nausea and gastroesophageal reflux, recurrent vomiting, and abdominal pain [11]. Roth *et al.*, (2021), reported serious hepatic complications like secondary sclerosing cholangitis and intra-hepatic microangiopathy, as well [12]. Another study reported terminal liver disease post-COVID-19 cholangiopathy, which required liver transplantation [13].

The study conducted by de Roquetaillade *et al.*, (2021), reported that COVID-19-related death occurred in 13% of patients due to secondary infection-related MODS in 26%, and fatal ischemic events [14].

In the current study, we found that hypertension, diabetes, previous history of IHD, and CKD were associated with higher complications but not with age or chronic chest

disease. These findings matched the results of many other studies. Tadic *et al.*, (2021), stated that hypertensive patients developed target organ damage that increased the risk of unfavorable outcomes in COVID-19 patients [15]. Sun *et al.*, (2020), demonstrated that COVID-19 patients with diabetes had a higher risk of complications, especially serious infections [16]. Docherty *et al.*, (2020), stated that chronic lung diseases increase the risk of severe outcomes [17]. Likewise, Rajan *et al.*, (2020), reported that patients with known coronary artery disease and heart failure were at higher risk than others to develop cardiovascular complications [18]. Podestà *et al.*, (2021), stated that CKD is associated with an increased risk of major cardiovascular events and higher mortality rates [19].

In Contrast to the current findings, a previous study reported great severity and serious complications of COVID-19 in men compared to women [20]. Also, Hwang *et al.*, (2020), reported that CKD was not significantly associated with Neurological diseases and death of COVID-19 patients [21].

5. Conclusion

Severe and critical COVID-19 with prolonged ICU stay is considered a multi-organ disease affecting both functional and biological status which needs a close follow-up of COVID-19 survivors from their families and their healthcare team for early screening and adequate treatment of fatal complications with physical and mental rehabilitation

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Ethical Approval Statement: Approvals have been obtained from the Ethical Committee of Fayoum Faculty of Medicine, Fayoum, Egypt.

Informed Consent Statement: Informed written consents for participation were taken and

signed by the eligible relatives before recruitment and randomization.

Availability of data and materials: The data sets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Conflicts of Interest: All authors declare no conflict of interest.

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