Pattern and Prevalence of Neurovascular Events among Covid-19 Patients

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Abstract

Background

The present COVID-19 situation has highlighted the importance of determining the pandemic's impact on healthcare. While several research have looked at the relationship between COVID-19 and neurological symptoms, the influence of the present pandemic on stroke outcomes has to be looked into more. Objectives: The current cross-sectional study was carried out to evaluate the short-term outcomes of stroke in Egyptian patients diagnosed with COVID-19 and to identify potential determinants of stroke outcomes in the short term. Methods: The current study was designed as a Cross section study that included All Patients 18 years or older with confirmed COVID- 19 presenting at the emergency department at Suez Canal university hospital. Results: The present study was designed as a cross-sectional study that included 75 patients over 18 years of age who confirmed COVID-19 presenting at the emergency department, Suez Canal university hospital fulfilling our inclusion criteria to be constituted. The prevalence of neurovascular events among the studied sample was 10% (five ischemic stroke patients, two hemorrhagic stroke patients, and one patient with cavernous sinus thrombosis). Conclusions: Neurovascular problems in COVID-19 are an important problem in clinical neurology. The hypercoagulability state might occur when there is hyperinflammation caused by a pathogenic virus. Increased blood cellular components and platelet might occur. A stimulation of the coagulation cascade is also observed. Additionally, an increased plasma concentration or viscosity during COVID-19 illness is described.

Keywords: Stroke - emergency department- covid- 19.

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Introduction:

The present COVID-19 situation has highlighted the importance of determining the pandemic's impact on healthcare. While several research have looked at the relationship between COVID-19 and neurological symptoms, the influence of the present pandemic on stroke outcomes has to be looked into more.

On March 11, 2020, the World Health Organization (WHO) declared COVID-19, the disease caused by the SARS-CoV-2, a pandemic. Characteristically, COVID-19 affects the respiratory system, producing symptoms ranging from mild upper-airway manifestations to pneumonia and severe acute respiratory distress syndrome. (Manuel et al., 2020) COVID-19 is increasingly recognized as a multi-system disease involving other organ systems (Tsivgoulis et al., 2020). Recently, it has become evident that COVID-19 can cause severe vascular damage and serious neurological manifestations. (Tsivgoulis et al., 2020). COVID-19 affects both the central nervous system (CNS) (24%) and the peripheral nervous system (PNS) (8.9%). (Munir et al., 2020). A growing number of case series and cohort studies have been published identifying neurological symptoms associated with COVID-19. (Tsivgoulis et al., 2020). Stroke has two types (ischemic stroke and hemorrhagic stroke) When the symptoms of a stroke last only a short time (less than an hour), this is called a transient ischemic attack (TIA) or mini-stroke. (S. W et al., 2012). Specific demographic, clinical, laboratory and radiological characteristics may be used as 'red flags' to alarm clinicians in recognizing COVID-19-related stroke. (Tsivgoulis et al., 2020) (Perry et al., 2020). However, this topic in emergency care has not been adequately studied. (Taylor et al., 2020). Our main objectives were to estimate the occurrence and survival outcome of neurovascular events among the studied sample of COVID-19 patients who attended the emergency departments in Suez Canal university hospital in Ismailia during the period of study.

As a result, the current cross-sectional study was carried out to evaluate the short-term outcomes of stroke in Egyptian patients diagnosed with COVID-19 and to identify potential determinants of stroke outcomes in the short term.

Methodology

Study site: the emergency departments at Suez

Canal University hospital, Ismailia city, Egyp

Study design

This was a cross sectional descriptive study included adult patients attended the study setting.

Study population

All Patients 18 years or older with symptoms or signs confirmed COVID - 19 presented at study setting at the period between October 2021 – January 2022.

Inclusion and exclusion criteria:

The study included Patients 18 years or older who presented to the ED at Suez Canal university hospital at the period of study with symptoms or signs confirmed of COVID–19 infection. The confirmed symptoms and signs were fever, cough, dyspnea, anosmia and the participants investigations showed CT findings highly suspected CORAD 3, CORAD 4 and CORAD 5, and positive PCR. Patients with traumatic brain injury with an external cause such as motor vehicle crashes and falls and those who have taken COVID-19 were excluded.

Sample size:

The sample size was calculated from the formula of descriptive cross-sectional study, i.e. N = Z2 p (100 _ p)/d2; where: N = estimated minimum sample size, Z = Standard deviation of 1.96 at 95% confidence interval, p = Prevalence/proportion in the study group = 23%. (Helms et al., 2020) and d = the margin of error on p, which is approximately 10 %. So, by calculation, the sample size is equal to 75 patients after the addition of 10% drop- out proportion. (Dawson B, Trapp RG., 2004).

Sampling technique:

A convenience sample technique included the patients fulfilled the research criteria who attended the emergency room during the period of study.

Data Collection

1- Patients was initially assessed at the emergency room of the emergency department of Suez Canal university hospitals.
2- Patients or their relatives signed an informed consent form that included the purpose and the type of the study.
3- The researcher assessed the patients directly to collect data.
4- Data was collected through a data collection sheet that includes socio demographic data, and medical history.
5- The patients were investigated till a confirmed diagnosis is reached by:

a. Clinical examination (symptoms and signs).

The signs of a neurovascular events are: Sudden numbness or weakness of the face, arm or leg, especially on one side of the body, Sudden confusion, Sudden trouble speaking, Sudden trouble seeing in one or both eyes. Sudden trouble walking, Sudden dizziness, loss of balance or coordination, Sudden severe headache with unknown cause. (S. W et al., 2012)

b. Positive finding of non-contrast brain CT or brain MRI.
c. Non contrast CT chest. (Highly suspicion COVID-19 viral infection with CT findings CORAD 3- CORAD 4 – CORAD 5).
d. PCR. (+VE PCR to confirm COVID-19 infection).
e. Blood glucose.
f. Serum electrolytes and renal function tests.
g. Complete blood count with differential, including platelet count.
h. Prothrombin time and international normalized ratio.
i. Activated partial thromboplastin time.
j. LDH and D-dimer.
k. Oxygen saturation.

6- Non-contrast CT brain was done to confirm findings of neurovascular manifestations (ischemic stroke, hemorrhagic stroke or cavernous sinus thrombosis). CT imaging was reviewed by the neurology team at Suez Canal University Hospitals (at 0 hour and 48 hours later).

7- Patients with neurovascular events were followed up in emergency by vital signs including: Blood pressure, Random Blood sugar, temperature, oxygen saturation and GCS every 6 hours and till disposition to see patient's fate.

Laboratory finding follow up was done every 48 hours to detect secondary bacterial infection and other complication.

ABG follow up was done every 12 hours to check the patient status for respiratory and metabolic improvement.

8- Evaluation of the patients using NIHSS score to Assess the severity of the disease and determine the suitable intervention according to the protocol of management of the hospital Suez Canal university.

Data analysis

It involves: data entry, data visualization, data manipulation and statistical analysis. The Statistical Package for Social Science SPSS Statistics version 15 (SPSS Inc., Chicago, IL, USA) software was utilized for data capture and statistical analysis.

Mean and standard deviation were estimated for each continuous variable. Student t-test, Mann Whitney test, Fischer exact test and chi-square test used to assess the statistical difference between variables, each test according to the type of variable. Study results was described in tables and graphs.

Multiple logistic regression analysis was used to study the effect of different factors on occurrence of neurovascular manifestations.

Ethical considerations:

Acceptance of the Suez Canal faculty of medicine ethical committee was obtained and an informed consent was obtained from all patients or relatives of participants before taking any data.

RESULTS

Characteristics of the studied sample

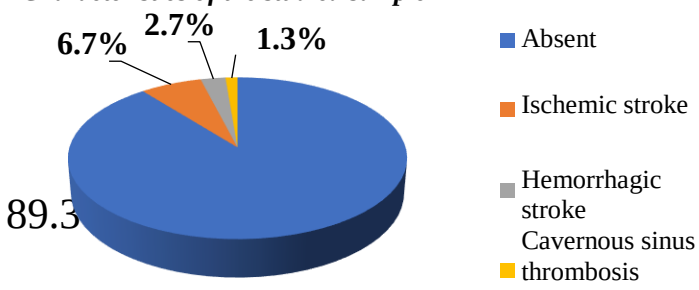


Figure 1. Occurrence of neurovascular symptoms in studied sample

Figure 1. Prevalence of neurovascular event among the studied sample

Figure 13 shows the prevalence of neurovascular event among the studied sample was 10% (five ischemic stroke patients,two hemorrhagic stroke patients and one patient with cavernous sinus thrombosis).

Table 1.Baseline characteristics of the studied sample and neurovascular events

Variables	Neurovascular events			p-value
	Total	Absent (n= 67)	Present (n= 8)	
Age, median (range)	62 (25 – 82)	61 (25 – 82)	62 (48 – 79)	0.891[a]
Gender, n (%)				
-Male	36 (48 %)	32 (47.8 %)	4 (50.0%)	0.905[b]
-Female	39 (52 %)	35 (52.2 %)	4 (50.0%)	
Occupation				
-Not employed /House wife	20 (26.7%)	18 (26.9 %)	2 (25.0%)	0.987[b]
-Retired	27 (36.0 %)	24 (35.8 %)	3 (37.5 %)	
-Skilled manual worker	7 (9.3 %)	6 (9.0%)	1 (12.5 %)	
-Semiprofessional/ Professional	21 (28.0%)	19 (28.4 %)	2 (25.0%)	
Smoking, n (%)				
-Absent	51 (68.0%)	47 (70.1 %)	4 (50.0%)	0.259[b]
-Present	24 (32.0%)	20 (29.9 %)	4 (50.0%)	
Chronic illness, n (%)				
-Absent	29 (38.7.0%)	28 (41.8 5)	1 (12.5%)	0.141[b]
-Present	46 (61.3 %)	39 (58.2 5)	7 (87.5%)	
	[a] P values are based Mann Whitney test. Statistical significance at P < .05. [b] P values are based on Fischer exact test. Statistical significance at P < .05.			

Mean age ± SD: 56.44 ± 15.06

Table 1 shows that the median age of COVID-19 patients presented with neurovascular events was 62 with range between 48 to 79 years. Males and females were almost equally represented and half of the patients were smokers. It was found that there is no statistically significant association between baseline characteristics of the studied sample and neurovascular events.

Table 2	**clinical characteristics of the studied sample and neurovascular events**			
Variables	**total**	**Neurovascular event**		**p-value**
		Absent (n= 67)	**Present (n= 8)**	
Fever				
-Absent	12 (16)	11 (16.4)	1 (12.5)	0.775 [b]
-Present	63 (84)	56 (83.6)	7 (87.5)	
Cough				
-Absent	4 (5.3)	4 (6)	0 (0)	0.478 [b]
-Present	71 (94.7)	63 (94)	8 (100)	
Dyspnea				
-Absent	11 (14.7)	10 (14.9)	**1 (12.5)**	0.855 [b]
-Present	64 (85.3)	57 (85.1)	**7 (87.5)**	
Oxygen saturation, median (range)	91 (66 – 96)	91 (80 – 96)	89 (66 – 93)	0.175[a]
Anosmia				
-Absent	51 (68)	48 (71.6)	3 (37.5)	0.101 [b]
-Present	24 (32)	19 (28.4)	5 (62.5)	
Headache				
-Absent	40 (53.3)	36 (53.7)	4 (50)	0.842 [b]
-Present	35 (46.7)	31 (46.3)	4 (50)	
Bone-ache				
-Absent	32 (42.7)	29 (43.3)	3 (37.5)	0.755 b
-Present	43 (57.3)	38 (56.7)	5 (62.5)	
[a] P values are based on Mann Whitney test. Statistical significance at P < .05. [b] P values are based on Fischer exact test. Statistical significance at P < .05.				

Table 2 shows that the most common presentations of COVID-19 patients presented with neurovascular events were fever, cough and dyspnea. The median O_2 saturation was 89% with range between 66 to 93%. It was found that there is statistically significant association between baseline characteristics of the studied sample and neurovascular events. The neurovascular symptoms ranged between decrease of the conscious level and limb weakness.

Table 3	**laboratory measures of patients with and without neurovascular**			
Variables	**Total sample**	**Neurovascular event**		**p-value**
	mean ± SD	**Absent (n= 67)** median (range)	**Present (n=8)** median (range)	
TLC	11.31 ± 5.91	9.6 (2.8 – 33.2)	12.5 (5 – 22)	0.239
Lymphocytes	15.3 ± 9.00	14 (2 – 44)	6 (6 – 30)	**0.034***
D-dimer	1.11 ± 1.49	0.6 (0.08 – 7.30)	1.2 (0.8 – 2.3)	**0.006***
CRP	72.84 ± 69.19	36 (6 – 280)	116 (16 – 120)	0.118
Na^+	139.15 ± 3.61	138 (132 – 145)	137 (132 – 143)	0.095
K^+	4.32 ± 0.64	4 (3.3 – 5.5)	4.3 (3.6 – 5)	0.717
LDH	415.4 ± 226.4	344 (110 – 998)	720 (230 – 782)	**0.002***
Serum creatinine	1.09 ± 0.70	0.9 (0.40 – 3.5)	0.65 (0.50 – 3.5)	0.346
PT	12.99 ± 1.14	13 (11 – 20)	13 (13 – 13)	0.512
INR	1.00 ± 0.18	1 (0.8 – 2.5)	1 (1 – 1)	0.565
	[a] P values are based on Mann Whitney test. Statistical significance at P < .05.			

Table 3. compares between patients with and without neurovascular event in terms of their laboratory measures. It was found that patients with neurovascular events had statistically significant lower lymphocyte count compared to stroke free patients (p=0.034). On the other hand, patients with neurovascular events had statistically significant higher D-dimer and LDH compared to stroke free patients (p=0.006) and (p=0.002), respectively.

Table 4. Logistic regression analysis of determinants of neurovascular events among COVID-19 patients

Variables	B	S.E.	OR	95% C.I.		p-value
				Lower	Upper	
Constant	-3.495	1.532	0.030			**0.023***
Age	-0.101-	0.061	0.904	0.803	1.018	0.095
Gender (male)	-0.625-	0.961	0.535	0.081	3.519	0.515
Chronic illness (present)	-2.290-	1.667	0.101	0.004	2.656	0.169
Lymphocytes	-0.058-	0.075	0.944	0.814	1.094	0.443
D-dimer	0.297	0.394	1.346	0.622	2.913	0.450
LDH	0.006	0.003	1.006	1.001	1.012	**0.032***

R^2=0.471 ANOVA<0.001; * Statistical significance < 0.05.

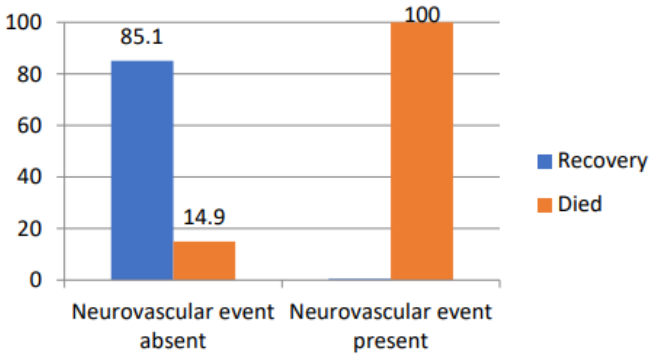
Table 4 shows logistic regression analysis of predictors of neurovascular events among COVID-19 patients. It shows that for every 1000 unit increase in the LDH level satisfaction, the likelihood to have neurovascular events increases by 6% (p=0.032).

II Outcome

Table 9. NIHSS mean of the patients of stroke (8 patients)

	Number of cases	mean ± SD
NIHSS of Stroke	**5**	**31 ± 9.3**
NIHSS of hemorrhagic Stroke	**3**	**32 ± 2.5**
NIHSS of total cases	**8**	**31 ± 7.6**

NIHSS: National Institutes of Health Stroke Scale



P values **<0.001** are based on Fischer exact test. Statistical significance at P < .05.

Figure 8. Association of morality with neurovascular event in COVID-19 patient

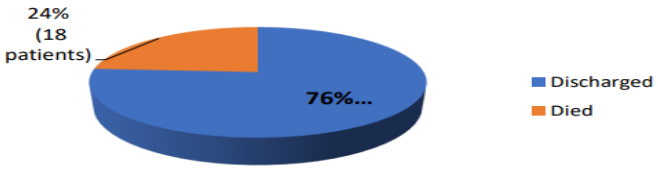


Figure 3. Outcomes of the studied patients after 48 hours

Figure 3. Outcomes of the studied patients shows that about one – quarter of the patients had died where about 76% of them had a recovery and discharged.

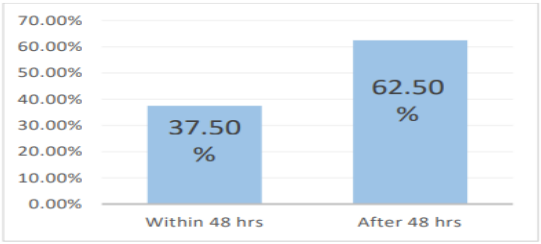
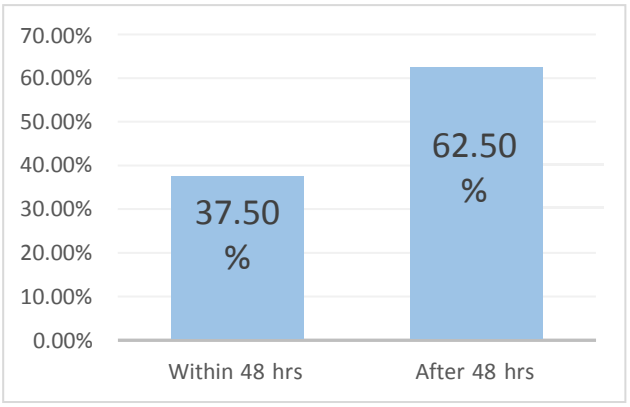


Figure 4. Mortality percentage of the patients with Neurovascular events associated Covid-19 according to time of Death. shows that ~~about~~ 3 patients (37.5%) had died within 48 hrs. of admission while 5 patients (62.5%) had died after 48 hrs. of admission.



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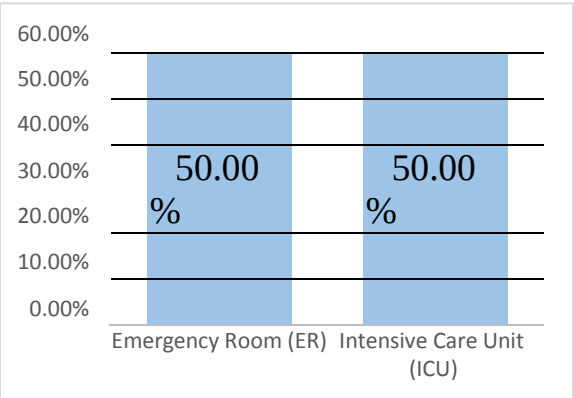

Figure 5 Mortality percentage of the patients with Neurovascular events associated Covid-19 according to Place of Death. shows that 4 out of 8 patients (50%) had died in Emergency Room (ER) at the hospital While 4 out 8 patients (50%) had died in the intensive Care Unit (ICU)

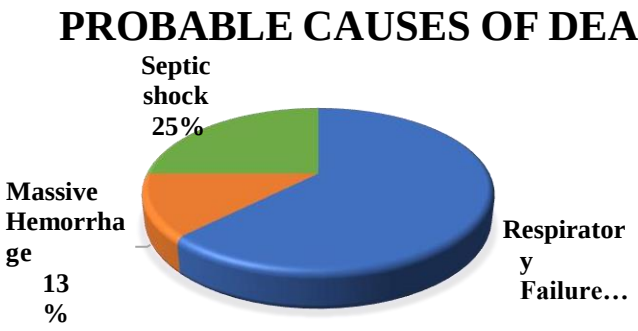

Figure 6. it shows that 25% of patients died duo to septic shock, 13 % died duo to massive hemorrhage and 62 % duo toRespiratory Failure.

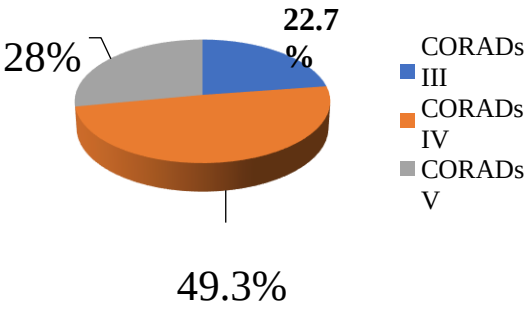

Figure 7. CORADS classifications among the studied sample

Figure 7 shows that about half of the patients had CORAD score IV while 28% of the had CORAD score IV.

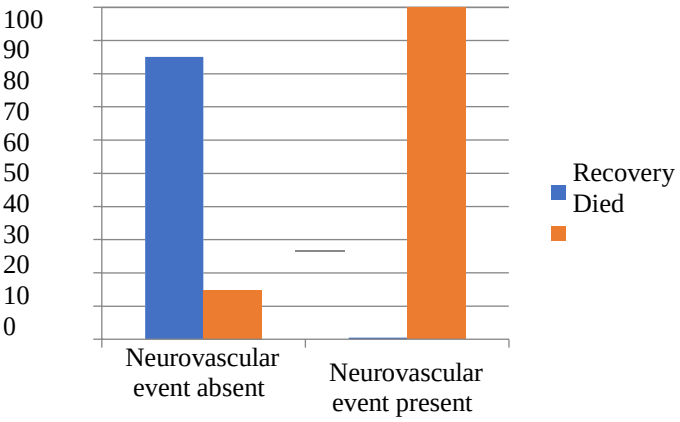

Figure 8. Association of morality with neurovascular event in COVID-19 patient

The present study was designed as a cross sectional study included 75 patients over 18 years of age confirmed COVID - 19 presenting at emergency departments, Suez Canal university hospital and fulfilled our inclusion criteria to be included. This study aimed at detecting the most common pattern of neurovascular events happening in COVID-19 patients and their prevalence.

Table 1 summarizes the baseline characteristics of the studied sample, where males and females were almost equally represented. About two thirds of the sample had chronic illness, where the most prevalent chronic illness was diabetes mellitus (38.7%), hypertension (32%) and ischemic heart disease (21.3%). Moreover, 32% of the patients were smokers. IHD (ischemic heart disease), CKD (chronic kidney disease), CLD (chronic liver disease), AF (atrial fibrillation).

Table 2 summarizes the most common presentations of COVID-19 patients presented to the emergency unit. The most common presentations were cough (94.7%), dyspnea (85.3%) and fever (84%). The mean O_2 saturation was 90 ± 4.23 with range between 66 to 96%. The neurovascular symptoms ranged between decrease of the conscious level (8 patients), limb weakness (4 patients) and one patient with bulging of the eye and surrounding tissue.

Table 3 summarizes the Laboratory measures of the studied sample. the mean total leucocytic count was 11.31 ± 5.91 while the mean lymphocytes were 15.3 ± 9.00. Regarding inflammatory markers, D-dimer ranges between 0.08 to 7.30 ng/mL and the mean CRP was 72.84 ± 69.19 mg/L. Moreover, the mean serum creatinine was1.09 ± 0.70 mg/ dl and the mean LDH level was 415.4 ± 226.4. TLC (total leucocytic count), CRP (C reactive protein), Na (sodium), K(potassium), LDH (lactate dehydrogenase), PT (prothrombin time), INR (international normalized ratio).

Figure 10. Outcomes of the studied patients shows that about one – quarter of the participant patients had died where about 76% of them had a recovery and discharged.

Figure 2 11. Mortality percentage of the patients with Neurovascular events associated Covid-19 according to time of Death. shows that ~~about~~ 3 patients (37.5%) had died within 48 hrs. of admission while 5 patients (62.5%) had died after 48 hrs. of admission.

Figure 4 13 shows the prevalence of neurovascular event among the studied sample was 10% (five ischemic stroke patients, two hemorrhagic stroke patients and one patient with cavernous sinus thrombosis).

Table 4 shows that the median age of COVID-19 patients presented with neurovascular events was 62 with range between 48 to 79 years. Males and females were almost equally represented and half of the patients were smokers. It was found that there is no statistically significant association between baseline characteristics of the studied sample and neurovascular events.

Table 5 shows that the most common presentations of COVID-19 patients presented with neurovascular events were fever, cough and dyspnea. The median O_2 saturation was 89% with range between 66 to 93%. It was found that there is statistically significant association between baseline characteristics of the studied sample and neurovascular events. The neurovascular symptoms ranged between decrease of the conscious level and limb weakness.

Table 6 compares between patients with and without neurovascular event in terms of their laboratory measures. It was found that patients with neurovascular events had statistically significant lower lymphocyte count compared to stroke free patients (p=0.034). On the other hand, patients with neurovascular events had statistically significant higher D-dimer and LDH compared to stroke free patients (p=0.006) and (p=0.002), respectively.

Table 7 shows that the mortality rate of all COVID-19 patients presented with neurovascular events was 100%, whereas only 15% of patients with no neurovascular event had died.

Table 8 shows logistic regression analysis of predictors of neurovascular events among COVID-19 patients. It shows that for every 1000 unit increase in the LDH level satisfaction, the likelihood to have neurovascular events increases by 6% (p=0.032).

DISCUSSION

The present COVID-19 situation has highlighted the importance of determining the pandemic's impact on healthcare. While several research have looked at the relation between COVID-19 and neurological symptoms, the influence of the present pandemic on stroke outcomes has to be looked into more.

As a result, the current cross-sectional study was carried out to evaluate the short-term outcomes of stroke in Egyptian patients diagnosed with COVID-19 and to identify potential determinants of stroke outcomes in the short-term.

Our Study revealed that the occurrence of neurovascular events was almost equal in both genders with males to female's ratio of 48 to 52. With 50 % of male's patients presented with symptoms and signs of Covid- 19 with neurovascular events especially Ischemic stroke as in Table 1. and the median age of covid-19 patients was 62 (25 -82) as in Table 1. And this result in consists with a cross-sectional study conducted by Hidayat et al., 2022 at Indonesia on 26,154 participants. It revealed that the median age of covid- 19 patients was 51 (89-38). Male percentage (61.5%) dominated the percentage of female patients (38.5%) as in Table 1

These results are consistent with the Oliveira et al.,2021 from Florida that found that severe patients were significantly older compared to their matching groups.

Our study revealed that about 32% of the sample size were smoking as in Table 1 which consist with the result of Elsheshiny et al., 2022 on 399 patients who revealed that smoking represents

about 19.5% of the sample size with Covid- 19. The reason of higher percentage in our study may be due to the higher percentage of males.

Our study revealed that the percentage of people had chronic illness was about 61.3% including Diabetes mellitus and Hypertension with prevalence of 38.7 and 32 respectively as in Table 1. which consist with the result of Elsheshiny et al., 2022 in Egypt that their study showed that DM consist of about 41.6% which is a close percentage to our results. Also, HTN in their study was about 46.8% which is a bit higher. Also, with Sylvana et al., 2022 who conduct a prospective observational cohort study in Al fayoum in Egypt on 66 - patients. They revealed that DM was about 21.2% and HTN was 27.3 %

The current study showed that there is a 1.3% had the risk of Atrial fibrillation as in Table 1. these results were in consistent with Elsheshiny et al., 2022 in Egypt who revealed a much higher percentage of about 11.7%. the reason behind this number may be due to the higher sample size they have.

Our study revealed that Cough was the most common symptoms of the Covid-19 patients with a 94.7% of the sample size as in Table 2. Which consists with Sylvana et al., 2022 who also revealed that cough was the most common presentation of

66.7 %. Dyspnea comes second with 85.3 % as in Table 2. Which consists with Sylvana et al., 2022 who also revealed that Dyspnea represents about 51.5%.

Our study showed that among Stroke patients Cough was the common Clinical presentation in about 100% of cases. In contrast to the current work, A Retrospective study carried out by Essmat.2022 at al Azhar- university in Egypt on 100 patients

revealed headache was the most common central CNS manifestation. These findings are in agreement with A cohort multicenter prospective study conducted in Egypt by Mekkawy et al., 2022 on 582 confirmed COVID-19 patients and the study of Agarwal et al.,2020 in Washington State on 404 COVID-19 patients. The reason behind this may be due to excess pro-inflammatory cytokine release, e.g., interleukin 1 (IL 1) and tumor necrosis factor-alpha (TNF-α), which promote trigeminal neural network sensitization, a key event in headache pathology.

However, in the study of Makda et al.,2020 in Pakistan the most common CNS manifestation was dizziness. In a meta- analysis conducted by Favas et al., 2021, the commonest symptom affecting the CNS was headache.

C-reactive protein or CRP serum was discovered to be an essential marker, which might change significantly in severe COVID-19 patients. CRP was a protein produced by the liver, which had a role as an initial marker of infection and inflammation.

we found that the mean of the CRP (mg/L) Level was 72.84 ± 69.19 as in Table 3. which consists with Sylvana et al., 2022 which revealed that CRP (mg/L) level was about 52.13±29.94. Also, a retrospective study in Wuhan on 214 patients with COVID-19 conducted by (Li Y., et al 2020) showed almost the same results. The elevated levels of CRP might be linked to the overproduction of inflammatory cytokines in severe patients with COVID- 19.

SARS-CoV-2 was found to cause CNS symptoms, including cerebrovascular strokes (ischemic, hemorrhagic, and CVST). COVID-19 has been associated with the broad family of cerebrovascular diseases in our study, all three stroke subtypes were detected with a greater preponderance of ischemic types.

The present study revealed that neurovascular events represent about 10.7% which account 10% of the sample size. ischemic stroke represents 6.7%, hemorrhagic stroke 2.7% and cavernous sinus thrombosis 1.3% as in figure 13. these finding was supported by Mao et al., 2020 at the beginning of Wuhan outbreak. Which is also consistent to a study recorded by Munir et al.,2020 who revealed a percentage of 5-5.7% of stroke manifestation. In contrast to a study recorded by Li y et al.,2020 which showed 4,7% ischemic stroke and 0.5% hemorrhagic stroke. Another study revealed by Whittaker et al.,2020 showed prevalence of stroke about of 1.5%, 3% respectively. this may be due to various risk factors as Hypertension, Diabetes mellitus, ischemic heart disease and lipid profile

The occurrence of ischemic stroke among COVID-19 patients could be attributed to the cytokine storm that causes endothelial dysfunction resulting from direct invasion of endothelial cells by the virus, which results from the interaction between the coronavirus S protein and the ACE-2 receptors, expressed in the capillary endothelium.

Endothelial dysfunction increases thrombin synthesis and decreases fibrinolysis, which leads to a hypercoagulable state.

This leads to the high rate of thrombotic complications observed in patients with COVID-19.

But the most significant outcome was the presence of neurovascular events in stroke patients with

100% and statistically significant (P-value of <0.001) which include symptoms like Disturbed level of conscious %10.7%, Motor Weakness 5.3% and bulging of the eye and surrounding tissue 1.3 % as in Table 2. Which in consists with (Essmat.2022) who revealed that headache was the most common neurological symptoms 78% and muscle weakness of 62%

Our Study revealed that about 24% of the patients died and the rest (76%) recovered and discharged with almost 100% mortality rate in Covid- 19 neurovascular patients as in Figure 8. These finding matched those of Mart Fàbregas et al., 2021 who conduct A prospective, observational, multicenter cohort study in Catalonia, Spain. They discovered that patients who had an ischemic stroke linked to COVID-19 had a more severe stroke. In comparison to patients without COVID-19, they reported a 3.1- fold increase in mortality risk within 72-hr of admission.

The significant in-hospital death rate linked with COVID-19 is due to the concomitant respiratory distress and multiorgan failure.

This may due to the category of patient we choose as most of them are COVID-19 grade IV TO V that developed ARDS and also had major neurovascular events like stroke hemorrhage and cavernous sinus thrombosis besides all of those patients intubated and admitted in ICU and some of them died in ER before admission.

Also, some stroke victims avoided obtaining emergency care in hospitals for fear of infection. This explains why there are fewer hospitalized stroke patients. Patients having mild strokes during the COVID phase may be less likely to seek medical care.

Roushdy et al., 2020 studied 93 Egyptian patients with acute ischemic stroke. They found that concern of contracting COVID-19 and a lack of healthcare resources prevented 11 percent of patients from receiving prompt stroke treatment. In this regard, Aref et al., 2021 who conduct A study at two stroke centers in Egypt had reported that in the COVID-19 era, fear of infection and lockdown issues were the most common causes of delayed arrival in ischemic stroke.

Our study showed that patients with neurovascular events have significantly lower lymphocytes count with median range 6 (6-30) than stroke free patients with (p=0.034) as in Table 3. Another case control study done by Elsheshiny et al., 2022 in Egypt on 399 patients revealed correlation between Lymphocytic count 0.86±0.12 with the outcome of the disease.

Our study showed that D- Dimer level in Covid-19 patients with stroke range from (0.8 – 2.3) with P-value of 0.006 as in Table 3. which consist with Sylvana et al., 2022 in Egypt which share a close result of about 0.1-5.0. which consist with Elsheshiny et al., 2022 in Egypt who also showed that there is an association between mean D-Dimer levels (r=0.668, P=0.001). Although, A retrospective study in Wuhan on 214 patients with COVID-19 conducted by Li Y., et al 2020 showed D- Dimer level of 6.9 (0.3–20.0) which is much higher than our study. This be considered as significant predictors for the outcomes of Covid-19 associated Stroke patients.

This could be due to a lack of samples for better understanding the relationship between an increase in d-dimer level and mortality outcome. The high d-dimer was suspected due to the inflammation in COVID-19 infection, which leads to the coagulation cascade. Therefore, the significance of mortality etiology was still inconclusive.

Our Study revealed that LDH level range from (230 -782) with median of 720 and also that for every 1000 unit increase in the LDH level satisfaction, the likelihood to have neurovascular events increases by 6% (p=0.032) as in Table 3. These results in agreement with Sylvana et al., 2022 in Egypt which show that the mean of LDH level was 726.5 ± 488.

Our study revealed that the NIHSS score (range from 0 - 42) of the patients of neurovascular events associated covid-19 was high which correlate with the severity of the disease with mean of 31 ± 7.6. as shown in table 5. With this means our patients not fit for thrombolytic therapy. And patients with cavernous sinus thrombosis and hemorrhagic stroke are contraindicated for thrombolytic therapy. These findings matched those of Mart-Fàbregas et al., 2021. They discovered that patients who had an ischemic stroke linked to COVID-19 had a more severe stroke. In comparison to patients without COVID- 19, they reported a 3.1- fold increase in mortality risk within 72 h of admission.

Our study revealed that about 62% of patients died duo to Respiratory failure followed by 25% duo to septic shock as shown in figure 14. And these results are in agreement with Elsheshiny et al., 2022 in Egypt who also showed that Respiratory failure was the most common cause of death with 5.19% of his patients.

Study Limitations:

This study has some limitations. First of all, Egypt as an undeveloped country had limited medical facilities. Almost all the

medical records are paper sheets. Retrieving

patients' data from the records was extremely difficult.

Shortage of comprehensive diagnostic work-up to identify the pathogenic mechanisms of cerebrovascular diseases.

The limitations of this study included the sample size is small, this is a single center study and may not reflect Egyptian population in general.

The data on vaccination status and its correlation with outcome did not come up with any credible results due to the insufficient data in Egypt as it was newly applied.

Our sample technique used is Convenience sampling method which is a weak method and vulnerable to bias.

There is no specialized unit to deal with covid-19 patients with stroke properly.

CONCLUSION

Neurovascular problems in COVID-19 are an important problem in clinical neurology. The hypercoagulability state might occur when there is a hyperinflammation caused by pathogenic virus. Increased blood cellular component and platelet might occur. A stimulation of coagulation cascade is also observed. Additionally, an increased plasma concentration or viscosity during COVID-19 illness is described.

Our study represents the number of COVID -19 patients with major neurovascular events like ischemic stroke, hemorrhage and cavernous sinus thrombosis with a prevalence of 10 % of COVID -19 patients. Divided into 6% ischemic stroke, 2% hemorrhage and 1% cavernous sinus thrombosis which is similar to the prevalence of stroke in Wuhan, China in pandemic of COVID-19.

In conclusion, we present a case series of a spectrum of major neurovascular events encountered among COVID-19 patients, including those with ischemic and hemorrhagic pathology. Although prognosis appears overall poor, higher initial GCS and lower D-dimer levels may indicate more favorable outcomes, a hypothesis that should be evaluated in future studies.

RECOMMENDATION

Our study shows the association between neurovascular events and COVID-19.

- So, we Recommend more researches to find out the causality between them, the causes of high mortality rate in our center more than other studies and how to improve the prognosis and life styles of patients.
- We recommended that larger comprehensive studies are mandatory to completely understand the association between COVID-19 and acute stroke. Also, to identify the specific pathogenesis of COVID-19 causing neurological manifestations.
- More researches on the efficacy of vaccination on the outcomes of covid-19 associated neurovascular events.
- Design tailored protocols for covid-19 patients with stroke in our hospital.
- More researches after application of stroke with covid protocol to assess the reduction of mortality rate.
- More researches to assess the risk factors of various neurological diseases (DM, HTN, smoking…. etc.) and how to minimize it in EGYPT.

LIST OF ABBREVIATIONS

ACE-1: Angiotensin converting enzyme-
1.**ACE2:** Angiotensin-converting enzyme
2. **COVID-19:** coronavirus disease.
CRP: C-reactive protein.
CVST: cerebral venous sinus thrombosis.
GCS: Glasgow coma scale.
IAT: Intra- arterial therapy.
ICH: Intracerebral hemorrhage.
ICU: Intensive Care Unit.
LDH: lactate dehydrogenase.
MRI: magnetic resonance imaging.
NIHSS: National Institutes of Health Stroke Scale.
SARS-CoV: severe acute respiratory syndrome coronavirus.
TNF: tumor necrosis factor.

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