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NEUROLOGICAL COMPLICATIONS OF COVID-19 INFECTION IN EGYPTIAN POPULATION, A MULTI-CENTER STUDY

By

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ABSTRACT

Background: COVID-19 infection can cause a variety of symptoms, including neurologic symptoms like anosmia, ageusia, or dysgeusia, as well as neurologic complaints like stroke, Guillain-Barre syndrome, encephalopathy, and a variety of others.

Objective: To detect the neurological complications of definite covid-19 infection patients, the relation with the onset and evolution of the infection, and compare these data with probable covid-19 infection patient.

Patients and methods: This were a multi-center observational retrospective – prospective study. Data were obtained from the archived files of the selected Covid-19 patients, in addition to patients admitted at Isolated ICU and inpatient rooms at Al-Azhar Specialized Hospital, Police Hospitals and Arab Contactor Medical Center. The duration of the recruiting period was from February 2021 till August 2021.

Results: Neurological complication was found in 97(33.2%) patients out of 292 covid-19 patients included in our study. Headache was the most prevalent neurological outcome. That present in 44 patients (16.9%). The presence of neurological complications was significantly associated with female gender (25.8 vs 15.9%), presence of comorbidities (40.2 vs 9.2%), hypertension (53.6 vs 20.5%), diabetes mellitus (DM) (44.3 vs 11.3%), HCV (7.2 vs 0.5%), and history of cerebrovascular stroke (CVS) (7 vs 0%). D-dimer, ferritin, C-reactive protein (CRP), platelets, international randomization ratio (INR) were noticeably higher among patients presented with neurological complications comparing to those who have not had any neurological issues. In prediction of stroke, two significant predictors including hypertension and CRP were found. Neurological involvement in Covid-19 patients carried a bad prognostic indication. It was associated with more frequent need for mechanical ventilation and higher risk of mortality. The neurological defects between the suspected and confirmed Covid-19 patients did not show significant differences except in cranial nerves affection that was higher among confirmed cases.

Conclusion: Patients with Covid-19 frequently have neurological symptoms. There was a significant association between the presence of neurological manifestations and mortality.

Keywords: COVID-19 infection, Neurologic, Complication, Mortality, Multi-center.

INTRODUCTION

SARS-CoV-2, an unusual coronavirus outbreak, is wreaking havoc on the world's population's health and, as a result, the worldwide economy. Although Fever, cough, and lethargy are the most prevalent symptoms of COVID-19. Other symptoms of the condition include headache, dyspnea, and diarrhea. In the most serious cases, pneumonia, acute respiratory distress syndrome, and multi-organ failure may occur *Asadi-Pooya and Simani (2020).*

The novel SARS-CoV-2 virus infects cells via the viral structural spike (S) protein, which attaches to the angiotensin converting enzyme 2 (ACE2) receptor and down-regulates ACE-2, resulting in increased synthesis of the vasoconstrictor Ang II and decreased production of the vasodilator angiotensin 1-7. Angiotensin II also acts as a proinflammatory cytokine when it binds to the angiotensin receptor 1. (AT1R). The Ang II – AT1R axis also activates NF-kB and metalloprotease 17, causing the mature form of epidermal growth factor receptor ligands and TNF-a to be produced. Lung alveolar epithelial cells, small intestine enterocytes, vascular endothelial cells, airway epithelia cells, and kidney cells all express the ACE2 receptor. Glial cells, neurons, the cerebral cortex, striatum, posterior hypothalamic area, substantia nigra, paraventricular nucleus, and the brain stem all have ACE2 receptors *(South et al., 2020)*.

Coronaviruses exhibit a number of characteristics in common, including neurotropism. The neurological system might be affected directly by the viruses or indirectly by the stimulation of immune-mediated processes. While the first effect can be seen during the acute phase of the sickness, the second can take days, weeks, or even months to appear after the acute phase has passed. *(Li et al., 2020)* Coronaviruses can infect immune-functioning macrophages, microglia, and astrocytes in the nervous system, causing nerve damage by direct infection (circulatory and neuronal), hypoxia, immunological injury, ACE2 assault, and other methods *(Obaidi et al., 2020)*.

Neurological manifestations were found in 78/214 patients (36.4 %) during the COVID-19 outbreak in Wuhan, China, and were divided into three categories: central nervous system (dizziness, headache, impaired consciousness, acute Cerebrovascular disease, encephalitis, and seizure), cranial and peripheral nervous system (taste impairment, smell impairment). The most prevalent symptoms in seriously impacted patients were stroke, ataxia, seizures, and a low level of awareness *(Mao, 2020)*.

Ischemic strokes believed to be induced by three basic processes in COVID-19: hypercoagulability, vasculitis, and cardiomyopathy with a global reduction in blood flow *(Beyrouti, 2020)*. While the etiology of hemorrhagic strokes in the existence of COVID-19 is unknown, it's likely that SARSCoV-2's affinity for ACE2 receptors, which are located in endothelial and arterial smooth muscle cells in the brain, permits the virus to injure intracranial arteries and burst vessel walls. Furthermore, hemorrhagic strokes may be caused by the cytokine storm that promotes the development of this sickness *(Corad-Artal, 2020)*.

Furthermore, many neurological illnesses (multiple sclerosis, Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy [CIDP], myasthenia) have an immunological etiology and may be aggravated or induced by COVID *Mao (2020)*. For all of these causes, the neurologic community must maintain a watchful eye on any potential neurological manifestations that may occur at the outset, during, or after COVID19.

The present work aimed to detect the neurological complications of definite covid-19 infection patients, and the

relation with the onset and evolution of the infection, and compare these data with probable covid-19 infection patient.

PATIENTS AND METHODS

Multi-center observational retrospective – prospective study, data was attained from the archived files of the selected Covid-19 cases, in addition to patient who was admitted at Isolated ICU and inpatient rooms at Al-Azhar specialized Hospital, Police Hospitals and Arab contactor medical centers. The duration of the recruiting period was from February 2021 to August 2021.

Inclusion criteria: All participants age above 18 years and may be classified into definite covid-19 infection (positive PCR test) and probable covid-19 infection (clinical, laboratory and chest radiology highly suggestive for covid-19 infection).

Exclusion criteria: Patients below 18 years and patients not fulfilling criteria of diagnosis of covid-19 infection.

Ethical issues: Approval was obtained from the ethical committee of the Faculty of Medicine, Al-Azhar University. At the time of the enrolment, written informed consents were obtained from the enrolled patients.

Data collection: I-data related to covid-19 infection: Demographic data including age, sex and BMI, Life style habits, comorbidities, concomitant therapies, clinical characteristics, chest imaging (High resolution thorax CT), laboratory tests for COVID-19 (CBC, CRP, D dimer, serum ferritin, LDH) and outcome of COVID-19 infection.

II-data related to neurological manifestation; Full neurological history, neurological examination, folstein Mini-Mental State examination, neurological imaging: - CT brain, MRI brain. - Neurophysiological assessment and EEG if needed and CSF study if needed.

Statistical analysis: All data were gathered, tabulated and statistically analyzed.

Qualitative data were presented as numbers and percentages and tested for in-between groups difference significance with Chi-square test if its assumptions were met, otherwise Fisher exact test or Monte-Carlo method were performed. Quantitative data were presented as mean ± standard deviation and tested for in-between groups difference significance with t-test assuming normality of the data distribution after confirmation of normality tests, otherwise nonparametric Mann Whitney U test was used.

Logistic regression and discriminant analysis models were built to predict mortality and stroke among Covid-19 patients after ensuring model fitness.

Receiver operating characteristics (ROC) curves were drawn for each predictive logistic regression model, then the area under the ROC curves was tested against the area obtained by chance which equal 0.5.

P-value< 0.05 was considered significant.

Statistical Package for the Social Sciences (SPSS) v 26 was used.

RESULTS

The study comprised 292 hospitalized individuals who had been diagnosed with covid-19. (263 males + 56 females). Ninety-seven patients had neurological abnormalities (33.2%). The most common neurological outcome was headache, with 44 patients reporting it (16.9%). This headache was usually characterized by bilateral frontal moderate to severe headache.

The presence of neurological complications was significantly associated with female gender (25.8 vs 15.9%), presence of comorbidities (40.2 vs 9.2%), hypertension (53.6 vs 20.5%), DM (44.3 vs 11.3%), HCV (7.2 vs 0.5%), and history of CVS (7 vs 0%). Patients with neurological manifestations were older than those without neurological affection **(Table 1)**.

Table (1): Demographic data and baseline factors of the patients

Groups / Parameters	No neurological manifestations (n = 195)		Neurological manifestations (n = 97)		P-value
	Number	66.8%	Number	33.2%	
Sex					
Female	31	15.9	25	25.8	0.04
Male	164	84.1	72	74.2	
Comorbidities any					
No	177	90.8	58	59.8	< 0.01
Yes	18	9.2	39	40.2	
Hypertension					
No	155	79.5	45	46.4	< 0.01
Yes	40	20.5	52	53.6	
DM					
No	173	88.7	54	55.7	< 0.01
Yes	22	11.3	43	44.3	
Smoking					
No	157	80.5	70	72.2	0.11
Yes	38	19.5	27	27.8	
Atrial fibrillation					
No	193	99	93	95.9	0.08
Yes	2	1	4	4.1	
Dyslipidemia					
No	195	100	95	97.9	0.11
Yes	0	0	2	2.1	
HCV					
No	194	99.5	90	92.8	< 0.01
Yes	1	0.5	7	7.2	
Ischemic heart disease					
No	188	96.4	90	92.8	0.17
Yes	7	3.6	7	7.2	
Chronic Kidney disease					
No	191	97.9	91	93.8	0.09
Yes	4	2.1	6	6.2	
History of Cerebrovascular stroke					
No	195	100	90	92.8	< 0.01
Yes	0	0	7	7.2	
PCR test for covid-19					
Positive	167	85.6	81	83.5	0.63
Negative	28	14.4	16	16.5	

D-dimer, ferritin, CRP, platelets, when comparing covid-19 patients were with neurological difficulties to covid-19 patients without neurological complications. INR were considerably higher **(Table 2)**.

Table (2): Demographic data and baseline factors of the patients

Groups / Parameters	No neurological manifestations (n = 195)		Neurological manifestations (n = 97)			P-value
	Mean	SD	Mean	SD		
Age	55.26	11.004	56.55	13.472	0.87	0.37*
Onset	.	.	12.85	12.795		
INR	1.033	0.1049	1.066	0.104	2.5	0.016*
WBCS	10.617	3.9042	10.11	4.2569	1.01	0.714
D-dimer	1576.4125	2507.57749	3145.3196	2872.08674	**5.22**	**0.0001¥**
CRP	134.749	110.1059	169.006	108.0263	**2.87**	**0.004¥**
Lymphocytes	20.7849	13.22456	17.7434	13.81826	**2.07**	0.037¥
Platelets	171.72	86.203	193.56	88.993	**2.74**	0.06¥
SPO2	78.53	9.452	77.66	9.382	0.74	0.45
Ferritin	514.20	817.780	1013.42	1138.695	**5.74**	0.0001¥

Independent samples t-test was used to compare between the two groups assuming normality of the variables' distribution. ¥: Mann Whitney U test was used assuming the distribution was not normal.

The reported neurological manifestations included headache in 44 patients (16.5%), taste impairment in 22 patients (8.27%), smell impairment in 22 patients (8.27%). Besides the headache, trigeminal neuralgia was detected in 6 patients (2.3%). Seizures occurred in 13 patients (4.9%), 7 of those patients (2.6%) were generalized Tonic-Clonic seizures, three patients (1%) with focal seizures, and 3 patients (1%) with focal to generalized seizures. Cranial nerve affection in 23 patients (8.7%), trigeminal nerve was the most common affected cranial nerve 6 (2.26%). speech abnormalities in 18 patients (6.8%). Thirteen of those patients with dysarthria (4.9%) and 5 presents with dysphasia (1.9%). Cerebrovascular disease (CVD) was found in 26 patients (9.7%), 20 patients with arterial infarction (7.5%), 4 patients were evaluated as hemorrhagic CVD (1.5%), and 2 as venous infarction (0.8%). Guillain-Barre syndrome present in 7 patients (2.6%). CNS infection present in 13 patients (4.9%). six of those patients were evaluated as viral infection (2.1%), 3 patients with bacterial infection (1.1%), and four patients with fungal infection (1.5%) **(Table 3)**.

Table (3): Covid-19 individuals have a wide range of neurological symptoms

Neurological complications	Frequency (total = 266)	Percentage
Headache	44	16.54
Anosmia	22	8.27
Loss of taste	22	8.27
Cranial nerve affection	23	8.65
Limb weakness	30	11.28
Meningeal irritation	4	1.50
Encephalitis	8	3.01
DCL	25	9.40
Seizure	13	4.89
Sensory affection	14	5.26
Abnormal speech	18	6.77
Muscle pain	14	5.26
Guillain-Barre syndrome	7	2.63
pain with eye movement	4	1.50
Visual deficit	11	4.14
trigeminal neuralgia	6	2.26

The neurological defects outcomes between suspected and confirmed Covid-19 patients did not show significant differences, except cranial nerve affection that was higher among confirmed cases. The patients with confirmed Covid-19 infection had higher platelets and ferritin, than suspected cases **(Table 4)**.

Table (4): Neurological defects among suspected and confirmed Covid-19 patients.

Groups / Parameters	Suspected (n = 44)		Confirmed (n = 248)		P-value
	Number	15.1%	Number	84.9%	
Outcomes					
Death	2	4.5	20	8.1	0.55
Discharge	42	95.5	228	91.9	
Acute stroke					
No	42	95.5	230	92.7	0.75
Yes	2	4.4	18	7.3	
Headache					
No	37	84.1	211	85.1	0.87
Yes	7	15.9	37	14.9	
Anosmia					
No	38	86.4	232	93.5	0.87
Yes	6	13.6	16	6.5	
Encephalitis					
No	43	97.7	241	97.2	1.00
Yes	1	2.3	7	2.8	
Cranial nerve affection					
No	43	97.7	241	97.2	0.22
Yes	1	2.3	22	8.9	
Limb weakness					
No	41	93.2	221	89.1	0.59
Yes	3	6.8	27	10.9	
Meningeal irritation					
No	44	100	244	98.4	1.00
Yes	0	0.00	4	1.6	
Seizure					
No	42	95.5	238	96	0.7
Yes	2	4.4	10	4	
DCL					
No	40	90.9	225	90.7	1.00
Yes	4	9.1	23	9.3	
Muscle pain					
No	41	93.2	236	95.2	0.48
Yes	3	6.8	12	4.8	
Guillain-Barre syndrome					
No	43	97.7	242	97.6	1.00
Yes	1	2.3	6	2.4	
Pain with eye movement					
No	43	97.7	245	98.8	0.48
Yes	1	2.3	3	1.2	
Visual defect					
No	43	97.7	240	96.8	1.00
Yes	1	2.3	8	3.2	
Trigeminal neuralgia					
No	44	100	242	97.6	0.6
Yes	0	0.00	6	2.4	
Sensory defect					
No	41	93.2	237	95.6	0.45
Yes	3	6.8	11	4.4	
Abnormal speech					
No	42	95.5	232	93.5	1.00
Yes	2	4.5	16	6.5	

In the regression model, we found two significant predictors including hypertension and CRP after adjusting for all predictors of the model. Hypertensive patients were 2.8 times more likely to get acute ischemic stroke after Covid-19 infection compared to normotensive patients. Additionally, for every one-point increase in CRP, the odds of stroke increased by 0.4% **(Table 5)**.

Table (5): Prediction of stroke among Covid-19 patients (suspected and confirmed) using logistic regression model

	B	S.E.	Sig.	Adjusted OR
PCR	-0.484	0.671	0.47	0.616
CRP	0.004	0.002	0.035	1.004
SpO2	0.058	0.035	0.098	1.059
Age	0.003	0.023	0.913	1.003
Hypertension	1.035	0.523	0.048	2.815
Ferritin	0	0	0.76	1
D-dimer	0	0	0.635	1
Lymphocytes	-0.001	0.02	0.955	0.999
WBCs	0.017	0.062	0.779	1.017
Platelets	-0.005	0.004	0.204	0.995
Constant	-7.242	3.517	0.039	0.001

In comparison between outcome of covid-19 patients with neurological complications and without neurological complications, we found that 40% of patients with neurological complications have died, while only 12% of patients without neurological complications have died.

DISCUSSION

Although SARS-CoV-2 is primarily a respiratory virus that causes pneumonia, it also affects the nervous system, severe cases are likely to result in multi-organ dysfunction and failure. Coronaviruses have been shown to infect brain tissue, according to new research, causing a variety of neurological symptoms and problems *(Pleasure et al., 2020)*.

The primary goal of this study was to describe any neurological complications seen by definite covid-19 infection patients, as well as their relationship to the beginning and progression of the illness, and to compare these findings to those experienced by probable covid-19 infection patients. The recruiting phase lasted for six months.

Neurological symptoms in hospitalized COVID-19 patients were assessed in this retrospective – prospective investigation. Ninety-seven patients out of 292 were found to have neurological involvement (33.2%). CNS, PNS, and skeletal muscles were among the neurological symptoms. The most prevalent usual symptom was headache (16.5%).

Our results showed that the presence of neurological complications was significantly associated with female gender, presence of comorbidities, hypertension, DM, HCV, and history of CVS. Patients with neurological manifestations were older than those without neurological affection. In agreement with the study of *Essmat (2021),* it has been shown that patients

with neurological affection were significantly older. In addition, they had significantly higher frequency of previous pulmonary morbidities. However, in the study of (Romagnolo et al., 2020) they noted that Covid-19 patients with neurological disorders are significantly older than those without neurological affection.

The present study showed that headache is the most common symptom that present in 16.5%, taste impairment in 8.2%, smell impairment in 8.2%, trigeminal neuralgia was detected in 2.3%, seizures occurred in 4.9%, cranial nerve affection in 8.7%, speech abnormalities in 6,8%, cerebrovascular disease (CVD) in 9.7%. four of those patients were evaluated as hemorrhagic CVD (1.5%), and 2 as venous infarction (0.8%). Guillain-Barre syndrome present in 1.5%, CNS infection present in 4.5%, (6 were evaluated as viral infection 2.1%, 1% patients with bacterial infection and 1.4% with fungal infection). However, in the study of *Yassin et al. (2021),* myalgia was in 22.2%, a problem with taste 19.6%, a problem with odor 18.3%, headache 12.1%, dizziness 11.3%, encephalopathy or cognitive dysfunction 9.4%, and ataxia or abnormal gait 2.1%. Nearly, 2.5% of COVID-19 patients had acute cerebrovascular diseases (CVD); which included ischemic stroke (IS), intracerebral hemorrhage (ICH), and cerebral venous sinus thrombosis (CVT).

In our study, headache the most common CNS manifestation. Taste and smell impairment were the most common manifestations affecting PNS. The severity of headache was reported to be moderate to severe. Headaches were reported to have tension-type quality and mostly located in the forehead region. Present on average, 2 days from onset of covid-19 symptoms. In the study of *Essmat (2021),* headache was the most common central CNS manifestation while smell and taste impairment were the commonest manifestations affecting the peripheral nervous system (PNS). These findings were in agreement with the study of *Agarwal et al. (2020)*. However, in the study of *Makda et al. (2020)*, the most common CNS manifestation was dizziness. In one meta-analysis, the commonest symptom affecting the CNS was headache while the commonest symptoms affecting the PNS was smell disturbance in agreement with our conclusions *(Bolay et al., 2020)*. The prevalence of anosmia and ageusia varies greatly between research, ranging from 5% in a China *(Mao et al., 2020)*, to over 80% in an Italian study *(Lee et al., 2020)*. Anosmia was found to be more common in females, younger patients, and those who were not hospitalized in multiple investigations. Anosmia cleared up on its own in most cases within 3 weeks, according to *(Lechien and Chiesa-Estomba, 2020)*.

Several possible underlying pathophysiological mechanisms have been proposed, particularly for headaches in the forehead and periorbital regions; one possibility is that SARS-CoV-2 has infected the trigeminal nerve terminals in the nasal cavity directly. The participation of endothelial cells of the artery walls with high expression of angiotensin-converting enzyme 2 is another potential underlying mechanism for trigemino-vascular activation (ACE2). The release of pro-inflammatory mediators and cytokines

during COVID-19, according to a third theory, may stimulate perivascular trigeminal nerve ends, causing headache *(Khatoon et al., 2020)*.

Cerebrovascular disease (CVD) was discovered in 26 participants in our investigation (9.7 percent). Four of these patients were diagnosed with hemorrhagic CVD (1.5%) and two with venous infarction (0.8 percent). According to recent research, venous and arterial thromboembolic consequences occur in 5–15 percent of patients with severe COVID-19 during the present pandemic *(Speeckaert et al., 2020)*. On average, 10 days after the onset of covid-19 symptoms, this symptom appears. The reason could be a combination of low-grade DIC and a localized pulmonary thrombotic micro-angiopathy. A considerable rise in D-dimers, elevated fibrinogen levels, mildly prolonged prothrombin time, and slight thrombocytopenia are all symptoms of COVID-19 coagulopathy. Furthermore, patients with COVID-19 have a transitory increase in antiphospholipid antibodies, which could play a role in thrombosis pathogenesis. Another probable cause is cytokine storm, which occurs frequently in COVID-19 patients who are extremely unwell. It inhibits anticoagulant pathways and causes the release of von Willebrand factor, which can lead to thrombosis in these patients *(Yaghi et al., 2020)*.

In our study, CNS infection present in 4.5%. Symptoms of viral encephalitis started to appear on average 7 days from onset of covid-19 symptoms. Two virus entry routes have been proposed: the first was through the trigeminal and olfactory nerve terminals. The enhanced FLAIR signal in the medial temporal lobe could be explained by infiltration through the olfactory system. Furthermore, signal alterations in the brainstem and thalamus could indicate a central invasion via the trigeminal system *(Virhammar, 2020)*. Increased permeability of the Blood Brain Barrier (BBB) due to high levels of pro-inflammatory cytokines in the CSF could be the second route of viral invasion *(Poyiadji and Colleagues, 2020)*.

Seizures occurred in 4.9%. Seizures usually started on average 12 days from onset of covid-19 symptoms. However, *Essmat (2021)* stated that, the frequency of seizures was 18% of patients with neurological affection. Infections of the central nervous system (CNS) and subsequent activation of neuro-inflammatory pathways have been shown to lower the seizure threshold and perhaps facilitate epileptogenesis in some people *(Elgamasy et al. 2020)*. Furthermore, the increase of inflammatory markers linked to SARS-CoV-2 infection could result in local cortical irritation, which could lead to seizures *(Hepburn et al., 2020)*.

In our study, Guillain-Barre syndrome present in 2.3%. Patients were diagnosed as Guillain-Barre Syndrome (GBS) on average 3 weeks after discharging with COVID-19 and re hospitalized. The possible framework is molecular mimicry, in which the pathogen has epitopes that are identical to those found in peripheral nerve components. Antibodies generated by the host immune system to resist the virus cross-react with peripheral nerves, resulting in neuronal dysfunction *(Zubair et al., 2020)*.

In the trying to predict all possible predictors of death among the Covid-19

patients. The regression model found three significant predictors including SpO2, hypertension, and d-dimer after adjusting for all predictors of the model. Hypertensive patients were 4.45 times more likely to die after Covid-19 infection compared to normotensive patients. Additionally, for every one-point decrease in oxygen saturation, the odds of death increased by 5%. Neurological involvement in Covid-19 patients carries a bad prognostic indication. It was associated with more frequent need of mechanical ventilation and higher risk of mortality *(Shekhar et al., 2020)*.

In the trying to predict all possible predictors of stroke among the Covid-19 patients, a multivariate binary logistic regression model found two significant predictors including hypertension and CRP after adjusting for all predictors of the model. Hypertensive patients were 2.8 times more likely to get acute ischemic stroke after Covid-19 infection compared to normotensive patients. Additionally, for every one-point increase in CRP, the odds of stroke increased by 0.4%. However, *Essmat's study (2021)* stated that the existence of neurological signs was found to be an independent predictor of mortality in the individuals investigated. *(Jain et al., 2020)* found a link between neurological symptoms and poor outcome in Covid-19 patients. *Chua et al. (2020)* identified the existence of neurological symptoms as a negative prognostic factor in Covid-19 patients in their systematic review and meta-analysis.

According to *Dorjee et al. (2020)*, the overall prevalence of death [percentage (95 percent confidence interval)] from COVID-19 was 20% in the United States and Europe, and 23% in China. 85 percent of individuals who died were over 60 years old, 66 percent were men, and 66 percent, 44 percent, 39 percent, 37 percent, and 27 percent, respectively, had hypertension, smoking history, diabetes, heart disease, and chronic kidney disease (CKD). all had increased sRRs of death. The prevalence of hypertension (55 percent), diabetes (33 percent), smoking history (23 percent), and heart disease (17 percent) among COVID-19 hospitalized patients in the United States was significantly higher than that of the general US population, implying that those with comorbidities are more susceptible to infection or disease progression.

Furthermore, *Khamis et al. (2021)* indicated that the multivariable logistic regression demonstrated that in-hospital mortality in admitted COVID-19 patients was associated with old age, heart diseases, liver diseases, those with higher ferritin levels, acute respiratory distress syndrome (ARDS), sepsis, and those that had ICU admission.

The neurological defects between the suspected and confirmed Covid-19 patients did not show significant differences except in cranial nerves affection that was higher in confirmed cases.

CONCLUSION

Neurological manifestations were communal in Covid-19 patients, with a significant relationship between the presence of neurological manifestations and mortality.

CONSENT FOR PUBLICATION

I confirm that all authors accept the manuscript for submission.

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المضاعفات العصبية لعدوى كوفيد -19 في مصر، دراسة متعددة المراكز

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خلفيه البحث: يمكن أن تسبب عدوى كوفيد 19 مجموعة متنوعة من الأعراض، بما في ذلك الأعراض العصبية مثل فقدان حاسة الشم، أو تقدم العمر، أو خلل الذوق، بالإضافة إلى شكاوى عصبية مثل السكتة الدماغية ومتلازمة غيلان باريه والاعتلال الدماغي وغيرها.

الهدف من البحث: إظهار أي مضاعفات عصبية لمرضى مصابين بفيروس كوفيد -19، وعلاقتها بظهور العدوى وتطورها، ثم مقارنة هذه البيانات مع مرضى مصابين بفيروس كوفيد -19 محتملين.

المرضى وطرق البحث: كانت هذه الدراسه بأثر رجعي متعدد المراكز - دراسة استباقية، تم الحصول على البيانات من الملفات المؤرشفة لمرضى كوفيد 19 المختارين، بالإضافة إلى المريض الذي تم قبوله في وحدة العناية المركزة المعزولة وغرف المرضى الداخليين في مستشفى الأزهر التخصصي ومستشفيات الشرطة والمقاولون العرب الطبي المراكز. كانت مدة الدراسه ستة أشهر.

نتائج البحث: تم العثور على المضاعفات العصبية في 97 (33.2٪) مريضاً من أصل 292 مريضاً بفيروس كوفيد -19 مشمولين في دراستنا. كان الصداع أكثر النتائج العصبية انتشارًا، حيث ظهر في 44 مريضًا (16.9٪).

ارتبط وجود المضاعفات العصبية بشكل كبير بالجنس الأنثوي (25.8 مقابل 15.9٪)، وجود أمراض مصاحبة (40.2 مقابل 9.2٪)، ارتفاع ضغط الدم (53.6 مقابل 20.5٪)، الداء السكري ((44.3 مقابل 11.3٪)، التهاب الكبد سي (7.2 مقابل 0.5٪)، وتاريخ CVS (7 مقابل0٪).

كان دي دايمر و فيريتين و البروتين التفاعلي سي والصفائح الدموية و معامل السيوله أعلى بشكل ملحوظ بين المرضى الذين يعانون من مضاعفات عصبية مقارنة بأولئك الذين لم يكن لديهم أي مشاكل عصبية. في التنبؤ بالسكتة الدماغية، وجدنا اثنين من المتنبئين المهمين بما في ذلك ارتفاع ضغط الدم و البروتين التفاعلي سي.

يحمل التأثر العصبي في مرضى كوفيد 19 مؤشرًا إنذاريًا سيئًا. كان مرتبطًا بالحاجة المتكررة للتهوية الميكانيكية وارتفاع مخاطر الوفاة.

لم تظهر العيوب العصبية بين مرضى كوفيد 19 المشتبه بهم والمؤكدين فرقًا معنويًا باستثناء إصابة الأعصاب القحفية التي كانت أعلى بين الحالات المؤكدة.

الاستنتاج: مرضى كوفيد -19 يعانون من أعراض عصبية بشكل متكرر، وهناك ارتباط كبير بين وجود المظاهر العصبية والوفيات.

الكلمات الدالة: عدوى كوفيد-19، عصبيه، مضاعافات، الوفيات، متعدد المراكز.