Neurological Manifestations of Hospitalized Patients with COVID-19 in Al-Imamain Al-Khadmain Medical City

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ABSTRACT

Background: In late 2019 many not-explained pneumonia cases observed in Wuhan, China. This outburst found to be caused by a novel-coronavirus (2019-nCoV). In COVID-19 patients, neurological manifestations such as impaired consciousness and stroke have been reported.

Objectives: To demonstrate the neurological manifestations of patients with COVID-19.

Method: This is a retrospective case series study performed at the COVID-19 isolation unit of Al-Imamain Al-Kadhimain Medical City throughout June-2020 to September-2020, 72 cases were selected. Severe group defined by CURB-65 ≥3 and were on CPAP. Neurological symptoms categorized into: central nervous system symptoms, peripheral nervous system symptoms and muscular symptoms.

Results: The average age was 60.9 ±11.7 years. Males were more in the severe group (*P*=0.008). Sixty-two (86.1%) patients had nervous system symptoms: Central nervous symptoms 58 (80.6%), peripheral nervous symptoms 45(62.5%) and skeletal muscles 39(54.2%). In central nervous symptoms, the most common complaints were headache 39 (54.2%). In peripheral nervous symptoms, the most common complaints were hypogeusia 41(56.9%). Forty-one (56.9%) patients had severe infection.

Conclusions: Neurological manifestation are common in patients with COVID-19 infection. Impaired consciousness was significant in severe COVID-19 patients. Stroke occurred with same significance in both non-severe and severe COVID-19 patients.

Keywords: COVID-19, Viral, Neurological.

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In the past two decades, there were three major highly pathogenic zoonotic outbreaks of beta coronaviruses[1-3]. The first was Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) in 2002, which infected over 8,000 people and killed 800. This was followed in 2012 by Middle East Respiratory Syndrome, MERS-CoV, a difficult to transmit but highly lethal virus, with 2,294 cases in 2019, with 35% mortality[1]. The third, SARS-CoV-2 is the cause of the severe respiratory disease COVID-19.

Three related factors combine to make this disease so dangerous: human beings have no direct immunological experience with this virus, leaving us vulnerable to infection and disease; it is highly transmissible; and it has a high mortality rate. The SARS-CoV-2 virus binds to the angiotensin-converting enzyme 2 (ACE2) via its spike (S) protein[1]. Transmembrane protein serineprotease 2 (TMPRSS2) is also required for viral entry into cells[4]. Similarly, the virus that caused the SARS pandemic in 2003, SARS-CoV-1, also binds to ACE2[5, 6]. ACE2 is a dipeptidyl carboxydipeptidase, a homologue of angiotensin-converting enzyme 1 (ACE1), and part of the renin angiotensin system (RAS). The ACE-2 receptor expression has recently been found on neurons and glial cells of several brain structures, including the cerebral cortex, the striatum, the posterior hypothalamic area, the substantia

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nigra, and brain stem[7,8]. Several mechanisms such as the transcribial route[9], the axonal transport and trans-synaptic transfer[10,11], and the hematogenous and/or lymphatic route[12] are currently discussed as possible viral access routes to the brain.

The aim of this study is to demonstrate the neurological manifestations of patients with (COVID-19).

Methods

This is a retrospective case series study that performed at the COVID-19 isolation unit of Al-Imamain Al-Kadhimain Medical City throughout the period from June 11, 2020 to September 15, 2020 over 3 months.

Seventy five patients, with a diagnosis of COVID-19 that based on clinical features, physical examination and positive RT-PCR. Only 72 cases were eligible for criteria of the study. Any new COVID-19 patient who confirmed by positive RT-PCR was enrolled in the study.

The study defines the exclusion criteria as the following:

1- Metabolic encephalopathy.
2- Presence of space occupying lesions.

All patients with COVID-19 enlisted in this research were diagnosed with agreement to the WHO interim guidelines. Only those cases proved by a positive-test to real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay from throat swab samples were included in the analysis[13]. All data represented by mean, value and frequency using demographical data, patients' clinical presentation, medical history, symptoms, clinical signs, laboratories findings, chest computed-tomographics (CT) findings were included from medical-records. Neurological symptoms were sorted out into three main areas: central-nervous system (CNS) symptoms or disease, peripheral-nervous system (PNS) symptoms and muscular symptoms. Acute cerebro-vascular insult included ischemic stroke and intra-cranial haemorrhage showed by CT-head. The date of disease onset was defined as the day when the disease clinical-features were noticed. The severity of COVID-19 was defined by the international guidelines for community-acquired pneumonia (CURB-65) [14]. Non-severe group defined by CURB-65 score ≤ 2 and not on CPAP, while severe group defined by CURB-65 ≥ 3 and were on CPAP. SARS-CoV-2 was guaranteed by real-time RT-PCR assay using SARS-CoV-2 nucleic acid detection material (PCR-fluorescent probe process, Zybio-Inc.) according to the manufacturer's protocol. Purpose of the study was carefully explained to the patients and oral informed consent obtained.

Results

A total of 72 hospitalized-patients with confirmed SARS-CoV-2 infection were encompassed in the present survey. Their average age was 60.9 ±11.7 years, and 47 (65.2%) were males, female were 25 (34.7%), *P* =0.01. Of these patients, who have underlying disorders was 52 (72.2%) and those without known risk factors was 20 (27.8%), *P*<0.001, 52 (72.2%) had at least one of the following underlying disorders: hypertension 35 (48.6%), diabetes 24 (33.3%), cardiovascular disease 15 (20.8%), malignancy 1 (1.4%), chronic renal failure 1 (1.4%), asthma 1 (1.4%) and epilepsy 1 (1.4%). Sixty-two (86.1%) patients had nervous system symptoms: CNS 58 (80.6%), PNS 45 (62.5%) and skeletal muscles 39 (54.2%). In patients with CNS symptoms, the most common complaints were headache 39 (54.2%) and dizziness 34 (47.2%). In patients with PNS symptoms, the most common complaints were hypogeusia 41 (56.9%) and hyposmia 30 (41.7%). According to the diagnostic criteria, 41 (56.9%) patients had severe and 31 (43.1%) patients had non-severe disease. The severe infection were found relatively in males (males = 29 vs. females = 12; *P*=0.008) and significantly older (65.2 ± 11.2 years vs. 55.1 ± 9.7 years; *P*<0.001), (Table 1).

The most common CNS presenting feature were headache in 39 (54.2%)

cases, followed by dizziness with 34 (47.2%) cases, then impaired consciousness 22 (30.6%) cases, and finally stroke 5 (6.9%) cases. In comparison between non-severe and severe COVID-19 patients, headache was 17 in non-severe group and 22 in severe group (p value was 0.92), dizziness was in non-severe group 15 and 19 in severe group p value was 0.86, impaired consciousness (DOC) was 2 in non-severe group and 20 in severe group p value was <0.001, stroke was 2 in non-severe group and 3 in severe group p value 0.88. The PNS symptoms include hypoguesia was the most frequent 41 (56.9%) patients followed by hyposomia in 30 (41.7%) patients, no difference between non-severe and severe COVID-19 patients regarding hypoguesia which was 19 in non-severe group and 22 in severe group p value 0.51. Hyposomia was 16 in non-severe group and 14 in severe group p value 0.1. Myalgia was found in 39 (54.2%), in non-severe group was 16 and in severe group was 23 no difference between the two groups p value 0.7, (Table 2).

Table 1: Baseline characteristics of the study populations.

Variables		Non-severe (n=31)	Severe (n=41)	p-value
Age, years (Mean ±SD)		55.1 ± 9.7	65.2 ± 11.2	**<0.001**
Sex (male 47/72 (65.2%) vs. female 25/72 (34.7%) , *P* =0.01)				
Risk factors no risk factors 20 (27.8%) vs. risk factors 52 (72.2%), *P*<0.001)	Hypertension No Yes	 15(48.4%) 16(51.6%)	 22(53.7%) 19(46.3%)	 **0.65**
	Diabetes mellitus No Yes	 22(71%) 9(29%)	 26(63.4%) 15(36.6%)	 **0.5**
	Ischemic cardiac disease No Yes	 26(83.9%) 5(16.1%)	 31(75.6%) 10(24.4%)	 0.39
	Who had risk factors	23(31.9)	29(40.2%)	0.7

Table 2: Relationship of neurological symptoms in non-severe and severe groups.

Variables	Non-severe (n=31)	Severe (n=41)	p-value
Headache	17	22	**0.9**
Dizziness	15	19	**0.8**
DOC	2	22	**<0.001**
Stroke	2	3	**0.8**
Hypoguesia Hyposomia	19 16	22 14	**0.5** **0.1**
Myalgia	16	23	**0.7**

Discussion

The mean age of patients with COVID-19 was 60.9 years, the mean for non-severe group was 55.1 years and for severe group 65.2 years. Older patients were more susceptible to have severe COVID-19 (p value < 0.001). This comes in agreement with L Mao et al, 2019[15].

Male gender was predominantly affected with COVID-19 incidence in this study and were more in the severe group. This was the same in a study of 425 patients with COVID-19 indicated that 56% were males[16]. Another study of 140 patients found that 50.7% were males[17]. A study performed in Baghdad, Iraq on 2111 patients[18] showed more male patients suffered from more severe manifestations and needed ICU admission, and non-invasive ventilation therapy while females had a lower case fatality rate than males. The severity in male group may be due to circulating ACE2 levels are higher in men than in women and in patients with diabetes or cardiovascular diseases[19].

Patients with COVID-19 infection tend to have at least one risk factors. Of our patients, who have underlying disorders were 52 out of 72 and without known risk factors were 20. This came in agreement with analysis of 1558 samples from 6 retrospective studies that were performed in China[20]. Among the most common precipitating factors in this study were hypertension, diabetes and ischemic heart disease. This goes with the agreement of L Mao et al, 2019 regarding diabetes mellitus (14%) and ischemic heart disease (7%) with no difference between the non-severe and severe group[15].

The most common presenting features were headache, followed by dizziness, then impaired consciousness, and finally stroke.

Headache was assessed in 51 studies, involving 16,446 COVID-19 patients. Of these, headache was reported in 20.1% of the population studied, ranging from 2.0[21] to 66.1%[22]. Dizziness was inquired into 13 surveys, of about 2236 COVID-19 patients. In approximate 7.0% (ranging from 2.5[23] to 21.4%[24]) of the COVID-19 patients were reported to have endured to dizziness, evenly reported among mild or moderate side by side with severe or critical cases.

Nine studies, with 2890 patients, reported impairment of consciousness (also titled “confusion” or “agitation”) in 5.1% of COVID-19 patients, extending from 1.4[25] to 69.0%[26] of the patients. As anticipated, impaired-consciousness was considered more repeatedly in severe or critical in comparison with mild or moderate COVID-19.

Two patients had stroke in non-severe group and 3 in severe group. Three of the stroke patients were ischemic stroke involve the MCA territory (one patient in non-severe group and 2 in severe group), two patients had haemorrhagic stroke (1 in non-severe group and 1 in severe group), 7.6-fold increase in the odds of stroke with COVID-19 compared with influenza was recently reported[27]. Three main mechanisms appear to be responsible for the occurrence of ischemic strokes in COVID-19. These entail a hypercoagulation-state, vasculitis, and cardiomyopathic diseases[28].

Hypoguesia was the most frequent followed by hyposomia, no difference between non-severe and severe COVID-19 patients. A multicenter-European study of 417 mild-to-moderate COVID-19 patients finalised the study 85.6% and 88.0% of patients showed olfactory and gustatory dysfunctions, respectively[29].

Myalgia clinical features of 1487 COVID-19 patients with out-patient management accomplished in Paris-France reviewed myalgia and body-aches 57%[30].

In conclusion; neurological manifestations are relatively common in patients with COVID-19 infection. Impaired consciousness was more significant to occur in severe COVID-19 patients, while stroke can occur with same significance in both non-severe and severe COVID-19 patients.

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