

SEIZURES IN CORONAVIRUS DISEASE-2019 IN THAILAND: CASE SERIES SURVEY

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Abstract. Medical services have been affected worldwide since the outbreak of COVID-19 pandemic. A number of patients with COVID-19 develop neurological manifestations, such as stroke, encephalopathy and seizures. In order to determine the relationship between COVID-19 and seizure disorders, a review of case series from 1 December 2019 to 7 July 2020 from seven hospitals in Thailand, which adequately detailed seizure occurrence or neurological manifestations, was carried out. Focus was placed on relationship of seizure/epilepsy and risk of COVID-19 infection, possible epileptogenic effects of the viral infection and management plans for control of seizures. Prevalence of acute symptomatic seizures among COVID-19 patients was 0.57%, indicating epilepsy patients in general were not more susceptible to COVID-19 infection. Issues on adverse interactions between antiepileptic drugs and antivirals, limited access to investigative diagnostic procedures, *eg* electroencephalography, CSF fluid and neuroimaging were of concern. In conclusion, prevalence of seizure in individuals with COVID-19 is low, but suitable plans for seizure management, antiepileptic medication-withdrawal seizures in patients with epilepsy during COVID-19 pandemic and implementation of appropriate telemedicine systems should be addressed.

Keywords: case study, COVID-19, epilepsy, seizure, Thailand

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INTRODUCTION

Beginning in December 2019, there was an increase in numbers of infection-related respiratory tract symptoms in Wuhan City, China, which led to the identification of a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as the causative agent (Zhu *et al*, 2020). The spread of SARS-CoV-2 infection is fueled by human-to-human transmission resulting in rapid dissemination of the infection among cities, countries and continents, until the World Health Organization (WHO) declared on 12 March 2020 that SARS-CoV-2 infection was pandemic and named the infection coronavirus disease 2019 or COVID-19 (WHO, 2020a). As of 7 July 2020, globally 11,500,302 people have been infected and 535,759 have died, a mortality rate of 4.66% (WHO, 2020b).

SARS-CoV-2 infects people of all ages and average mortality rate varies considerably among countries, depending on patients' age, co-morbidities and management approaches (Huang *et al*, 2020). In hospitals COVID-19 mortality rate is higher in the elderly, in males and in those with comorbidities, such as chronic cardiac disease, non-asthmatic chronic pulmonary disease, chronic kidney disease, liver disease and obesity, than in the young or in previously healthy people (Docherty *et al*, 2020; Zhou *et al*, 2020). Typical symptoms of COVID-19 are fever, common cold or flu-like symptoms (Guan *et al*, 2020; Wang *et al*, 2020; Zhou *et al*, 2020), and in severe cases, patients develop progressive dyspnea and hypoxemia (Docherty *et al*, 2020; Guan *et al*, 2020; Wang *et al*, 2020; Yang *et al*, 2020; Zhou *et al*, 2020). There have been some case reports of atypical clinical presentations or asymptomatic clinical

states, such as afebrile, no coughing, diarrhea, thrombocytopenia, renal dysfunction and confusion (Tin *et al*, 2020).

Previous reports indicated coronaviruses are neurotropic, causing abnormal neurological symptoms and signs related to inflammation and demyelination (Bohmwald *et al*, 2018). For example, a SARS outbreak in Hong Kong, China in 2003 resulted in a substantial number of patients with encephalitis and encephalomyelitis (Hung *et al*, 2003; Lau *et al*, 2004). One series reported 23% of SARS-CoV patients develop seizures (Li *et al*, 2016) and another of seizures in Middle East respiratory syndrome coronavirus (MERS-CoV) infection with an occurrence of 8.6% (Saad *et al*, 2014).

Data on neurologic manifestation in patients with COVID-19 are limited. Mao *et al* (2020), in an examination of neurological symptoms in 214 patients with COVID-19 in China, reported 24.8% of patients with central nervous system involvement: dizziness (16.8%), headache (13.1%), altered mental status (8%), acute stroke (3%), loss of coordination (0.5%) and seizures (0.5%), and 8.9% with peripheral nervous system involvement: hypogeusia (5.6%) and hyposmia (5.1%), both being more evident in severe cases. Compared to SARS- and MERS-CoV, SARS-CoV-2 appears to have a lower risk for seizures (Hung *et al*, 2003; Lau *et al*, 2004; Saad *et al*, 2014; Mao *et al* 2020).

Here, we describe three COVID-19 patients with seizures from case series obtained from seven hospitals in Thailand during 1 December 2019 to 7 July 2020. The findings were analyzed with the aim to answer the following questions: 1) how often does COVID-19 cause acute symptomatic seizure and what are the proposed mechanisms?; 2) how

does COVID-19 influence patients with epilepsy?; 3) is an epileptic patient a more susceptible host for COVID-19?; and 4) what are the appropriate seizure management protocols in patients with seizures during COVID-19 pandemic?

MATERIALS AND METHODS

Patients

Medical records of COVID-19 patients ($n = 527$) admitted to seven hospitals in Thailand, namely, Bamrasnaradura Infectious Diseases Institute, Nonthaburi Province; Chakri Naruebodindra Medical Institute, Samut Prakan Province; Prasat Neurological Institute, Bangkok; Phramongkutklao Hospital, Bangkok; Rajavithi Hospital, Bangkok; Rajprachasamasai Institute, Samut Prakan Province; and Trang Hospital, Trang Province during 1 December 2019 to 7 July 2020 were retrieved with names redacted and subjected to descriptive analysis. Results are reported as numbers and percent.

The research protocol was approved by the Institution Review Boards of the Phramongkutklao Hospital (S069h/63) while other centers' approval processes were exempted. The need for patient consent was waived due to the retrospective nature of the study and also it was allowed not to obtain the consent approach during communicating disease outbreak. Descriptive analysis was performed and the result was simply reported as number and percent.

RESULTS

Among 527 patients with COVID-19 admitted to the seven study medical centers in Thailand, there were three Thai patients with seizures related to definitive

COVID-19 infection (Table 1).

Patient A, admitted to Chakri Naruebodindra Medical Institute, is a 53-year-old male with no comorbid disease. COVID-19 infection was confirmed by positive nasal swab using an RT-qPCR assay for SARS-CoV-2 (Bustin and Nolan, 2020). The patient presented with acute fever, subsequently developed bilateral pneumonitis and hypoxemia; and was treated with antiretroviral drugs (*hydroxychloroquine, azithromycin, favipiravir*). On Day 13 of the illness, pneumonia worsened and on Day 14 a generalized tonic-clonic seizure episode of two minutes occurred, which was controlled by intravenous diazepam. The patient was intubated and prescribed sedating agents. Computed tomography (CT) X-ray and CT venography of the brain were unremarkable. Intravenous levetiracetam 1,000 mg/day was commenced for seizure prevention. Subsequently, there was no recurrence of seizure and upon improvement of clinical status sedating agents, intubation and levetiracetam treatment were discontinued. The patient was discharged on Day 28 according to the hospital guideline (unpublished).

Patient B, admitted to Trang Hospital in Trang Province, is a 20-year-old male with a history of amphetamine abuse but no prior report of seizure, who developed symptoms of upper respiratory tract infection and COVID-19 test using RT-qPCR was positive. When afebrile and with a negative second COVID-19 test the patient was discharged on Day 14 post-admission. The following day the patient developed a brief generalized tonic-clonic seizure, followed by catatonia lasting one day. Upon re-admission, CT and magnetic resonance imaging (MRI) of the brain were

Table 1
Seizures in Thai admitted patients with COVID-19: clinical survey from 7 medical centers in Thailand.

No.	Medical center	Total number of patients admitted with COVID-19	Number of patients with severe COVID-19	Number of patients that developed seizure	Number of patients with underlying epilepsy
1.	Bamrasnaradura Infectious Diseases Institute	205	5	0	0
2.	Chakri Naruebodindra Medical Institute	152	14	1 ^a	0
3.	Rajavithi Hospital	77	27	1 ^b	0
4.	Prasat Neurological Institute	36	0	0	0
5.	Rajprachasamasai Institute	32	1	0	0
6.	Phramongkutklao Hospital	20	1	0	0
7.	Trang Hospital	5	0	1 ^c	0
Total		527	48 (9.11%)	3 (Seizure prevalence 0.57%)	0

a: Seizure in severe COVID-19 case, no status epilepticus, electroencephalography - not done, magnetic resonance imaging (MRI) of the brain - not done, lumbar puncture - not done.

b: Seizure in non-severe COVID-19 case, no status epilepticus, electroencephalography - not done, magnetic resonance imaging (MRI) of the brain - not done, lumbar puncture - not done.

c: Seizure in non-severe COVID-19 case, no status epilepticus, electroencephalography - not done, magnetic resonance imaging (MRI) of the brain - not done, lumbar puncture - negative for COVID-19 in cerebrospinal fluid.

unremarkable. An electroencephalogram (EEG) was not performed. Cerebrospinal fluid (CSF) showed no white blood cells and normal CSF protein and sugar levels. Nasal swab and CSF for COVID-19 were negative. Valproate 1000 mg/day for seizure prevention was administered and upon absence of any recurrence of seizure the patient was discharged on Day 2 after the second admission post-second admission without any apparent neurological sequelae.

Patient C, admitted at *Rajavithi* Hospital in Bangkok, is a 43-year-old female with alcoholism who developed low graded fever five days prior to admission. Body temperature was 38°C and presented with mild dyspnea. Nasal swab for COVID-19 using RT-qPCR was positive. On Day 2 post-admission (11 days after alcohol withdrawal), there were generalized tonic-clonic seizures. Brain CT imaging, electroencephalography and lumbar puncture were not performed. Levetiracetam 2,000 mg/day was administered. Upon subsequent absence of seizures, the patient was discharged on Day 12 with no apparent neurological sequelae.

DISCUSSION

Prevalence of seizures among COVID-19 patients

A review of the literature on occurrences or neurological manifestations conducted by searching public databases, www.pubmed.gov and <https://scholar.google.co.th/>, from 1 December 2019 to 7 July 2020, using a variety of keywords, eg COVID-19, electroencephalography, epilepsy, neurological manifestation, novel coronavirus, and seizure, ten COVID-19 series were uncovered (Table 2).

From a retrospective multicenter study (Lu *et al*, 2020) conducted in 42 hospitals in China during 18 January - 18 February 2020, there were 304 patients diagnosed with COVID-19 infection and 108 (35%) patients developed severe symptoms. Eleven neurologists assessed their histories and found that there were no patients previously diagnosed with epilepsy. Eighty-four patients (27%) have both abnormal brain function and metabolic derangements, which could potentially induce seizures. Two patients (0.6%) developed seizure-like symptoms in the context of stressful events and hypocalcemia. Neither acute symptomatic seizure nor status epilepticus was identified in this case series. Vollono *et al* (2020) in Italy reported a patient who presented with focal status epilepticus. Pinna *et al* (2020) in Chicago, IL, noted among 150 patients, 50 (33%) presented with abnormal neurological symptoms, of whom 13 (26%) developed seizures. In addition, there was no patient developing seizure from the reports of Huang *et al*, 2020, Chen *et al*, 2020, and Helms *et al*, 2020. Only one patient with severe COVID-19 developed a seizure (Arentz *et al*, 2020).

Overall, from this current review, prevalence of seizures among COVID-19 patients is approximately 0.45% compared to 0.57% among the case series in Thailand over the same survey period.

COVID-19 and acute symptomatic seizure and proposed mechanisms

Seizures in Patient A would be considered acute and symptomatic, as it was related to severe pneumonitis, and possibly combined with direct virus involvement of the brain as the seizure duration was quite prolonged; however, brain MRI, EEG, or lumbar puncture

Table 2
Seizures in patients with COVID-19: literature review.

No.	Reference	Total number of patients admitted with COVID-19	Number of patients with severe COVID-19	Number of patients that developed seizure	Number of patients with underlying epilepsy
1.	Guan <i>et al</i> , 2020	1,099	67	0	0
2.	Wang <i>et al</i> , 2020	138	36	0	0
3.	Yang <i>et al</i> , 2020	710	52	0	0
4.	Mao <i>et al</i> , 2020	214	88	1 ^a	0
5.	Lu <i>et al</i> , 2020	304	108	0	0
6.	Huang <i>et al</i> , 2020	41	13	0	0
7.	Chen <i>et al</i> , 2020	99	17	0	0
8.	Helms <i>et al</i> , 2020	NA	58 ^b	0	7 ^c
9.	Pinna <i>et al</i> , 2020	650	NA	13 ^d	0
10.	Arentz <i>et al</i> , 2020	NA	21	1	0

a: Seizure in severe COVID-19 case, no status epilepticus.

b: Eight patients underwent electroencephalography, only non-specific changes were detected.

c: Seven patients had had previous neurologic disorders including transient ischemic attack, partial epilepsy and mild cognitive impairment.

d: These 13 patients were among 50 (out of 650) COVID-19 patients with neurological issues

NA: data not available.

would be required to demonstrate direct brain involvement. Patient B developed catatonia right after seizure, suggesting a drug effect from an underlying amphetamine abuse. Patient C developed a seizure on Day 11 after alcoholic withdrawal, not typical of an alcoholic withdrawal seizure. In addition, the patient's COVID-19 status was not severe, thus the etiology of seizure would likely be multifactorial. Etiologies of seizures in these three patients were significantly different so that no conclusion could be made regarding a direct effect from SARS-CoV-2 infection.

SARS-CoV-2 may cause seizures in several ways: (i) by direct viral neuroinvasion (viral encephalitis), (ii) by triggering immune system (autoimmune

encephalitis), (iii) by the hypoxia or metabolic derangements arising from systemic involvement and other organ failures, and (iv) by complications due to therapeutic interventions (Tsai *et al*, 2020). Although acute symptomatic seizures in COVID-19 are infrequently reported, it may be an under-recognized condition, especially in individuals with altered mental status where EEG is always not available. In order to confirm non-convulsive seizures, in particular non-convulsive epilepticus status, Salzburg Consensus EEG Criteria (Leitinger *et al*, 2015) need to be rigorously followed for diagnosis, otherwise subtle signs or subclinical seizures could be missed.

COVID-19 and patients with epilepsy

Frequency of seizures among patients

with epilepsy and viral infection might be increased due to such triggering factors as high fever, hypoxemia, electrolyte/metabolic derangements, psychosocial stress, and insomnia, among others. In addition, difficulty in accessing regular medication due to the pandemic could result in drug withdrawal syndromes, as has happened during the SARS outbreak/pandemic in 2003. For example, Lai *et al* (2005) in Taiwan reported 22% of 227 patients with epilepsy could not obtain their usual medication, resulting in 12% having uncontrolled seizures and 2% developing status epilepticus.

Physicians should be alert to potential drug interactions between antiviral and anticonvulsant treatments. Liver and renal impairment in severe COVID-19 patients will require dosage adjustment of antiepileptic agents (Anderson and Hakimian, 2014). Administration of anti-COVID-19 drugs, *eg* azithromycin, chloroquine or hydroxychloroquine, has been reported to cause prolongation of ECG QT-interval (Wu *et al*, 2020), while carbamazepine, lacosamide, phenytoin and rufinamide also can carry risk of cardiac conduction abnormalities, such as prolonged QT-interval, PR interval, arrhythmia, and hypotension (Asadi-Pooya *et al*, 2020). Thus, co-administration of these two groups of drugs should be considered with caution and regular ECG surveillance is recommended (Auerbach *et al*, 2018).

In Thailand, after the implementation of lock-down measures, many patients had difficulty accessing medical services due to unavailability of public transportation and a feeling of insecurity of going outside. Many hospitals have used telemedicine to interview patients and medication delivery services are provided for patients (Ohannessian *et al*, 2020).

Epilepsy patients are encouraged not to allow prescriptions to lapse and to access telemedicine service to ensure their stable status.

Patients with epilepsy and increase susceptibility to COVID-19

To date there is no convincing evidence suggesting epilepsy can be an underlying predisposing disease or taking of antiepileptic medications enhances susceptible to this viral infection. From the literature review only few patients have underlying epilepsy (Table 2) and no patient in the Thai case series was previously diagnosed with epilepsy (Table 1). Any susceptibility to SAR-CoV-2 infection would more likely depend on other factors, *eg* old age, and other comorbidities than epilepsy.

Appropriate seizure management protocol during COVID-19 pandemic

Treatment approaches for both seizures in epilepsy patients and symptomatic seizures in non-epilepsy patients are similar and consistent with accepted principles of epilepsy management (Perrucca, 2015). Physicians should be aware of subclinical seizures or non-convulsive status epilepticus in patients with altered mental status without obvious convulsions. In an emergency setting, airway, breathing and circulation are the first considerations requiring prompt treatment. In the meantime, identification of triggering factors and appropriate management of hypoxemia, pyrexia and metabolic derangements should be rapidly determined.

For initial symptomatic seizures, prescribing antiepileptic medications should be considered in cases with high risks of seizure recurrence (prolonged seizure, serial seizures, status epilepticus and single seizure with underlying brain

lesion or abnormal EEG). Managing recurrent seizures especially in status epilepticus during a pandemic is challenging as it increases the opportunity of spreading infection to medical personnel, and short-term antiepileptic prophylaxis during acute and transitional phases would be justified (Pandey *et al*, 2016). On the other hand, individuals presenting with a first brief seizure without epilepsy and low risk of seizure recurrence should be observed along with proper symptomatic supportive treatments rather than prescribing antiepileptic medications as there may be adverse effects from medication or drugs interaction with anti-COVID-19 treatments.

Thai patients received a short-term course of anticonvulsants to raise threshold of subsequent seizures and simplify medical management. This provided adequate seizure control as eventually the patients regained consciousness and had no further convulsions. However, during a COVID-19 pandemic in many countries, including Thailand, one concern is an inability to provide EEG recordings thereby allowing non-convulsive seizures to be under-recognized.

Proposed suitable national management protocol for people with epilepsy during COVID-19 epidemic

The Neurological Association of Thailand under the Royal College of Physician of Thailand and Department of Medical Services, Ministry of Public Health, Thailand provided national guidelines for physicians and neurologists on how to deal with neurological patients in the time of COVID-19 pandemic (Sithinamsuwan and Boonyapisit, 2020). In addition, physicians should inform patients that epilepsy does not increase

the risk of infection and encourage compliance with medication to avoid breakthrough seizures from antiepileptic treatment withdrawal. As the government regulation of staying at home may interfere with patients' ability to visit hospitals, telemedicine systems for evaluation and treatment, video or phone consultations as well as other kinds of telecommunications should be implemented. Medicine should be made available across the country through the postal system. These actions have been shown to be helpful for patients with epilepsy (Ohannessian *et al*, 2020).

In conclusion, a very low occurrence of seizures among COVID-19 patients likely reflects low CNS involvement, either from direct viral involvement or immune mediated process. Thus, COVID-19, to date, manifests non-neurovirulence or non-neuroinvasive pathology with low seizure occurrence among infected patients.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

- Anderson GD, Hakimian S. Pharmacokinetic of antiepileptic drugs in patients with hepatic or renal impairment. *Clin Pharmacokinet* 2014; 53: 29-49.
- Arentz M, Yim E, Klaff L, *et al*. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA* 2020; 323: 1612-4.

- Asadi-Pooya AA, Attar A, Moghadami M, Karimzadeh I. Management of COVID-19 in people with epilepsy: drug considerations. *Neurol Sci* 2020; 41: 2005-11.
- Auerbach DS, Biton Y, Polonsky B, *et al.* Risk of cardiac events in Long QT syndrome patients when taking antiseizure medications. *Transl Res* 2018; 191: 81-92.
- Bohmwald K, Galvez NMS, Rios M, Kalergis AM. Neurologic alterations due to respiratory virus infections. *Front Cell Neurosci* 2018; 12: 386.
- Bustin SA, Nolan T. RT-qPCR testing of SARS-CoV-2: a primer. *Int J Mol Sci* 2020; 21: 3004.
- Chen N, Zhou M, Dong X, *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395: 507-13.
- Docherty AB, Harrison EM, Green CA, *et al.* Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020; 369: m1985.
- Guan WJ, Ni ZY, Hu Y, *et al.* Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382: 1708-20.
- Helms J, Kremer S, Merdji H, *et al.* Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med* 2020; 382: 2268-70.
- Huang C, Wang Y, Li X, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395: 497-506.
- Hung EC, Chim SS, Chan PK, *et al.* Detection of SARS coronavirus RNA in the cerebrospinal fluid of a patient with severe acute respiratory syndrome. *Clin Chem* 2003; 49: 2108-9.
- Lai SL, Hsu MT, Chen SS. The impact of SARS on epilepsy: the experience of drug withdrawal in epileptic patients. *Seizure* 2005; 14: 557-61.
- Lau KK, Yu WC, Chu CM, Lau ST, Sheng B, Yuen KY. Possible central nervous system infection by SARS coronavirus. *Emerg Infect Dis* 2004; 10: 342-4.
- Leitinger M, Beniczky S, Rohracher A, *et al.* Salzburg Consensus Criteria for Non-Convulsive Status Epilepticus--approach to clinical application. *Epilepsy Behav* 2015; 49: 158-63.
- Li Y, Li H, Fan R, *et al.* Coronavirus infections in the central nervous system and respiratory tract show distinct features in hospitalized children. *Intervirology* 2016; 59: 163-9.
- Lu L, Xiong W, Liu D, *et al.* New onset acute symptomatic seizure and risk factors in coronavirus disease 2019: a retrospective multicenter study. *Epilepsia* 2020; 61: e49-53.
- Mao L, Jin H, Wang M, *et al.* Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020; 77: 683-90.
- Ohannessian R, Duong TA, Odone A. Global telemedicine implementation and integration within health systems to fight the COVID-19 pandemic: a call to action. *JMIR Public Health Surveill* 2020; 6: e18810.
- Pandey S, Rathore C, Michael BD. Antiepileptic drugs for the primary and secondary prevention of seizures in viral encephalitis. *Cochrane Database Syst Rev* 2016; 2016: CD010247.
- Perucca E. General principles of medical management. In: Shorvon S, Perucca E, Engel J, editors. *The treatment of epilepsy*. 4th ed. Chichester West Sussex, UK: John Wileys & Sons Ltd; 2015. p. 110-23.
- Pinna P, Grewal P, Hall JP, *et al.* Neurological manifestations and COVID-19: experiences from a tertiary care center at the Frontline. *J Neurol Sci* 2020; 415: 116969.
- Saad M, Omrani AS, Baig K, *et al.* Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: a single-center experience in Saudi Arabia. *Int J Infect Dis* 2014; 29: 301-6.
- Sithinamsuwan P, Boonyapisit K. Management

- of epileptic patients. In: Charnnarong N, Apiwattanakul M, editors. Guidelines for management of neurological patients in the COVID-19 pandemic era. 1st ed. Bangkok, Thailand: Tanapress; 2020 .p. 34-6. [in Thai]
- Tin SS, Wiwanitkit V. Uncommon atypical presentations of COVID-19: important and should not be under recognized! *J Health Sci Med Res* 2020; 38: 153-8.
- Tsai S, Lu M, San S, Tsai C. The neurologic manifestations of coronavirus disease 2019 pandemic: a systemic review. *Front Neurol* 2020; 11: 498.
- Vollono C, Rollo E, Romozzi M, *et al.* Focal status epilepticus as unique clinical feature of COVID-19: a case report. *Seizure* 2020; 78: 109-12.
- Wang D, Hu B, Hu C, *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; 323: 1061-9.
- World Health Organization (WHO). Coronavirus disease 2019 (COVID-19) situation report - 78, 2020 [cited 2020 Apr 07]. Available from: URL: <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200407-sitrep-78-covid-19.pdf>
- World Health Organization (WHO). Coronavirus disease 2019 (COVID-19) situation report - 169, 2020 [cited 2020 Jul 07]. Available from: URL: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200707-covid-19-sitrep-169.pdf?sfvrsn=c6c69c88_2
- Wu CI, Postema PG, Arbelo E, *et al.* SARS-CoV-2, COVID-19, and inherited arrhythmia syndromes. *Heart Rhythm* 2020; 17: 1456-62.
- Yang X, Yu Y, Xu J, *et al.* Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020; 8: 475-81.
- Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; 395: 1054-62.
- Zhu N, Zhang D, Wang W, *et al.* A novel coronavirus from patients with pneumonia in China. *N Engl J Med* 2020; 382: 727-33.