

# New Onset of Mania in COVID-19 Infection: A Report of Two Cases

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## Abstract

**Background:** Those who have infected with coronavirus disease 2019 (COVID-19), experience a range of symptoms, from mild and self-resolving respiratory illnesses to severe respiratory complications, as well as a range of the emotional symptoms of fear, guilt, anger, or anxiety due to the need of quarantine isolation. Clinical cases with a new onset of psychiatric symptoms in the acute stage or aftermath of COVID-19 have also been described in the literature. The impact of COVID-19 on psychological health across all stages of illness has become an area of interest in psychiatry. **Methods:** We at Johor Bahru, Malaysia, would like to report two patients without any history of any known psychiatric illness, who had their first manic episodes during the acute stage of COVID-19 infection. **Results:** Patient A was a 29-year-old married female patient, had a COVID-19 infection which were treated smoothly. But unfortunately, the devastating news of her husband's hospitalization for COVID-19 infection and the death of her sister-in-law due to the deadly virus came on the day of her discharge. Since she developed a picture of a manic episode with as elated mood, irritability, talkativeness, increased energy, decreased need for sleep, spending spree, reckless driving, excessive ideas concerning COVID-19 infection, and excessive sexual drive. She subsequently responded to treatment and was discharged with daily 600 mg of oral lithium carbonate, 200 mg of oral chlorpromazine, and 1,000 mg of sodium valproate Chrono. Patient B was a 31-year-old married homemaker and she presented herself to the emergency department for stage COVID-19 infection and witnessed resuscitation and eventual deaths of several patients diagnosed with COVID-19 infection. She was so frightened that she had become easily distracted, increasingly irritable, and talkative. Having reduced need for sleep at night, she would repeatedly call her friends and family around the clock to check if they had COVID-19 infection. She claimed to have the power to heal bone fractures with naked eyes. Furthermore, she started to see supernatural creatures around her at home. She subsequently responded to daily 750 mg of lithium carbonate and 1,000 mg of amisulpride during a 14-day inpatient stay. **Conclusion:** We content that our two patients had a new onset of manic episode after COVID-19 infection. We suggest that manic symptoms may have been triggered through an episode of COVID-19.

**Key words:** bipolar disorder, decreased need for sleep, distraction, mania  
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## Introduction

The World Health Organization declared the novel coronavirus disease 2019 (COVID-19) outbreak as a pandemic on March 11, 2020 ([www.who.int/director-general/speeches/detail/who-director](http://www.who.int/director-general/speeches/detail/who-director)). Those who have COVID-19 infection experience a range of symptoms, from mild and self-resolving respiratory illnesses to severe respiratory complications requiring intensive medical attention. The experience of quarantine due to COVID-19 infection causes the emotion of fear, guilt, anger, or anxiety revolving around

the worst possible disease outcome, worsening the preexisting psychiatric disorder [1]. Emerging evidence has elaborated examples of cases where new onset of psychiatric symptoms is manifested in the acute stage or aftermath of COVID-19 [2]. The impact on psychological health across all stages of illness has become an area of interest in psychiatry. We at Johor Bahru, Malaysia (Figure 1), illustrate two patients without history of any known psychiatric illness, who had

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their first manic episodes during the acute stage of COVID-19 infection.

## A Report of Two Cases

### Case 1

Patient A is a 29-year-old married female patient, without a history of any medical or psychiatric illnesses, neither a smoker nor a substance abuser. She also denied any family history of psychiatric illness. Premorbidly, she was described as a loving



**Figure 1.** Map of Johor Bahru, Malaysia (photo courtesy: www.mbjb.gov.my). Johor Bahru is the capital city of the state of Johor, Malaysia. Johor is the second highest populous state in Malaysia. Johor Bahru is on the southern tip of the peninsular Malaysia, and is bordering with Singapore to the south with Johor Channel. The dot line represents a high-speed rail under construction. Johor is 296 km to Kuala Lumpur, the capital of Malaysia, and is 188 km to Malacca on the northwestern direction, and is 731 km to Kuching of Sarawak. Internationally, Johor is 613 km to Medan, the capital of Aceh province of Indonesia, and 914 km to Jakarta, the capital of Indonesia.

**Table 1.** Clinical staging of COVID-19 by the Ministry of Health, Malaysia

Staging	Description
1	Asymptomatic
2	Symptomatic, no pneumonia
3	Symptomatic, pneumonia
4	Symptomatic, pneumonia, requiring supplemental oxygen
5	Critically ill with multi-organ involvement

Source: Ministry of Health, Malaysia (www.covid-19.moh.gov.my)

person and a responsible clerk at a manufacturing factory. On July 26, 2021, she started showing flu-like symptoms, cough, and sore throat, three days after, her sister-in-law tested positive for COVID-19. She was subsequently tested COVID-19 positive through antigen rapid test kit in the nearest screening center and was ordered for home quarantine. According to the family, she did not show any abnormal behavior besides expressing minor worries about her own health status. She could interact with family as usual and had good sleep and appetite. On day 4 of illness, she sought medical consultation due to shortness of breath and was immediately admitted to a tertiary hospital for stage 4 COVID-19 infection (Table 1).

Despite requiring oxygen supplementation through venturi mask up to 60% in ward, the patient was energetic and had slept late at night for two days after admission. According to her husband, she constantly posted messages on social media at midnight and sent flirty texts to her husband throughout her entire admission. She was treated with dexamethasone intravenously up to 24 mg daily, which was then changed to oral dose to 4 mg daily upon discharge, making it a total of a 15-day course of steroid regimen. She was discharged home without complication on day 10 of illness. Unfortunately, the devastating news of her husband's hospitalization for stage 4 COVID-19 infection and the death of her sister-in-law due to the deadly virus came on the day of her discharge. Since then, she was noted by family to show elated mood, irritability, talkativeness, increased energy, decreased need for sleep, spending spree, and reckless driving. She had excessive ideas concerning COVID-19 infection, such as possessing an ability to predict who will be the next person to contract COVID-19 infection. Despite her husband's unfit physical state following discharge, she demanded to have up to five sexual intercourses daily with him.

The patient was then brought to psychiatric attention and received inpatient psychiatric care on day 24 of COVID-19 infection. Results of general examinations including neurological examination were unremarkable. Her full blood picture, renal and liver profiles, and thyroid function test were not remarkably deranged in findings (Table 2). Her clinical presentation corresponded to the picture of a manic episode with the differential diagnosis of brief reactive psychosis.

On ward, the patient started to receive many oral medications which include daily sodium valproate up to 600 mg BID, lithium carbonate up to 600 mg QD, and chlorpromazine up to 200 mg BID. She also needed many parenteral administrations of haloperidol, midazolam, and promethazine for rapid tranquilization. Her condition was improved and was subsequently discharged after a nine-day hospitalization. Upon discharge, her medications were further adjusted to oral lithium carbonate 600 mg qhs, oral chlorpromazine 200 mg qhs, and sodium valproate Chrono 1,000 mg qhs. Three weeks later, she was reassessed, and was noted to be achieving full remission during her psychiatric outpatient clinic appointment.

### Case 2

Patient B is a 31-year-old married homemaker and she presented herself with a medical history of diabetes mellitus

**Table 2.** Summary of relevant investigation findings and pharmacological management for patients in Cases 1 and 2

	Case 1			Case 2	
Method of confirmed COVID-19 diagnosis	RTK-Ag			RT-PCR RdRp = 19.00 E = 18.14	
Chest X-rays	Bilateral lower zone ground-glass opacity (day 4) Improving bilateral lower zone ground-glass opacity (day 8)			Bilateral lower zone ground-glass opacity (day 6)	
Highest oxygen requirement	Venturi mask 60%			Nasal prong 4 L	
Blood gas analysis					
pO <sub>2</sub> (80–100 mmHg)		76		60	
pCO <sub>2</sub> (32–48 mmHg)		37		34	
HCO <sub>3</sub> (22–26 mmol/L)		26.9		25.9	
Related blood investigations	Day 4	Day 8	Day 26	Day 5	Day 19
Hb (12.0–15.0 g/dL)	13.6	12.2	13.7	14.3	12.4
WBC (4.0–10.0×10 <sup>9</sup> /L)	4.9	9.3	7.30	5.76	8.06
LYM (1.0–3.0×10 <sup>9</sup> /L)	0.8	1.2	1.90	-	2.72
Neutrophils (2.0–7.0×10 <sup>9</sup> /L)	4.0	8.4	4.18	-	4.63
Platelet (150–410×10 <sup>9</sup> /L)	243	422	293	203	522
Na (136–145 mmol/L)	139	136	140	-	142
K (3.5–5.1 mmol/L)	2.73	4.85	3.51	-	3.25
BUN (2.8–8.1 mmol/L)	3.0	3.4	2.2	-	1.3
Creatinine (44–80 μmol/L)	64	54	52	-	64
AST (5–32 U/L)	48	46	36	-	44
ALT (5–33 U/L)	25	49	43	-	58
ALP (35–104 U/L)	62	59	97	-	53
Total bilirubin (≤ 21 μmol/L)	6.4	8.7	12.6	-	8.2
CK (26–132 U/L)	592	105	-	-	-
LDH (135–214 U/L)	746	558	-	-	-
C-RP (< 5 mg/L)	61.8	32.2	-	-	-
Ferritin (13–150 mcg/L)	330.8	-	-	-	-
TSH (0.27–4.20 mIU/L)	-	-	1.250	-	1.320
Free T4 (12.0–22.0 pmol/L)	-	-	21.30	-	21.80
Medical treatments	IV Augmentin 1,200 mg, tid (day 4–10) IV dexamethasone 24 mg, qd (day 4–8) IV dexamethasone 12 mg, qd (day 9) IV dexamethasone 8 mg, qd (day 10) Tab dexamethasone 8 mg, qd (day 11–12) Tab dexamethasone 4 mg, (day 13–14) Tab dexamethasone 2 mg, (day 15–16)			Tab dexamethasone 8 mg, qd (day 5) Tab metformin 500 mg, bid Tab amlodipine 5 mg, qd	
Psychiatric treatment and discharge medication	IM haloperidol 10 mg (up to 3 doses) IM midazolam 10 mg (up to 9 doses) IM promethazine 25 mg (up to 9 doses) Tab lithium carbonate 600 mg, qhs Tab chlorpromazine 200 mg, qhs Tab sodium valproate chrono 1,000 mg, qhs			IM haloperidol 10 mg (up to 4 doses) IM midazolam 10 mg (up to 4 doses) IM promethazine 50 mg (up to 4 doses) IM zuclopenthixol acetate 100 mg (1 dose) Tab lithium carbonate 750 mg, qhs Tab amisulpride 400 mg qam/600 mg qhs	

RTK-Ag, antigen rapid test kit; RT-PCR, reverse transcription polymerase chain reaction; RdRp, RNA-dependent RNA polymerase; E, envelope protein gene; Hb, hemoglobin; WBC, white blood cell; LYM, lymphocyte; Na, sodium; K, potassium; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; CK, creatine kinase; IM, intramuscular; IV, intravenous; LDH, lactate dehydrogenase; C-RP, C-reactive protein; Tab, tablet; TSH, thyroid stimulating hormone; Free T4, free thyroxine, qd, once a day; bid, two times per day; tid, three times per day; qam, once every morning; qhs, once every night at bedtime

and hypertension well-controlled with oral metformin and amlodipine. She had no previous psychiatric, smoking, or illicit substance use histories. On August 31, 2021, she was tested positive for COVID-19 infection using reverse transcription-polymerase chain reaction (RT-PCR) after a four-day history of fever and runny nose. The source of COVID-19 was undetermined in this patient as no close contact of the

illness was reported by the patient. She was ordered for home quarantine. On day 5 of illness, she presented herself to the emergency department for stage 4 COVID-19 (Table 1) and received oxygen supplementation up to nasal prong 4 l/min and oral dexamethasone 8 mg daily. In the emergency department, she witnessed resuscitation and eventual deaths of several patients diagnosed with COVID-19 infection, which

were intensely traumatizing to her. She was so frightened that she escaped from the hospital the following day.

Since then, the patient has become easily distracted, increasingly irritable, and talkative. Having reduced need for sleep at night, she would repeatedly call her friends and family around the clock to check if they had COVID-19 infection. She claimed to have the power to heal bone fractures with naked eyes. Furthermore, she started to see supernatural creatures around her at home.

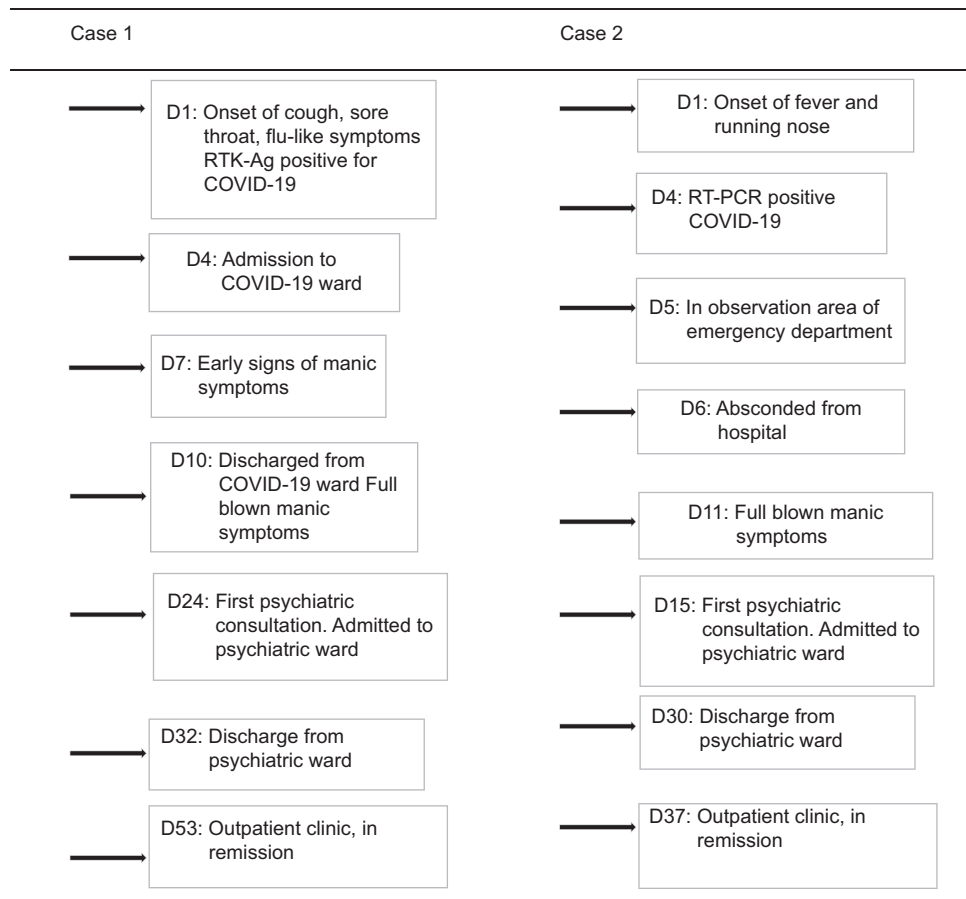
With increasing severity of her mental condition, the patient was admitted to the psychiatric ward on day 15 of COVID-19 infection for inpatient psychiatric management. The working differential diagnoses were acute mania and delirium. On general examination, she was an obese female with height of 155 cm and weight of 110 kg (body mass index = 45.79 kg/m<sup>2</sup>), who was oriented to time, place, and person. The results of other systemic examinations including the neurological examination were unremarkable. Blood investigations were not remarkably abnormal except isolated mild elevation of serum alanine aminotransferase at the level of 58 U/L, with no remarkable change compared to the value of 57 U/L in year 2008 (Table 2). On the ward, she showed no fluctuation or alteration of cognition, orientation or consciousness, making a differential diagnosis of delirium unlikely. She was initially hostile and aggressive, hence was

given many parenteral sedations including zuclopenthixol acetate, midazolam, and promethazine. She subsequently responded to oral lithium carbonate up to 750 mg daily and amisulpride up to 1000 mg daily during a 14-day inpatient stay. Residual symptoms were resolved in a week following her discharge from the ward.

### Comment

According to the *Diagnostic and Statistical Manual of Mental Disorders, the Fifth Edition (DSM-5)* [3], the proposed criteria for manic episodes have at least 4 out of 7 criteria of one-week duration of almost daily persistently elevated mood, and goal-directed behavior. Those symptoms and signs include inflated self-esteem or grandiosity, decrease need for sleep, more talkative or pressured speech, flight of ideas, easily distracted, increased goal-directed activity or psychomotor agitation, and excessive involvement in activities with potentially painful consequences [3].

With recent intensive research, patients with COVID-19 infection experience possibly neurological sequelae and neuropsychiatric manifestations. In several reports, delirium, depression, anxiety, and fatigue have been accounted for the majority of neuropsychiatric manifestations following the COVID-19 infection [2, 4]. Several articles are describing new



**Figure 2.** Timeline of illness for cases 1 and 2 counted from onset of COVID-19 infection. D, day; RT-CPR, reverse transcription polymerase chain reaction; RTK, antigen rapid test kit.

onset of mania or psychosis in patients who have contracted from this virus.

Among the initial reports on patient with COVID-19 infection published from China, the United States, and the United Kingdom, all cases outlined the first manic presentations of subjects aged from 30 to 50 years following COVID-19 infection [5-7]. As for our patients, both young women developed progressively worsening manic symptoms within a week after being diagnosed as stage 4 COVID-19 with full blown manic episode within two weeks. The onset was preceded by remarkable emotional trauma and life events in the middle of the progression of their COVID-19 infection (Figure 2). There was otherwise no remarkable neurological finding in both patients. Despite the presence of mild deranged blood parameters as elaborated in Table 2, the diagnosis of delirium was excluded in Case 2 as evidenced by fully orientated throughout the entire course of admission, and her manic symptoms which persisted after her full recovery from COVID-19 infection responded well to mood stabilizers.

The exact mechanism of acute mania as a result of COVID-19 infection is yet to be determined, but the involvement of monoamine, pro-inflammatory cytokine, and interleukin as a result of viral infection has been hypothesized as a significant trigger [8-10]. On the other hand, steroids are known to be associated with various psychiatric disorders [11]. However, the relatively short duration of steroid use in both of our cases makes the occurrence of exogenous corticosteroid-induced manic episodes less likely.

Neuropsychiatric manifestations are increasingly reported among survivors of COVID-19 infection. We hope that those two reported cases will serve to increase awareness among clinicians in early detection and management of symptoms in the middle of the COVID-19 pandemic, aiming at minimizing the disease burden as a result of COVID-19 infection. In future, more research is required to look at the incidence of manic episodes as a result of COVID-19 infection given the potential association of both conditions (National Institute of Health Ministry of Health, Malaysia, wrote a letter for clearance on behalf of authors' ethics committee for human experiments for approving publication of this case report

[reference number = NIH.800-4/4/1 Jld.104(46) and date of the letter = December 8, 2021] without the need of obtaining a signed informed consent from the patients).

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## Conflicts of Interest

The authors report no actual or potential conflicts of interest.

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