

A Family Cluster of Coronavirus Disease (COVID-19) Infection with Different Clinical Manifestations

Soedarsono

Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Airlangga, Surabaya, Indonesia.

Corresponding Author:

Soedarsono, MD., PhD. Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Airlangga. Jl. Mayjen Prof. Dr. Moestopo No. 6-8 Surabaya 60131, Indonesia. email: ssoedarsono@gmail.com.

ABSTRAK

Coronavirus Disease 2019 (COVID-19) yang disebabkan oleh Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) oleh WHO telah dinyatakan sebagai pandemi global. Selama pandemi, kecurigaan infeksi COVID-19 adalah pada pasien yang menunjukkan gejala klinis COVID-19. Beberapa gejala klinis COVID-19 yang baru dikenal telah dilaporkan baru-baru ini. Hal ini menyebabkan kesulitan untuk mengidentifikasi COVID-19 hanya berdasarkan gejala klinis. Real-Time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) mutlak diperlukan untuk menegakkan diagnosis. Kami melaporkan satu keluarga yang terinfeksi COVID-19 dengan manifestasi klinis yang berbeda satu sama lain. Kasus kluster dalam keluarga ini menunjukkan potensi penularan COVID-19 pada orang yang awalnya tidak memiliki gejala tetapi pada perjalanan penyakitnya menunjukkan gejala karena periode inkubasi yang bervariasi antara 5-14 hari. Orang tanpa gejala ini tetap berpotensi untuk menularkan virus. Laporan kasus ini menguraikan temuan epidemiologis, klinis, radiologis, laboratorium, dan berbagai manifestasi klinis yang berbeda dalam satu keluarga dengan COVID-19 di Indonesia. COVID-19 ditularkan dari orang yang tidak menunjukkan gejala pada masa inkubasi.

Kata kunci: COVID-19, SARS-CoV-2, gejala klinis, orang tanpa gejala.

ABSTRACT

Coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) had been declared as a global pandemic by WHO. During the pandemic, a suspicion of COVID-19 infection could be found on patients presented with clinical symptoms of COVID-19. However, several new clinical symptoms of COVID-19 had also been reported recently. This caused difficulties to identify COVID-19 based on the clinical symptoms only. Real-Time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) was absolutely needed to determine the correct diagnosis. We report a family cluster of COVID-19 with different clinical manifestations to show a potential COVID-19 transmission in person who has no symptoms initially but may develop symptoms later as the incubation period varies from 5-14 days. This asymptomatic person remains potential to transmit the virus. This report describes the epidemiological, clinical, radiological, laboratory findings, and different clinical manifestation of a family cluster of COVID-19 case in Indonesia. COVID-19 was transmitted from asymptomatic person in the incubation period.

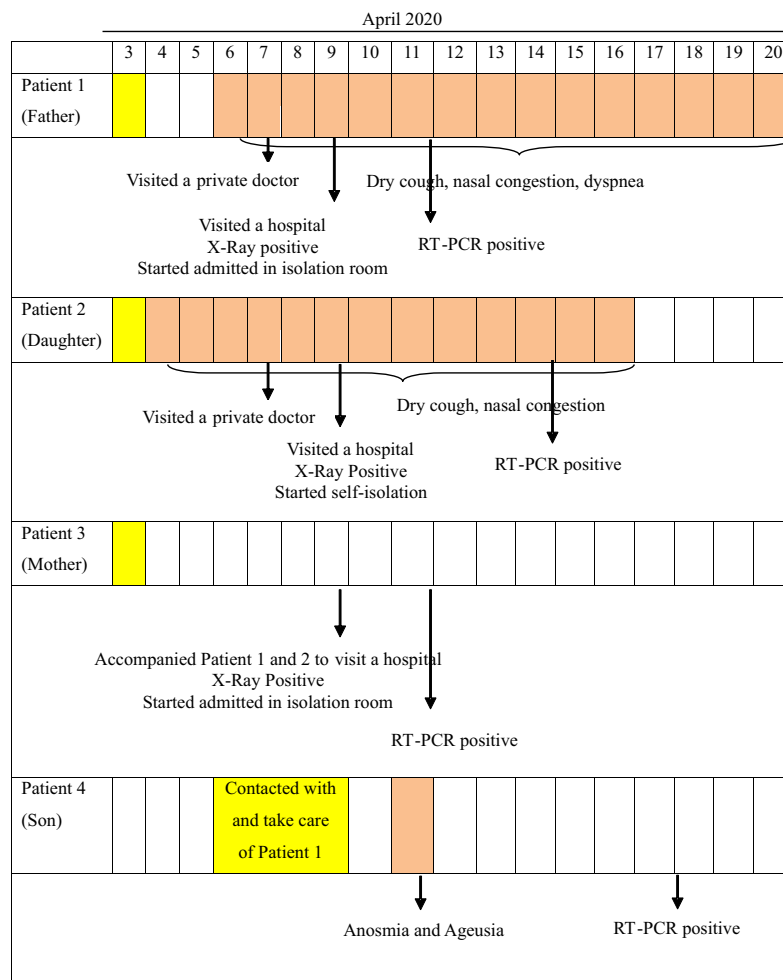
Keywords: COVID-19, SARS-CoV-2, clinical manifestation, asymptomatic person.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which first found in Wuhan, China and had been declared as a global pandemic by the World Health Organization (WHO) on 11 March 2020.¹⁻⁴ The common clinical symptoms and laboratory findings caused by this COVID-19 infection were fever, dry cough, dizziness, headache, sore throat, rhinorrhea, chest pain, dyspnea, myalgia, malaise, arthralgia, fatigue, sputum production, anorexia, diarrhea, nausea, and vomiting. Recently, anosmia (loss of smell sense) and ageusia (loss of taste sense) had been reported as the symptoms of confirmed COVID-19 patients in the previous studies.^{5,6} Generally, laboratory findings showed normal range of WBC count, reduced lymphocyte

count, and elevated C-reactive protein level. Radiological manifestation of COVID-19 were patchy ground glass opacity with or without consolidation involving multiple lobes, mainly in the peripheral zone, accompanied by halo sign, vascular thickening, crazy paving pattern, or air bronchogram sign.⁷⁻¹⁰ However, several new clinical symptoms of COVID-19 had also been reported recently. This caused difficulties to identify COVID-19 based only the clinical symptoms.

A better understanding of diagnosis and transmission of COVID-19 are needed. This report describes the epidemiological, clinical, radiological, laboratory findings, and different clinical manifestation of a family cluster of COVID-19 case in Indonesia.



Boxes filled with yellow are the dates of close contacted; boxes filled with orange are the dates of symptoms.

Figure 1. Clinical timeline of symptoms' onset of a family cluster and their contacts.

CASE ILLUSTRATION

These case histories began when Patient 2 (daughter of Patient 1 and Patient 3) initially presented with dry cough and nasal congestion since 4th April 2020 (symptoms' onset/illness day 1). Then, Patient 1 (father) became unwell and developed dry cough and nasal congestion on 6th April 2020 (2 days after the symptoms' onset of Patient 2). Patient 3 (mother) presented no symptom. Patient 4 (son of Patient 1 and Patient 3) presented very mild symptoms in only 1 day and recovered on 11th April 2020. Clinical timeline of symptoms' onset was presented in **Figure 1**.

This family lived closely in a particular neighborhood. Patient 1, 2, and 3 lived together in one house, while Patient 4 lived in the different house and frequently came to his parents' house, especially when Patient 1 felt sick. Patient 2 has not worked for a long time before this pandemic. Patient 2 also stated that she stayed home along this pandemic. Patient 3 was a housewife with no activity outside. Patient 1 was a worker who also routinely attended religious activities in mosque even in this pandemic time. This was a risk factor of COVID-19 infection and the patient was suspected and considered as indexed case.

Patient 1 was a 58 year old man presented with dry cough and nasal congestion since 6th April 2020 (symptoms' onset). This patient had no co-morbid, but he was a smoker. He visited a private doctor on 7th April 2020 and chest X-ray examination showed infiltrate on basal of the right lung (**Figure 2**). On 9th April 2020, he visited our hospital and second chest X-ray on the same day showed bilateral infiltrate on both of the lung (**Figure 2**). He was directly hospitalized in isolation room. At presentation, laboratory examination showed elevated C-reactive protein (CRP) to 92.7 mg/L and low lymphocyte to 22.06% (**Table 1**). On the following day, dyspnea was occurred and his 3rd chest X-ray on 10th April 2020 showed progressive infiltrate in sub pleural and basal of both of lungs (chest X-ray developed/ progressed into more severe). The following lab examination showed reduced lymphocyte to 19.40%. He was prescribed antibiotic of Levofloxacin IV, antipyretic, antitusive, vitamin C supplement and

oxygenation. He was tested positive for SARS-CoV-2 by Real-Time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) assay on 11th April 2020. After confirmed as COVID-19 positive, this patient received Chroloquine 2 times a day, 400 mg as an antiviral. Laboratory examination showed reduced lymphocyte to 11.93% on 17th April 2020. Secondary bacterial infection got worse and Levofloxacin was changed to Cephalosporin. Bacterial culture was not evaluated due to cost limitation. The three times of RT-PCR evaluation every 5 days remained positive, while clinical condition which had been worsen in the previous days, was improved now. The following evaluation of RT-PCR showed negative for SARS-CoV-2 and patient was in good condition.

Patient 2 was a 34 year old woman (daughter of Patient 1 and Patient 3) presented with dry cough and nasal congestion since 4 April 2020. He visited a private doctor on 7th April 2020 then visited a hospital with Patient 1 due to persistent symptoms on 9th April 2020. She was prescribed symptomatic drugs. Laboratory examination showed normal percentage of lymphocyte to 38.89% (**Table 1**). Chest X-ray showed pulmonary nodule infiltrate in the right paracardial (**Figure 2**). She started self-isolation on 9th April 2020 and was tested using RT-PCR assay on 14th April 2020. The RT-PCR assay test showed a positive result for COVID-19. She received symptomatic drugs without antiviral. All symptoms were improved and she was recovered. RT-PCR test was negative for COVID-19 on 17th April 2020.

Patient 3 was a 63 year old woman (mother of Patient 2 and Patient 4) presented no symptom. This patient had co-morbid of Type 2 Diabetes Mellitus (T2DM). On 9th April 2020, she accompanied Patient 1 and Patient 2 to a hospital, under the instruction of doctor, she was recommended to get a chest X-ray due to abnormal chest X-ray results found in Patient 1 and Patient 2. Her chest X-ray showed infiltrate bilateral in the basal of both of the lungs (**Figure 2**). Laboratory examination showed low lymphocyte to 22.76% (**Table 1**). She was then admitted to the isolation room (triage) on the same day and was prescribed

Table 1. Summary of clinical features and laboratory results of the family cluster infected with COVID-19, at presentation.

	Patient 1 (Father)	Patient 2 (Daughter)	Patient 3 (Mother)	Patient 4 (Son)
Age (years)	58	34	63	30
Sex	Man	Woman	Woman	Man
Occupation	Retired	Unemployed	Housewife	Employee
Co-morbid	-	-	Type 2 Diabetes Mellitus	-
Fever	-	-	-	-
Body temperature (0C)	38.2	37,4	36.4	NA
Cough	+	+	+	-
	(Dry)	(Dry)	(Dry)	
Dyspnea	-	-	-	-
Headache	-	-	-	-
Myalgia	-	-	-	-
Sore throat	-	-	-	-
Nasal congestion	+	+	-	-
Fatigue	-	-	-	-
Anosmia	-	-	-	+
Ageusia	-	-	-	+
Gastrointestinal symptoms (diarrhea)	-	-	-	-
Chest x-ray infiltrates	+	+	+	-
Isolation room (triage)	+	-	+	-
Self-isolation	-	+	-	+
White blood cell (10 ³ /uL)	11.66	6.28	6.65	NA
Normal range 3.8-10.6	(↑)			
Lymphocyte (%)	22.06	36.89	22.76	NA
Normal range 25-40	(↓)		(↓)	
Hemoglobin (g/dL)	15.84	14.31	14.59	NA
Normal range 13.2-17.3				
Sodium (Na) (mmol/l)	120.80	NA	NA	NA
Normal range 125-147				
Potassium (K) (mmol/l)	3.50	NA	NA	NA
Normal range 3.5-5.0				
Chloride (Cl) (mmol/l)	99.60	NA	NA	NA
Normal range 95-105				
Glucose (md/dL)	126	NA	199	NA
Normal range <145				
Blood urea nitrogen (mg/dL)	13.1	NA	NA	NA
Normal range 10-20				
Creatinine (mg/dL)	0.82	NA	NA	NA
Normal range 0.62-1.10				
SGOT/AST (U/L)	82	75	NA	NA
Normal range 0-50	(↑)	(↑)		
SGPT/ALT (U/L)	51	69	NA	NA
Normal range 0-50	(↑)	(↑)		
C-reactive protein (mg/L)	92.7	NA	NA	NA
Normal range <6	(↑)			

NA=not available; +=positive (yes); -=negative (no); ↑=above normal range; ↓=below normal range.

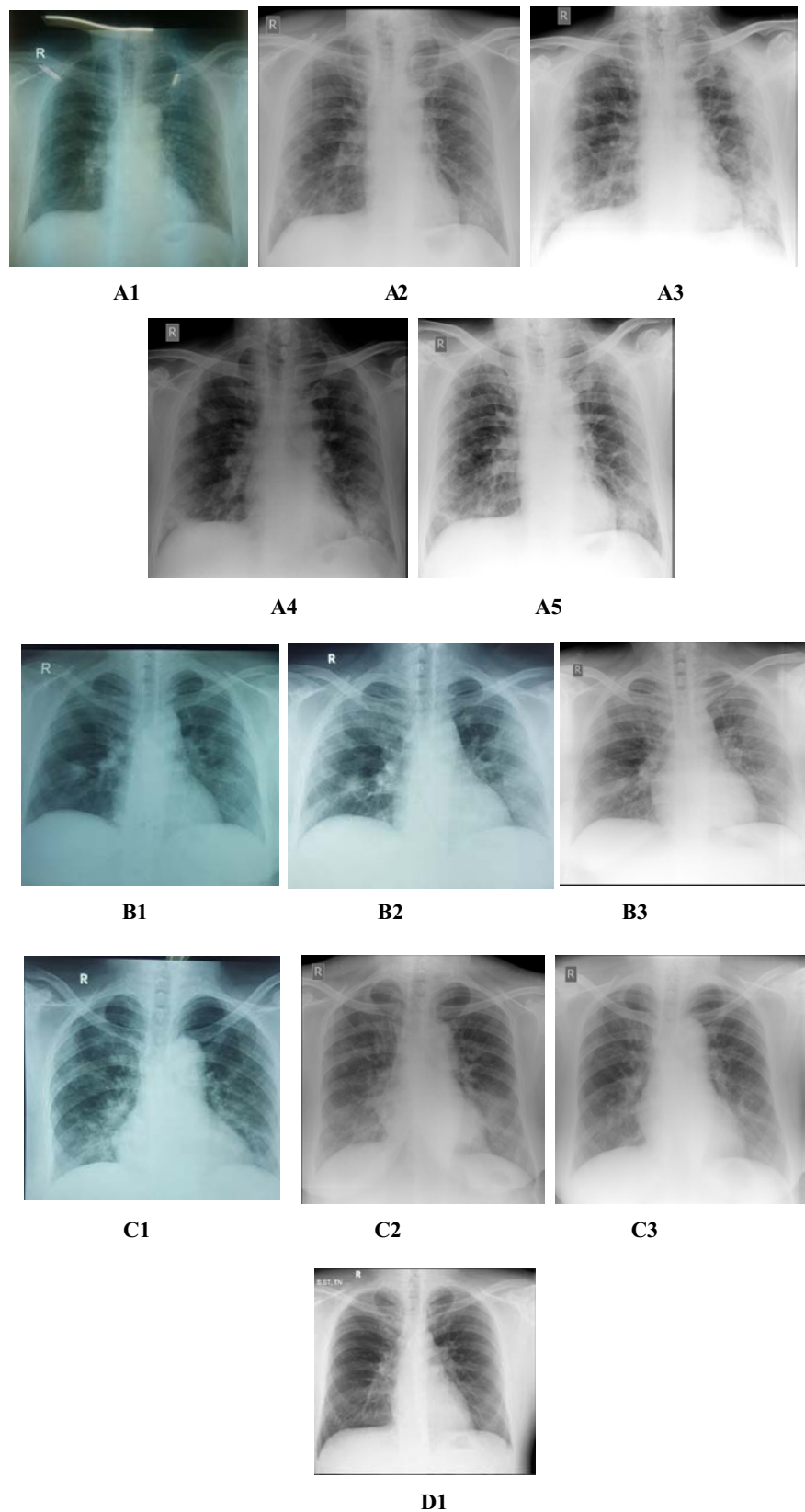


Figure 1. Chest radiograph of all patients. A. Patient 1; B. Patient 2; C. Patient 3; D. Patient 4; A1. 7th April 2020; A2. 9th April 2020; A3. 10th April 2020; A4. 20th April 2020; A5. 1st May 2020; B1. 7th April 2020; B2. 9th April 2020; B3. 17th April 2020; C1. 9th April 2020; C2. 14th April 2020; C3. 20th April 2020; D1. 10th April 2020).

only multivitamins. The RT-PCR test showed positive for SARS-CoV-2 on 11th April 2020. Chest X-ray examination on the 5th day of hospitalization showed improvement. On the 6th day, patients asked to be discharged from hospital and start her self-isolation at home. She still had no symptoms until she was tested negative for COVID-19, 3 weeks away from the first RT-PCR test.

Patient 4 was a 30 year old man (son of Patient 1 and Patient 3). This patient stated that he had implemented both social and physical distancing, hand hygiene, and wear mask when he was outside his house. He frequently visited and looked after Patient 1 (father), since Patient 1 felt sick. He also stated that he was in close contact with Patient 1. Chest X-ray on 10th April 2020 showed normal lungs (**Figure 2**). On 11th April 2020, he reported very mild symptoms such as anosmia and ageusia in a very short time which lasted only one day and recovered on the same day. He was tested positive for COVID-19 on 17th April 2020. Due to very mild symptoms, he started self-isolation at home. He was not prescribed any drugs and finished his 14 days of self-isolation. He was later tested negative for COVID-19, 3 weeks after the first RT-PCR test.

DISCUSSION

This family cluster of COVID-19 showed that infection caused by SARS-CoV-2 can present with different clinical manifestations. Patient 1, as suspected of indexed case, had no symptoms initially but developed symptoms later on. He also had a progressive severity of disease but then improved and recovered in one month. While Patient 2 who was most likely transmitted by Patient 1, initially showed symptoms of dry cough and nasal congestion then recovered in a short time. Patient 3 had no symptoms, while Patient 4 only presented with ageusia and anosmia in just a day and recovered. Chest X-ray of Patient 1, 2, and 3 showed abnormalities, while chest X-ray of Patient 4 showed normal lungs. RT-PCR of all patients also showed positive for COVID-19. These findings indicated that COVID-19 can be transmitted by asymptomatic carriers during the incubation period. A study in China also

reported the transmission of COVID-19 from asymptomatic carriers during the incubation period in a familial cluster.¹¹ Approximately 80% of infected individuals remain asymptomatic or present only with minor symptoms, whereas 15% become moderately to severely ill with cough and shortness of breath, and 5% require intensive care. Elderly people with underlying diseases, such as cardiovascular disease, diabetes mellitus, hypertension, chronic respiratory disease and malignancies, are at greater risk of developing severe COVID-19.¹² COVID-19 can affect all groups of ages and asymptomatic infection has been well described. In the large Chinese report, 2% of infections were in individuals below 20 years old. Similarly, in South Korea, 6.3% of nearly 8000 infections were in those younger than 20 years old. Pneumonia is the most frequent serious manifestation of infection, characterized primarily by fever, cough, dyspnea. There are no specific clinical features that can differentiate COVID-19 from other viral respiratory infections.¹⁰

Patient 1, as the indexed case, was in more severe condition and hospitalized for around 1 month due to persistent clinical manifestation, heavier dyspnea, followed by extendedly worsening of serial chest X-ray and a secondary bacterial infection from laboratory examination. Patient 3 had no symptoms but she was hospitalized for a week and was discharged for self-isolation, despite the remained positive result of RT-PCR. This was according to the guideline in Indonesia which allows COVID-19 patients with RT-PCR positive to implement self-isolation if the symptoms are very mild and patients are in good condition. Patient 2 and 4 started self-isolation for 14 days after confirmed for COVID-19. This was due to very mild symptoms of those patients. Self-isolation was done under supervision and monitored by Surabaya local public health authorities. Antiviral was only given to Patient 1, following the policy of hospital, which antiviral was only given to patient with moderate to severe symptoms of disease. Patients with mild symptoms were treated with symptomatic drugs.

Patient 1 was known as an active smoker. Smoking is a risk factor for many respiratory

infections, and could also trigger disease progression in those infected.¹³ Previous studies have shown that smokers are more likely to contract influenza and exhibit more severe symptoms than nonsmokers.¹⁴ Smoking was reported to be a risk factor for Middle East respiratory syndrome coronavirus (MERS-CoV) infection and associated with high mortality.¹⁵ The mechanisms in which smoking increases the risk of worsening pneumonia include altered airway architecture, inhibition of airway ciliary clearance and reduced immune function.¹⁴ The proportion of patients with severe symptoms was 21.2% among current smokers and 42.9% among past smokers, which was higher compared with those who had never smoked (14.5%). Only 4.7% of those who had never smoked developed critical outcomes.⁸

Co-morbidities such as cardiovascular disease, diabetes mellitus, chronic lung disease, hypertension and malignancies are believed to increase the risk of mortality.¹⁰ Although in this family cluster, Patient 3 had a co-morbidity of type 2 diabetes mellitus (T2DM) and presented with no symptoms. She was hospitalized and recovered in less than a week. This finding showed that patient with T2DM also had chance to recover from COVID-19.

There were some uncompleted data such as laboratory examination including procalcitonin due to the expensive cost of some examinations, which was not covered by the government because the hospital was not a referral hospital for COVID-19.

CONCLUSION

Physicians should be aware and raise suspicion on asymptomatic person who has no symptoms initially but may develop symptoms later because this asymptomatic person was able to transmit the virus. Diagnosis of COVID-19 should not only on clinical manifestations. Radiological and laboratory testing should be used in the diagnosis and RT-PCR was absolutely needed to confirm COVID-19.

CONFLICT OF INTEREST

We are exempt from ethical approval from The Second Islamic Hospital Surabaya

Institutional Review Board as it is not required in our hospital for a case report.

ACKNOWLEDGMENTS

Author thanks to Mayta Rithmala, M.D. and nurses of outpatient clinic and ward room of The Second Islamic Hospital Surabaya.

REFERENCES

1. World Health Organization. Novel coronavirus – China. <http://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/>. 12 January 2020.
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5).
3. World Health Organization Director-General's opening remarks at the media briefing on COVID-19. March 2020.
4. World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it. [https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-\(covid-2019\)-and-the-virus-that-causes-it](https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it) (accessed Mar 24, 2020).
5. Russel B, Moss C, Rigg A, Hopkins C, Papa S, Van Hemelrijck. Anosmia and ageusia are emerging as symptoms in patients with COVID-19: what does the current evidence say?. *Ecancer*. 2020; 14: ed98. <https://doi.org/10.3332/ecancer.2020.ed98>.
6. Benezit F, Turnier P, Declerck C, et al. Utility of hyposmia and hypogeusia for the diagnosis of COVID-19. *Lancet Infect Dis*. 2020. [https://doi.org/10.1016/S1473-3099\(20\)30297-8](https://doi.org/10.1016/S1473-3099(20)30297-8).
7. Yang X, Xu J, Shu H, 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. [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5).
8. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020. <https://doi.org/10.1056/NEJMoa2002032>; PMID: 32109013; epub ahead of press.
9. Han R, Huang L, Jiang H, Dong J, Peng H, Zhang D. Early clinical and CT manifestation of coronavirus disease 2019 (COVID-19) pneumonia. *Am J Roentgenol*. 2020;215:1-6.
10. International Pulmonologists's Consensus on COVID-19: 2nd Edition. 2020. India.
11. Ye F, Xu S, Rong Z, et al. Delivery of infection from asymptomatic carriers of COVID-19 in a familial cluster. *Int J Infect Dis*. 2020;94:133-8.
12. Komiyama M, Hasegawa K. Smoking cessation as a public health measure to limit the coronavirus disease

- 2019 pandemic. 2020;15:e16. <https://doi.org/10.15420/ecr.2020.11>.
13. Groskreutz DJ, Monick MM, Babor EC, et al. Cigarette smoke alters respiratory syncytial virus-induced apoptosis and replication. *Am J Respir Cell Mol Biol* 2009;41:189–98. <https://doi.org/10.1165/rcmb.2008-0131OC>; PMID: 19131644.
 14. Arcavi L, Benowitz NL. Cigarette smoking and infection. *Arch Intern Med*. 2004;164:2206–16. <https://doi.org/10.1001/archinte.164.20.2206>; PMID: 15534156.
 15. Park JE, Jung S, Kim A, Park JE. MERS transmission and risk factors: a systematic review. *BMC Public Health* 2018;18:574. <https://doi.org/10.1186/s12889-018-5484-8>; PMID: 29716568.