Epidemiology and clinical characteristics

Update March 2021 – what's new?

- Updated figures for asymptomatic patients, pre-symptomatic patients, and infection fatality ratio.

The mean incubation period for COVID-19 is 4-5 days. Patients may be infectious for 2-3 days prior to the onset of symptoms however.

The strongest risk factor for severe disease is advanced age. Other risk factors include cardiopulmonary comorbidities, obesity, HIV, and diabetes mellitus.

The spectrum of COVID-19 clinical presentations includes asymptomatic infection, a respiratory tract infection that may range from mild to severe, and atypical manifestations such as diarrhoea, skin manifestations, hyperglycaemic syndromes and large vessel strokes.

SARS-CoV-2 is a betacoronavirus closely related to SARS-CoV and MERS-CoV. It is an enveloped, non-segmented, positive sense RNA virus. It is thought to have originated in bats but the animal responsible for transmission to humans remains unknown.

Epidemiology

The median incubation period for COVID-19 is estimated to be 4-5 days, with an interquartile range of 2-7 days. Based on patients' viral shedding patterns and on epidemiological modelling, patients appear to be infectious for 2-3 days prior to the onset of symptoms, and the contribution of pre-symptomatic infections to the overall pandemic may be substantial.[1-7] The basic reproductive number for the virus is approximately 2.2 (meaning that on average each person spread the infection to two others).[8] A male preponderance of cases has been noted globally both in terms of absolute case numbers, and in severe disease.[9-11] Risk factors for severe disease include older age, cardiopulmonary comorbidities, obesity, HIV, and diabetes mellitus. Very few cases which required hospitalisation have been reported among children under the age of 15 years (~1%).

Clinical characteristics – what to look for

Truly asymptomatic COVID-19 patients (as distinguished from pre-symptomatic patients) comprise approximately 20% of COVID-19 cases.[12-14] Around half the patients who are asymptomatic at the time of diagnosis are actually pre-symptomatic however.[15,16] Among symptomatic patients in China, 81% developed mild disease, an estimated 14% developed severe disease (with hypoxaemia, marked tachypnoea and extensive lung infiltrates), while 5% became critically ill (with respiratory failure, septic shock and/or multiorgan dysfunction).[17] Because of the strong effect of age on disease severity, the proportions of mild, severe, and critical cases seen in a country will partially depend on that country's population age structure.

The most common presenting symptom has been fever in approximately 90%, but importantly this may only be present in a minority of patients on admission.[11,18] A cough is present in two-thirds of patients, but sputum production is only reported by one third of patients, as is dyspnoea. Myalgia, a sore throat, nausea, vomiting, and diarrhoea are all present in less than one fifth of cases.[11,18,19] Anosmia (loss of sense of smell) and dysgeusia (alteration of the sense of taste) have also emerged as relatively common, early, and moderately specific symptoms.[20,21] Atypical manifestations are

increasingly being recognised, including large vessel strokes in young patients, diabetic ketoacidosis/hyperglycaemic hyperosmolar syndrome, unexplained abdominal pain and various dermatological manifestations.[22,23]

Abnormalities are visible on chest X-ray in at least 60% of hospitalised COVID-19 patients, with chest CT scans being more sensitive.[11,18,24] These are typically bilateral patchy ground glass opacities, though other patterns have been described.[11,25] However, a normal chest X-ray or chest CT scan does not rule out COVID-19. This is especially true of patients with mild disease, in whom a majority of chest X-rays may be normal.[26]

Outcomes and prognosis

The vast majority of cases will make a full recovery, although this may take several weeks, particularly in severe cases. In a minority of cases, COVID-19 has been associated with rapid progression to acute respiratory distress syndrome (ARDS), multiple organ failure and sometimes death. Internationally, the case fatality ratio has ranged between 0.7-7%, and is partially determined by the particular population's age distribution, the pandemic's burden on the healthcare system at the time, and the extent to which mild or asymptomatic cases are diagnosed.[9,27] The infection fatality ratio (which includes both asymptomatic and symptomatic patients) is estimated at around 0.8% overall, though again there is substantial age-related variability, from <1 per 10,000 cases in those less than 30 years to 12% in those over 80 years of age.[28] Full recovery from COVID-19 may take several weeks, and in a minority, symptoms can persist for >1 month (now often referred to as "long-COVID", see module 11). A multisystem inflammatory syndrome resembling Kawasaki disease has also been described, occurring almost exclusively in patients aged <21 years ("MIS-C syndrome"), and typically appearing 2-3 weeks after the primary infection.[29]

References

1. Du Z, Xu X, Wu Y, Wang L, Cowling BJ, Meyers LA. Serial Interval of COVID-19 among Publicly Reported Confirmed Cases. Emerg Infect Dis. 2020;26(6).
2. Yu P, Zhu J, Zhang Z, Han Y, Huang L. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. J Infect Dis. 2020.
3. Tindale L, Coombe M, Stockdale JE, Garlock E, Lau WYV, Saraswat M, et al. Transmission interval estimates suggest pre-symptomatic spread of COVID-19. medRxiv. 2020:2020.03.03.20029983.
4. Nishiura H, Linton NM, Akhmetzhanov AR. Serial interval of novel coronavirus (COVID-19) infections. Int J Infect Dis. 2020;93:284-6.
5. Nishiura H, Kobayashi T, Suzuki A, Jung SM, Hayashi K, Kinoshita R, et al. Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). Int J Infect Dis. 2020.
6. Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, et al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. New England Journal of Medicine. 2020.
7. Gandhi M, Yokoe DS, Havlir DV. Asymptomatic Transmission, the Achilles' Heel of Current Strategies to Control Covid-19. New England Journal of Medicine. 2020.
8. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med. 2020.
9. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA. 2020.
10. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368:m1091.

11. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020.
12. Buitrago-Garcia D, Egli-Gany D, Counotte MJ, Hossmann S, Imeri H, Ipekci AM, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. PLoS Med. 2020;17(9):e1003346.
13. Byambasuren O, Cardona M, Bell K, Clark J, McLaws M-L, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. medRxiv. 2020:2020.05.10.20097543.
14. Pollock AM, Lancaster J. Asymptomatic transmission of covid-19. BMJ. 2020;371:m4851.
15. Yanes-Lane M, Winters N, Fregonese F, Bastos M, Perlman-Arrow S, Campbell JR, et al. Proportion of asymptomatic infection among COVID-19 positive persons and their transmission potential: A systematic review and meta-analysis. PLoS One. 2020;15(11):e0241536.
16. He J, Guo Y, Mao R, Zhang J. Proportion of asymptomatic coronavirus disease 2019: A systematic review and meta-analysis. J Med Virol. 2021;93(2):820-30.
17. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020.
18. Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A, et al. Clinical Characteristics of Covid-19 in New York City. N Engl J Med. 2020.
19. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020.
20. Giacomelli A, Pezzati L, Conti F, Bernacchia D, Siano M, Oreni L, et al. Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. Clin Infect Dis. 2020.
21. Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and Covid-19 in patients presenting with influenza-like symptoms. Int Forum Allergy Rhinol. 2020.
22. Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP, et al. Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young. N Engl J Med. 2020.
23. Galvan Casas C, Catala A, Carretero Hernandez G, Rodriguez-Jimenez P, Fernandez Nieto D, Rodriguez-Villa Lario A, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. Br J Dermatol. 2020.
24. Wong HYF, Lam HYS, Fong AH-T, Leung ST, Chin TW-Y, Lo CSY, et al. Frequency and Distribution of Chest Radiographic Findings in COVID-19 Positive Patients. Radiology.0(0):201160.
25. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients. AJR Am J Roentgenol. 2020:1-7.
26. Weinstock MB EA, Russell JW, et al. Chest x-ray findings in 636 ambulatory patients with COVID-19 presenting to an urgent care center: a normal chest x-ray is no guarantee. J Urgent Care Med. 2020;14(7):13-8.
27. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)2020. Available from: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf.
28. Pastor-Barriuso R, Pérez-Gómez B, Hernán MA, Pérez-Olmeda M, Yotti R, Oteo-Iglesias J, et al. Infection fatality risk for SARS-CoV-2 in community dwelling population of Spain: nationwide seroepidemiological study. BMJ. 2020;371:m4509.
29. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet. 2020.