Clinical Profile of Coronavirus Disease 2019 Comparing the First and Second Waves: A Single-Center Study from North India

Abstract

Background and Objectives: Severe acute respiratory syndrome coronavirus 2, caused by the novel coronavirus disease 2019 (COVID-19), led to a devastating pandemic that hit majority of the countries globally in a wave-like pattern. The characteristics of the disease varied in different geographical areas and different populations. This study highlights the epidemiological and clinical characteristics of COVID-19 during two major waves in North India. Materials and Methods: Clinical characteristics and outcomes of all COVID-19-reverse transcription-polymerase chain reaction-positive patients, admitted from March 2020 to June 2021, to a tertiary care center in North India, were studied retrospectively. Results: During this period, total of 5652 patients were diagnosed having COVID. Patients who were incidentally diagnosed as COVID-positive (n=667) with other unrelated comorbid conditions and patients admitted under level 1 facility (n=1655; 1219 from first and 436 from second wave) were excluded from final analysis. Males were most commonly affected in both waves, with male to female ratio 4:1 in first and 3:1 in second wave. First wave had significantly more people with co-morbidities like diabetes mellitus and hypertension (P<0.001), whereas younger age group (age <40 years) were significantly more affected in second wave (P= 0.000). Fever was the most common presenting complaint in both waves, followed by cough and breathlessness. Patients during first wave had more severe disease at presentation and high mortality compared to the second wave. Conclusion: Majority of the patients with COVID-19 infection presenting to our hospital were young during the second wave. Fever was noted as presenting manifestation. Mortality was low during the second wave as compared to the first wave, likely to be due to proper protocol-based treatment resulting in better outcomes.

Keywords: Comorbidities, coronavirus disease 2019, first wave, pandemic, second wave, severe acute respiratory syndrome coronavirus 2

Introduction

Coronaviruses have been reported as a cause of mild and moderate respiratory infections for over 50 years. Even though this group of viruses has been isolated from many different animals, bats are accepted as a major natural reservoir of coronaviruses. Recently detected coronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) (2002), and middle east respiratory syndrome-CoV (2012) completely altered all known approaches about this virus group because these viruses caused severe acute respiratory infections and nosocomial outbreaks. The first outbreak of coronavirus disease 2019 (COVID-19) occurred in Wuhan, Hubei province, in early December 2019 where several patients with viral pneumonia were found to be epidemiologically associated with the Huanan Seafood Market in Wuhan. At present, the whole world has faced the challenge of this pandemic.

In various countries, the first wave, the second wave, and the third wave have already happened. India has suffered from the first and second waves and preparing itself for the upcoming danger of the third wave. Despite the same virus and pandemic, different countries and regions have observed considerable disparities in the patterns, clinical manifestations as well as the outcome. A study from India suggested that the second COVID-19 wave in India began on February 11, 2021. As per this study, the virus was much more infectious than the first wave, though the number of daily deaths per infection was lower compared with the first wave. The study shows that there is a higher disease burden in lower socioeconomic groups. A milder disease...
pattern is seen in children with COVID-19 as compared with adults.\textsuperscript{[3]}

The end of the first wave was likely to be a result of a combination of factors – effective implementation of government interventions, increase in awareness, and most importantly, the experience gained by the medical professionals in treating the disease over the initial months. There was a rapid rise in number of COVID-19 patients during the second wave. The sudden surge in the number of cases after a relatively long “cooling” time may be attributed to highly infectious double mutant variant of SARS-CoV-2 (B.1.617 lineage), to negligent the behavior of the population, and to the relaxation of interventions.\textsuperscript{[6-8]}

The number of daily deaths was also high during the second wave, but the overall case fatality rate was low compared to the first wave.

In our part of the country, we too noticed some dissimilarities between disease profile during the first and second waves. Therefore, we planned to analyze all the demographic and clinical data, laboratory parameters, and outcomes of COVID-19 patients admitted in our hospital during both waves. The objective of this study was to describe the clinical characteristics of COVID-19 patients admitted in our hospital during the first and second waves so as to understand the trend of the disease and to plan the effective and better implementation of treatment strategies and future management of patients.

Materials and Methods

Study settings and data collection

This study was conducted in Dayanand Medical College and Hospital (DMCH), Ludhiana, Punjab. DMCH, Ludhiana, is a 1625-beded, tertiary care referral hospital in the center of Punjab. DMCH is catering patients from various states, more frequently from Punjab, Haryana, Himachal Prades, and Jammu and Kashmir. We collected data of all reverse transcription-polymerase chain reaction (RT-PCR)-positive, COVID-19 patients admitted in our hospital during the first and second waves on their demographic, epidemiological, clinical, laboratory parameters, oxygen requirement, treatment as well as outcome. The data were collected from March 2020 to June 2021. DMCH, Ludhiana, has dedicated facilities to manage COVID-19 patients as well as well-equipped emergency area. Patients with all levels of severity were admitted in the hospital. All the COVID-19 facility areas were divided into level 1, level 2, and level 3 areas, and patients were admitted in these areas as per the clinical condition and oxygen requirement. All the patients reaching in triage area were assessed by the dedicated COVID team. At the arrival in the emergency, vital signs including blood pressure, pulse rate, respiratory rate, oxygen saturation, and temperature were checked for all the patients. In the meantime, patients and their family members were interviewed regarding onset of symptoms, history of presenting complaints as well as history of contact and travel. Date of onset of symptoms and date of first RT-PCR positive (in patients where it was done already) were noted. Baseline investigations including hemogram, liver and kidney function tests, C-reactive protein (CRP) levels, D-dimer levels, interleukin-6 (IL-6) levels, serum ferritin, and chest X-ray were done for all symptomatic patients and computed tomography (CT) chest and CT pulmonary angiography in those at risk of severe disease. Elderly patients with age >60 years and those with comorbid conditions such as hypertension, coronary artery disease, diabetes mellitus, chronic obstructive airway disease, chronic liver or kidney disease, immune-compromised state, and obesity were considered high risk for progression to severe disease.

Patient segregation as per symptomatology and facility

Level 1 facility

Patients with mild symptoms, oxygen saturation >94% on room air with normal chest X-Ray or CT Chest, with no evidence of lower respiratory tract involvement were considered for level 1 facility.

Level 2 facility

Patients with radiologically proven pneumonia, with oxygen saturation <94%, with evidence of lower respiratory tract involvement clinically, or on chest X-ray or CT chest were shifted to level 2 facility.

Level 3 facility

Patients with tachypnea, shock, respiratory distress, or oxygen saturation between 92% and 94% or below this with lower respiratory tract involvement and patients who were confused, drowsy, or in shock were shifted to level 3 facility.

Sample collection and processing

Throat and nasopharyngeal samples were collected for all patients suspected of SARS-CoV-2 infection using Dacron swabs by the trained infection control nurses. All the samples were immersed in viral transport medium (VTM) immediately and transported in triple-layered packaging to the microbiology laboratory. The samples were processed in a biological safety cabinet (Type IIB). RNA was extracted from VTM fluid followed by real-time RT-PCR using the standardized National Institute of Virology, Pune, protocol.\textsuperscript{[9]}

As per the hospital policy, follow-up nasopharyngeal and throat swabs for RT-PCR were sent after 10–14 days of symptom onset or 2–3 days of symptom resolution. If the follow-up RT-PCR was positive, another sample was sent after 4 days. Patients were discharged after negative RT-PCR tests. They were advised for home isolation once the patient was off oxygen for more than 48 h. Outcomes were recorded as discharge or death.
All patients were started on antibiotics as per guidelines at that time. All patients received azithromycin or antibiotics as per sepsis. In the case of oxygen requirement, steroids were started along with LMWH. Patients in levels 2 and 3 received injection remdesivir, steroids, and therapeutic dose of LMWH. Few patients received tocilizumab as per clinical and laboratory parameters.

Ethical clearance was taken from the Institutional Ethical Committee, vide number DMCH/RandD/2021/115

Statistical analysis

Continuous data were presented as mean standard deviation, if normally distributed, and median (interquartile range [IQR]), if data were nonnormal. Categorical variables were presented as frequency and percentages (n; %). Comparability of groups was analyzed by Chi-square test, Student’s t-test, or Mann–Whitney test as appropriate. IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA) software was used for statistical analyses.

Results

During the year 2020 first wave and 2021 second wave, a total of 5652 patients were admitted in the hospital. Out of these, 667 patients were excluded from final analysis due to various reasons like patients with incidental diagnosis of COVID-19 positivity, patients presenting to the hospital with poisoning, poly-trauma, terminal malignancy, obstetrics/gynecological indications, elective surgeries and procedures and patients whose data was incomplete. Level-1 patients were also excluded, as we planned to analyze the various parameters of patients admitted in level 2 and level 3 only. First wave had more number of patients in level 1 as compared to second wave. Finally 1744 patients from the first wave and 1596 from the second wave were included for the analysis [Figure 1].

In the first wave, out of 1744 patients, 509 (29%) were female and 1235 (71%) were male. More female patients, i.e., 598 (37%), were admitted during the second wave as compared to the first wave. In the second wave, patients below 40 years of age group were more as compared to the first wave (P = 0.000) [Table 1 and Figure 1]. More number of patients had diabetes mellitus and hypertension during the first wave as compared to the second wave [Figure 2]. Majority of the patients had more than two comorbid conditions during the first wave as compared to the second wave [Figure 3]. Fever and cough as presenting symptoms were found more commonly during the second wave as compared to the first wave [Table 1]. On comparing the oxygen requirement during both waves, more number of patients were on HFNC during the first wave (P = 0.000) as compared to NRBM, while more were seen on NRBM during the second wave and difference was statistically significant (P = 0.050) [Table 2]. Patients received medications as per clinical situation. One hundred and ninety-two patients during the first wave received medications as per clinical situation. One hundred and ninety-six patients during the second wave and difference was statistically significant (P = 0.000) [Table 2].

| Wave | 1 (n=1744), n (%) | 2 (n=1596), n (%) | P |
|------|------------------|------------------|---|
| Age group | | | |
| <20 | 16 (1) | 40 (3) | 0.000 |
| 21-30 | 48 (3) | 121 (8) | 0.000 |
| 31-40 | 128 (7) | 191 (12) | 0.000 |
| 41-50 | 263 (15) | 266 (17) | 0.000 |
| 51-60 | 484 (28) | 366 (23) | 0.000 |
| 61-70 | 517 (30) | 360 (23) | 0.000 |
| >70 | 288 (17) | 252 (16) | 0.000 |
| Age, median (IQR) | | | 0.000 |
| Gender | | | |
| Female | 509 (29) | 598 (37) | 0.0001 |
| Male | 1235 (71) | 998 (63) | 0.0001 |
| COVID diagnosis | | | |
| Antigen | 348 (20) | 254 (16) | 0.0001 |
| RT-PCR | 1055 (60) | 1218 (76) | 0.0001 |
| CT-chest | 73 (4) | 54 (3) | 0.226 |
| Anti-SARS Ab | 50 (3) | 36 (2) | 0.265 |

| Number of comorbidities | | | 0.0001 |
| 0 | 441 (25) | 584 (37) | 0.0001 |
| 1 | 483 (28) | 510 (32) | 0.0001 |
| 2 | 585 (34) | 353 (22) | 0.0001 |
| 3 | 184 (11) | 125 (8) | 0.0001 |
| 4 | 42 (2) | 24 (2) | 0.0001 |
| 5 | 7 (0) | 0 | 0 |

| Comorbidities | | | |
| DM | 906 (52) | 684 (43) | 0.0001 |
| HT | 770 (44) | 549 (34) | 0.0001 |
| CAD | 185 (11) | 141 (9) | 0.085 |
| HF | 8 (0) | 5 (0) | 0.500 |
| PVD | 5 (0) | 1 (0) | 0.127 |
| Prostatic valve | 4 (0) | 3 (0) | 0.794 |
| CKD | 147 (8) | 94 (6) | 0.914 |
| Renal Tx | 5 (0) | 2 (0) | 0.308 |
| CLD | 60 (3) | 56 (4) | 0.914 |
| HCV | 14 (1) | 6 (0) | 0.110 |
| HBsAg | 6 (0) | 1 (0) | 0.076 |
| HIV | 3 (0) | 2 (0) | 0.727 |
| Drug addict | 9 (1) | 13 (1) | 0.287 |
| Obesity | 222 (13) | 88 (6) | 0.000 |
| COAD | 22 (1) | 6 (0) | 0.005 |
| Asthma | 23 (1) | 19 (1) | 0.740 |
| ILD | 3 (0) | 3 (0) | 0.913 |
| Cancer | 18 (1) | 14 (1) | 0.646 |

Contd...
Table 1: Contd...

| Wave  | 1 (n=1744), n (%) | 2 (n=1596), n (%) | P  |
|-------|-------------------|-------------------|----|
| Chest pain | 46 (3)            | 28 (2)            | 0.083 |
| Loss of taste/smell | 12 (1)            | 17 (1)            | 0.241 |
| Loose stools | 43 (2)            | 29 (2)            | 0.197 |
| Vomiting | 51 (3)            | 41 (3)            | 0.531 |
| Altered sensorium | 66 (4)           | 33 (2)            | 0.003 |
| Asymptomatic | 21 (1)            | 38 (2)            | 0.010 |

IQR: Interquartile range; RT-PCR: Reverse transcriptase-polymerase chain reaction; CT: Computed tomography; DM: Diabetes mellitus; HT: Hypertension; CAD: Coronary artery disease; HF: Heart failure; PVD: Peripheral vascular disease; CKD: Chronic kidney disease; CLD: Chronic liver disease; HCV: Hepatitis C virus; HBsAg: Hepatitis B Ag; COAD: Chronic obstructive airway disease; ILD: Interstitial lung disease; SARS Ab: Severe acute respiratory syndrome, corona virus antibodies; SOB: Shortness of breath

methylprednisolone pulse therapy. About 156 patients received tocilizumab during the first and second waves. Two patients of level 2 received monoclonal antibody cocktail regimen (casirivimab and imdecvimab).

Hospital stay and final outcome

There was a significant difference between the hospital stay of patients during the first wave, median 8 (IQR: 5–13), and in the second wave, 7 (5–12) (P = 0.009), with a maximum stay of 54 days in the first wave as compared to 45 days in the second wave. One thousand two hundred and fifty-one (78%) patients were discharged from hospital in the second wave as compared to 1151 (66%) of the first wave and 593 (34%) expired from the second wave in comparison to 345 (22%) of the second wave. There was a significant difference in the final outcome of patients (P = 0.0001) [Table 2].

Laboratory parameters

CRP values were high at baseline in the first wave, 85.39 (IQR: 31–166.89), compared to the second wave, 65.7 (IQR: 23.77–139.2) (P = 0.000). Similarly, there was a significant difference in D-dimer at admission in the first wave, 636 (315–1000), and the second wave, 404 (IQR: 222–849.25) (P = 0.000). There was not much difference in ferritin at admission 506 during the first wave (IQR: 232–1000) versus 508.85 during the second wave (IQR: 237.5–1031.25).

Other laboratory parameters are mentioned in Table 3.

Discussion

Since the initial reports of COVID-19 in early December 2019, the novel coronavirus outbreak continues to strain modern society, and its pathogenesis remains to be fully elucidated. A public health challenge has appeared due to mutations of the SARS-CoV-2 virus which makes it highly contagious. For example, the SARS-CoV-2 lineage B.1.1.7, which was first detected in the United Kingdom in November 2020, is estimated to be 40%–80% more transmissible than the wild-type SARS-CoV-2.[6,7]

Using one of the largest North Indian patient populations across a range of clinical services, including OPD, IPD, and ICU admission, we assessed the associations between various demographic factors including age, sex, and ethnicity on CoV-2 infection testing, clinical severity, and mortality in the first wave and the second wave of COVID-19. All the patients were managed as per the severity of the disease. Time-to-time standard diagnostic and treatment protocols as well as guidelines issued by the government for the management were followed. In our study, there was a difference in the age of patients in the first wave 60 (IQR: 50–67) and the second wave 55 (IQR: 42–66) (P = 0.000). As per our hospital data, during the second wave of COVID-19, patients below 40 years of age group were more in number as compared to the first wave. This age pattern is comparable to a study by Soni et al., median age 33 years;[10] a study by Gupta et al.,[11] where mean age was 40.3 years; and another study from a tertiary care hospital in northern India in comparison to data by China (median age – 56 years).[12] New York (median age – 63 years)[13] or Italy (median age – 63 years),[14] where patients were of higher age.

The other difference noted was that there were more females, 598 (37%), during the second wave as compared to 509 (29%) during the first wave. The reasons for the same may be that the second wave of COVID-19 affected all the age groups and genders equally, with preponderance for younger age group and elderly during the first wave. This was in concordance with first-wave data from Wuhan, China, where majority of the patients were in the sixth decade.[15] Fever was present in 73% of our patients in the second wave and 63% during wave one, followed by cough and...
breathlessness. It is similar to other reports across the globe, including a report from Bangladesh where 89% of patients had fever at presentation and a Chinese cohort in which 44% had fever at the time of presentation and 88% developed fever during the hospital stay.[12,16‑19] In the present study, the first wave cohort had significantly higher incidence co-morbidities as compared to the second (P=0.0001). This could be because of predominance of elderly patients in the first wave. A study by Saxena et al. showed that comorbidities such as diabetes mellitus and chronic diseases of lungs, heart, and kidneys were found to be common in symptomatic group and this was found to be statistically significant.[17]

There are various biomarkers such as CRP, D-dimer, IL-6, ferritin, LDH, besides total leukocyte count, low albumin, and high creatinine to predict disease severity. These markers were found quite high in patients with moderate-to-severe COVID disease. Patients with high D-dimers or rising levels were started empirically with LMWH, to prevent deep venous thrombosis as well as to prevent acute PTE.

The median hospital stay in China ranged from 4 to 33 days, and outside China hospitals, it ranged from 4 to 21 days outside of China.[15] Severity at presentation was more during the first wave. Patients with severe disease at presentation had longer hospitalization. This is similar to our study; the median duration of hospital stay in our study was 8 days in the first wave and 7 days during the second wave, with a maximum stay of 54 days in the first wave compared to 45 days in the second wave. It favors the better outcome in patients admitted during the second wave, maybe due to better treatment options available. Mortality was 22% during the second wave as compared to 34% during the first wave (P = 0.00001). Mortality was more than double in males as compared to females (68% vs. 32%).

The strengths of our study were that our study population was large and all the data were captured meticulously. There
Table 3: Laboratory parameters of patients during the first and second waves

|                                      | Wave 1            | Wave 2            | P    |
|--------------------------------------|-------------------|-------------------|------|
|                                      | Median (IQR)      | Median (IQR)      |      |
| RBS/diabetes_Pr. RBS                 | 160 (119-241)     | 150 (108.5-242)   | 0.013|
| RBS/diabetes_HBA1C                   | 7.9 (6.75-9.95)   | 7.8 (6.7-9.9)     | 0.968|
| CRP                                  |                   |                   |      |
| At admission                         | 85.39 (31-166.89) | 65.7 (23.7-139.2) | 0.000|
| At discharge                         | 18.79 (3.5-78)    | 24.23 (6.14-83.125) | 0.017|
| D-dimer                              |                   |                   |      |
| At admission                         | 636 (315-1000)    | 404 (222-849.25)  | 0.000|
| At discharge                         | 496 (254-1000)    | 387 (194-1113)    | 0.032|
| Ferritin                             |                   |                   |      |
| At admission                         | 506 (232-1000)    | 508.85 (237.5-1031.25) | 0.821|
| At discharge                         | 560.8 (232.25-1077.75) | 569.45 (295.875-1087.75) | 0.621|
| IL-6                                 |                   |                   |      |
| At admission                         | 50.43 (13.875-135.1) | 52.51 (18.54-150.51) | 0.300|
| At discharge                         | 26 (7.16-91.13)   | 44 (12.29-201.1)  | 0.124|
| LDH                                  |                   |                   |      |
| At admission                         | 354 (258-516.75)  | 403 (283-564)     | 0.000|
| At discharge                         | 312 (212.75-478.75) | 424 (286.5-692)  | 0.000|
| Hemoglobin                           |                   |                   |      |
| At admission                         | 12.1 (10.4-13.5)  | 12.2 (10.8-13.5)  | 0.014|
| At discharge                         | 11.8 (9.9-13.2)   | 11.9 (10.2-13.3)  | 0.029|
| Hematocrit                           |                   |                   |      |
| At admission                         | 37 (32.425-41.1)  | 37.8 (33.7-41.525) | 0.002|
| At discharge                         | 36 (30.7-40)      | 36.5 (32-40.4)    | 0.044|
| TLC                                  |                   |                   |      |
| At admission                         | 9.7 (6.9-14.8)    | 9.3 (6.2-13.4)    | 0.000|
| At discharge                         | 11.2 (8-16.4)     | 10.6 (7.5-15.2)   | 0.007|
| DLC-N                                |                   |                   |      |
| At admission                         | 82 (71-89.05)     | 81.8 (71-89)      | 0.350|
| DLC-L                                |                   |                   |      |
| At admission                         | 10 (5.6-19)       | 11 (6-20)         | 0.044|
| Platelets                            |                   |                   |      |
| At admission                         | 207 (150-279)     | 192 (150-259.25)  | 0.013|
| At discharge                         | 220.5 (147.75-320.25) | 220 (154-314) | 0.515|
| At discharge                         | 14.1 (11.7-16.8)  | 13 (11.8-15.6)    | 0.156|
| INR                                  |                   |                   |      |
| At admission                         | 1.12 (1.05-1.28)  | 1.1 (1.06-1.23)   | 0.075|
| At discharge                         | 1.245 (1.0775-1.5025) | 1.23 (1.09-1.42) | 0.753|
| APTT                                 |                   |                   |      |
| At admission                         | 26.095 (21.575-36.725) | 31 (27.1-36.725) | 0.139|
| At discharge                         | 1.415 (1.1-25.705) | 30.5 (107-47.175) | 0.606|
| Fibrinogen                           |                   |                   |      |
| At admission                         | 194 (0.985-457.5) | 1.1 (0.91-158)    | 0.036|
| At discharge                         | 1.98 (1.98-1.98)  | 0.51 (0.07-0.95)  | 0.221|
| Blood urea                           |                   |                   |      |
| At admission                         | 42 (28-71)        | 36 (25-57)        | 0.000|
| At discharge                         | 52 (35-112)       | 47 (31-83.75)     | 0.000|
| Creatinine                           |                   |                   |      |
| At admission                         | 0.94 (0.7-1.5)    | 0.83 (0.67-1.18)  | 0.000|
| At discharge                         | 0.9 (0.61-1.985)  | 0.78 (0.59-1.4)   | 0.000|
| Na                                   |                   |                   |      |
| At admission                         | 137 (134-140)     | 138 (134-140)     | 0.060|

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are few limitations in our study. It was a single-center, retrospective study. We do not have much information on mild cases as we did not include level 1 cases in our analysis.

Conclusions

COVID-19 virus affected almost all of the countries. During the second wave, both young and old patients were affected as compared to the first wave. Fever and tachypnea were the most common presenting manifestations during the second wave. Patients during the first wave had more comorbidities. The overall mortality rate was less during the second wave as compared to the first wave, maybe due to better treatment options, team management, and better facilities. Seeing the severity of
the disease, all the nations are taking extensive measures to accelerate the vaccination drive in order to control the pandemic at the earliest.

**Ethical clearance**

Ethical clearance was taken from the Institutional Ethical Committee, vide number DMCH/RandD/2021/115.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Fung TS, Liu DX. Human coronavirus: Host-pathogen interaction. Annu Rev Microbiol 2019;73:529-57.
2. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 2019;17:181-92.
3. Yu P, Hu B, Shi ZL, Cui J. Geographical structure of bat SARS-related coronaviruses. Infect Genet Evol 2019;69:224-9.
4. Ranjan R, Sharma A, Verma MK. Characterization of the second wave of COVID-19 in India. Current Science 2021;121:85-93. doi: 10.18520/cs/v121/i1/85.
5. Sarangi B, Reddy VS, Oswal JS, Malshe N, Patil A, Chakraborty M, et al. Epidemiological and clinical characteristics of COVID-19 in Indian children in the initial phase of the pandemic. Indian Pediatr 2020;57:914-7.
6. Davies NG, Abbott S, Barnard RC, Jarvis CI, Kucharski AJ, Munday JD, et al. Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. Science 2021;372:eabg3055.