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Original Article

# Clinical characteristics and treatment outcomes of SARS-CoV-2 delta variant outbreak, Pingtung, Taiwan, June 2021

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**KEYWORDS**
Coronavirus disease 2019;
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*Background:* An outbreak of SARS-CoV-2 Delta variant infection occurred in Pingtung, Taiwan, in June 2021. In this study, we aimed to elucidate the clinical characteristics of the Delta-variant SARS-CoV-2 infection and the treatment outcome of antiviral agents in patients from Pingtung County in Southern Taiwan.
*Methods:* A total of 11 patients with Delta-variant COVID-19 were consecutively admitted to a governmental hospital in June 2021. Baseline characteristics and treatment outcome were evaluated.
*Results:* All patients were symptomatic. The most common symptoms were cough (72.7%), followed by fever (54.5%), headache (18.2%) and dysosmia/dysgeusia (18.2%). Two patients developed pneumonia without mechanical ventilation requirement. Compared to patients without pneumonia, those with pneumonia had higher aspartate aminotransferase (AST) (21.0 vs. 126.0 IU/L, $P = 0.03$) and lactate dehydrogenase (LDH) (143.1 vs. 409.0 IU/mL,

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$P = 0.03$), and ferritin (0.2 vs. 2.0 mg/L, $P = 0.046$) levels. Pneumonia improved after 2-week treatment, and no mortality occurred after 30 days of diagnosis. The median duration of viral shedding duration of viral shedding was 16.5 days (range 11—42 days) (defined by time to repeated negative real-time reverse transcriptase polymerase chain reaction (RT-PCR) or a cycle threshold (CT) value $\geq$ 30).

*Conclusion:* We demonstrated the clinical characteristics of Delta-variant COVID-19 and treatment outcome of antiviral agents. The risk factors attributed to pneumonia were higher serum AST, ferritin, and LDH levels.



## Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first found in China in 2019, has caused the coronavirus disease 2019 (COVID-19) pandemic.[1,2] More than 100 million people over 210 countries have been diagnosed with COVID-19 and 3 million people have died from it. Taiwan had few domestic cases owing to extensive public health infrastructure and pre-COVID-19 experience.[3,4] However, there were outbreaks in Taiwan in May 2021, affecting more than 10,000 patients.

Patients with COVID-19 have various symptoms, including fever, cough, rhinorrhea, or other systemic symptoms such as diarrhea and hepatitis.[2] Patients are at risk of developing pneumonia, and the mortality rate is approximately 2%—5%.[5,6] The risk factors for increased severity include old age, comorbidities, and some serum inflammatory markers.[7] Updated treatment regimens include antiviral agents, immune-based adjunctive therapy, and vaccination. Among these, vaccination is the best way to prevent the disease.[8]

Recently, the Delta variant of SARS-CoV-2 has emerged and spread globally.[9] An outbreak of COVID-19 caused by the Delta variant occurred in Southern Taiwan. Previously, two imported COVID-19 cases from Peru were thought to be the main cause of this outbreak. As a result, 17 patients were infected with the Delta variant of SARS-CoV-2. Therefore, we aimed to elucidate the clinical features and risk factors of Delta-variant COVID-19 and treatment outcome of antiviral agents in patients from Pingtung, Taiwan.

## Patients and methods

### Patients

A total of 11 patients with COVID-19 were consecutively isolated in negative pressure wards at a governmental hospital in Pingtung, Taiwan, in June 2021. All patients met the reporting criteria for COVID-19 and had a positive nasopharyngeal swab test result for the Delta variant of SARS-CoV-2, either by real-time reverse transcriptase polymerase chain reaction (RT-PCR) or virus culture in the laboratory of the Taiwan Centers for Disease Control and Prevention (CDC) or other designated hospital laboratories. Information on travel history, underlying diseases, and clinical presentation were collected during case investigation. Laboratory tests were performed within 12 h of admission. Treatment regimens were provided according to the guidelines of the Taiwan CDC. Patients with hepatitis B or C infections were excluded from the study. Data collection and analysis were determined by the Taiwan Ministry of Health and Welfare to be part of a continuing public health outbreak response. Therefore, the requirement of institutional board review approval was waived.

### Laboratory analyses

Biochemical analyses were performed using a multichannel autoanalyzer (Hitachi Inc., Tokyo, Japan). Hepatitis B surface antigen (HBsAg) was examined using a standard quantitative chemiluminescent microparticle immunoassay (ARCHITECT HBsAg, Abbott Diagnostics). HCV antibodies (anti-HCV) were measured using third-generation enzyme immunoassay (Abbott Laboratories, North Chicago, IL, USA). The duration of viral shedding is defined as the time from symptoms to repeated negative RT-PCR or a CT value $\geq$ 30).

### Statistical analyses

Frequencies were compared between groups using the $\chi^2$ test with Yates correction or Fisher's exact tests. Variables means are presented as means $\pm$ standard deviations and were compared using analysis of variance, Student's t-test, or the nonparametric Mann—Whitney test. Statistical analyses were performed using SPSS 20 statistical package (SPSS, Chicago, IL, USA). All statistical analyses were based on two-sided hypothesis tests, with a statistical significance of $P < 0.05$.

## Results

### Patient characteristics

As shown in Table 1, the mean age was 59.9 years (range: 15—88 years); men comprised 63.6% (n = 7) of the cohort. None of the patients had been administered COVID-19 vaccines. Two patients had elevated AST or ALT levels; HBsAg and anti-HCV were both negative.

**Table 1** Characteristics of the 11 COVID-19 patients.

| | All patients (n = 11) |
|---|---|
| Age (years, mean (SD)) | 59.9 (19.9) |
| Male, n (%) | 7 (63.6) |
| Diabetes history, n (%) | 3 (27.3) |
| Hypertension history, n (%) | 5 (45.5) |
| AST (IU/L, mean (SD)) | 40.1 (55.1) |
| ALT (IU/L, mean (SD)) | 26.3 (22.4) |
| LDH (IU/L, mean (SD)) | 191.5 (114.6) |
| CRP (mg/L, mean (SD)) | 28.4 (54.8) |
| Platelet count (x$10^3u$/L, mean (SD)) | 200.0 (73.3) |
| Creatinine (mg/dL, mean (SD)) | 1.0 (0.4) |
| HBsAg seropositivity, n/N (%) | 0/7 (0) |
| Anti-HCV seropositivity, n/N (%) | 0/7 (0) |
| D-dimer (mg/L, mean (SD)) | 1.2 (1.3) |
| Ferritin (mg/L, mean (SD)) | 0.6 (0.9) |
| BMI (kg/$m^2$, mean [SD]) | 25.0 (2.8) |

Note: SD: standard deviation; COVID-19: coronavirus disease 2019; LDH: Lactate dehydrogenase; CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; HBsAg: Hepatitis B surface antigen; HCV: hepatitis C virus.

### Clinical characteristics of COVID-19 patients with or without pneumonia

Two patients developed pneumonia on admission. Compared to patients without pneumonia, those with pneumonia had higher AST (21.0 vs. 126.0 IU/L, $P = 0.03$), lactate dehydrogenase (LDH) (143.1 vs. 409.0 IU/mL, $P = 0.03$), and ferritin (0.2 vs. 2.0 mg/L, $P = 0.046$) levels (Table 2). The progression and recovery of patients with pneumonia are shown in Figs. 1 and 2. These patients recovered after a 2-week treatment regimen. One had oxygen supply with high flow nasal cannula and tapered to nasal cannula supply gradually after treatment. Another one had nasal cannula supply at diagnosis and weaned from any oxygen supply gradually.

### Clinical features of the 11 patients with COVID-19

Among the patients, all patients were symptomatic. The most common symptoms were cough (72.7%), followed by fever (54.5%), headache (18.2%) and dysosmia/dysgeusia (18.2%), and two (18.2%) developed pneumonia without mechanical ventilator support requirement during admission (Table 3). On progression, the two patients with pneumonia received remdesivir, dexamethasone, tocilizumab, and colchicine. Furthermore, six patients received casirivimab (600 mg) and imdevimab (600 mg), owing to old age and comorbidities. In these patients, this regimen prevented the development of severe diseases. In all patients, no adverse effects were observed after drug administration and no 30-day mortality was recorded.

### Duration of viral shedding

Six out of the eleven patients were negative detection of SARS-CoV-2 RNA when hospital discharge (Table 4). The median and mean duration of viral shedding were 16.5 and 19.0 days (range 11–42 days), respectively.

## Discussion

In the current study, we demonstrated the clinical features of Delta-variant COVID-19 and therapeutic effects of antiviral agents in patients. All patients were symptomatic on diagnosis, and two patients developed pneumonia. The efficacy of the current medications against COVID-19 was fair; there were no obvious adverse side effects in the study. Elevated AST, ferritin, and LDH levels were associated with the development of pneumonia.

COVID-19 has caused huge health and economic burdens globally. The first case of COVID-19 in Taiwan was diagnosed in January 2020. At that time, the mortality rate was at 1.3%.[10] Taiwan had few domestic cases, until small outbreaks occurred in May 2021.[11] The dominant viral strains included the Alpha and Beta variants[12]; however, the Delta variant cluster emerged in June 2021.

**Table 2** Characteristics of the 11 COVID-19 patients with or without pneumonia.

| | Pneumonia (n = 2) | Without pneumonia (n = 9) | P value |
|---|---|---|---|
| Age (years, mean (SD)) | 72.0 (1.4) | 57.2 (21.3) | 0.19 |
| Male, n (%) | 1 (50.0) | 6 (66.7) | 1.00 |
| Diabetes history, n (%) | 0 (0) | 3 (33.3) | 1.00 |
| Hypertension history, n (%) | 0 (0) | 5 (55.6) | 0.46 |
| AST (IU/L, mean (SD)) | 126.0 (110.3) | 21.0 (4.2) | 0.03 |
| ALT (IU/L, mean (SD)) | 58.0 (48.1) | 19.2 (5.3) | 0.10 |
| LDH (IU/L, mean (SD)) | 409.0 (38.2) | 143.1 (42.2) | 0.03 |
| CRP (mg/L, mean (SD)) | 111.5 (107.6) | 10.0 (13.9) | 0.06 |
| Platelet count (x$10^3u$/L, mean (SD)) | 166.5 (51.6) | 207.4 (80.1) | 0.48 |
| Creatinine (mg/dL, mean (SD)) | 1.0 (0.5) | 1.0 (0.4) | 0.81 |
| D-dimer (mg/L, mean (SD)) | 1.0 (0.3) | 1.2 (1.5) | 0.48 |
| Ferritin (mg/L, mean (SD)) | 2.0 (0.8) | 0.2 (0.1) | 0.046 |
| BMI (kg/$m^2$, mean [SD]) | 21.7 (2.1) | 25.7 (2.5) | 1.00 |

Note: SD: standard deviation; COVID-19: coronavirus disease 2019; LDH: Lactate dehydrogenase; CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; HBsAg: Hepatitis B surface antigen; HCV: hepatitis C virus.

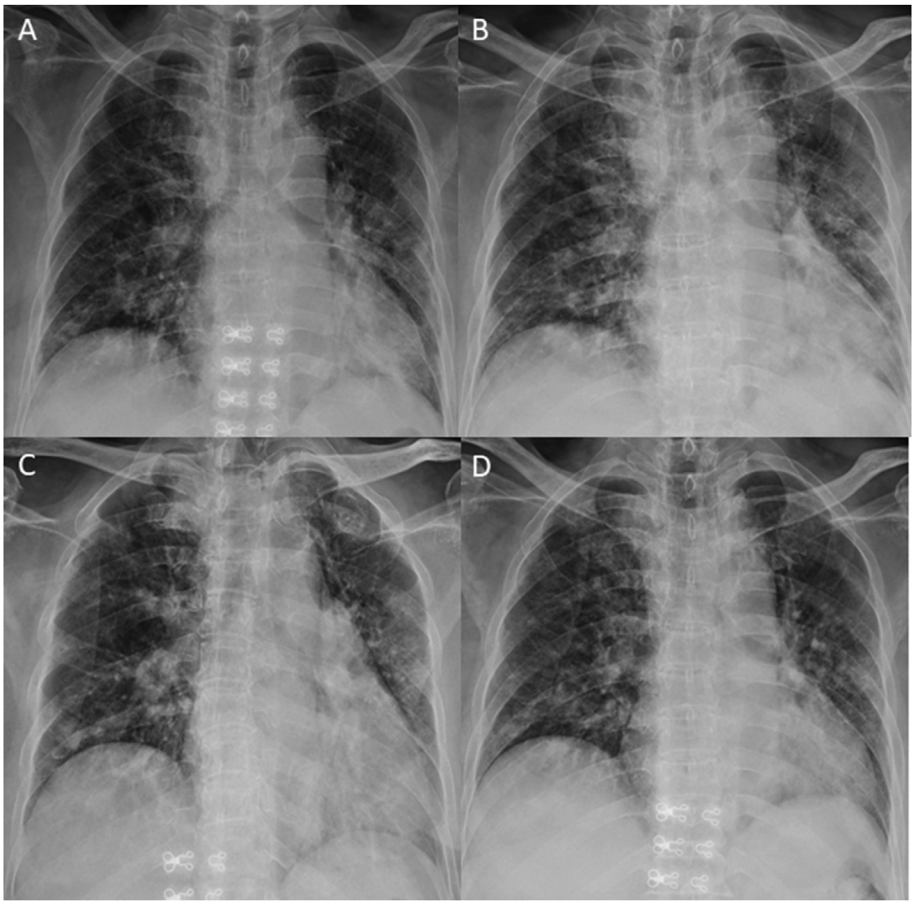


**Figure 1** Chest X-rays of a patient with pneumonia on days 1 (A), 5 (B), 10 (C), and 14 (D) after admission.

Symptoms of COVID-19 caused by the Delta variant are different from those of the traditional ones.[13] COVID-19 mortality was approximately 2%—5% in various areas[3] and 3%—5% in Taiwan after the first outbreak in May 2021. In this study, cough and fever were the most common symptoms, and only two patients developed dysosmia and dysgeusia. Symptoms among Asians may be different from those of Caucasians, thereby requiring further studies. Rare mortality was reported during the outbreak of the Delta-variant COVID-19 in Southern Taiwan. The duration of viral shedding was reported 17 days,[14] and it was similar in the study.

The risk factors for severe COVID-19 include old age, male sex, obesity, and elevated inflammatory marker and hepatic enzyme levels.[7,15] In the study, ferritin, LDH, and AST were associated with pneumonia progression, which was consistent with the findings of previous studies. The risk factors for severe disease require further large-scale studies.

Recently, the Delta variant has emerged in India and has gradually spread to other countries.[9] This variant has become the dominant cause of COVID-19 in England. Vaccination aims to prevent its progression, in conjunction with the strategy of quarantine.[16] However, vaccine effectiveness against the Delta variant seems unsatisfactory.[17]

The treatment regimens include antiviral agents, immune-based therapies, and adjunctive therapeutic agents. Previous medications, such as chloroquine and azithromycin, have been proven to be ineffective and may even be harmful.[18] In this study, all patients were treated according to the guidelines of the Taiwan CDC with good efficacy. Remdesivir was used in patients with an oxygen saturation of $<$94% in room air and had promising effects.[19] Dexamethasone may lower the mortality in hospitalized patients with COVID-19.[20] Casirivimab and imdevimab may interrupt the progression of pneumonia and shorten the duration of hospitalization[21]; these drugs were used in early disease stages, in accordance with the Taiwan CDC guidelines. Colchicine has also been demonstrated to decrease the mortality and hospitalization rate.[22] Therefore, we treated patients with pneumonia with 0.5 mg colchicine a day since admission. These drugs were administered to our patients and showed satisfactory efficacy.

The current study has some limitations, including a relatively small number of cases and a short-term follow-up. We lack the data of the second attack rate owing to not all the 17 delta variant patients in Pingtung being admitted to our hospital, and we were short of comprehensive data in epidemic investigation. Although participants were enrolled from a medium-sized hospital, the therapeutic regimens were regularly updated, and the efficacy was consistent with that reported in previous studies. Our study is the first study to describe the clinical characteristics of Delta-variant COVID-19 and treatment outcome of antiviral agents in Taiwan.

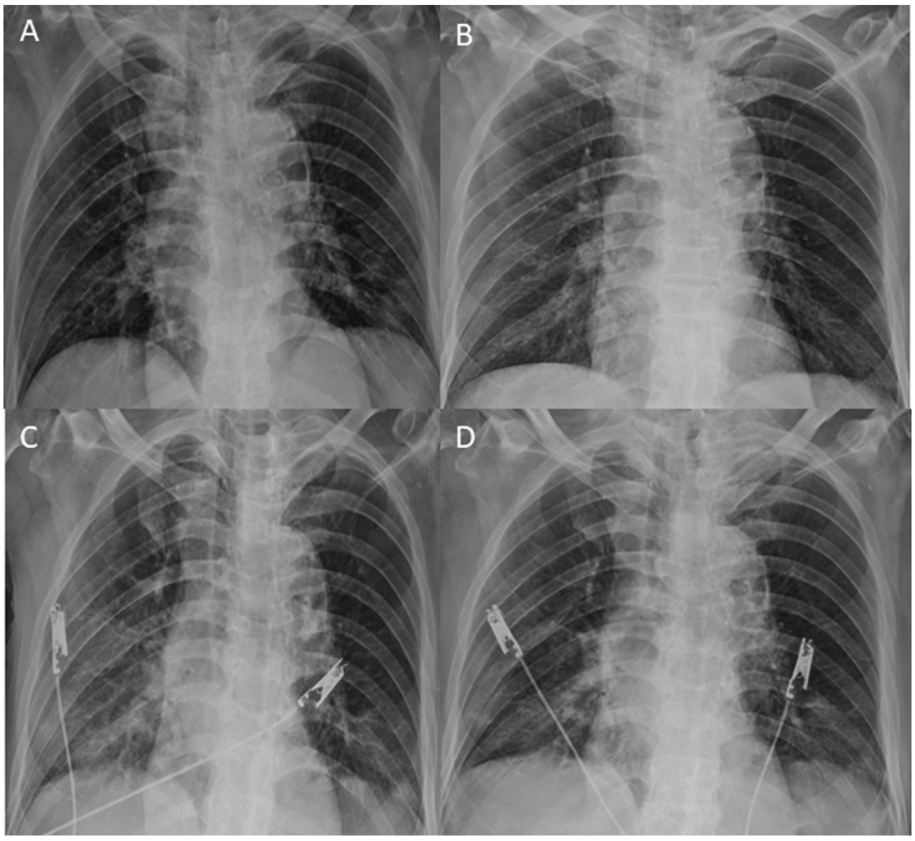


**Figure 2** Chest X-rays of another patient with pneumonia on days 1 (A), 5 (B), 10 (C), and 14 (D) after admission.

**Table 3** Clinical features of the 11 COVID-19 patients.

| Characteristic | All patients (n = 11) |
|---|---|
| **Clinical features, n (%)** | |
| Fever | 6 (54.5) |
| Cough | 8 (72.7) |
| Headache | 2 (18.2) |
| Dysosmia and dysgeusia | 2 (18.2) |
| **Disease severity, n (%)** | |
| Upper respiratory infection | 8 (72.7) |
| Pneumonia without mechanical ventilatory support | 2 (18.2) |
| Pneumonia with mechanical ventilatory support | 0 (0) |
| **Therapeutic agents, n (%)** | |
| Casirivimab + imdevimab | 6 (54.5) |
| Dexamethasone | 2 (18.2) |
| Remdesivir | 2 (18.2) |
| Tocilizumab | 2 (18.2) |
| Colchicine | 2 (18.2) |
| **Outcome, n (%)** | |
| 30-day mortality | 0 (0) |

Note: COVID-19: coronavirus disease 2019.

**Table 4** CT values of the 11 COVID-19 patients when admission and hospital discharge.

| Patient | CT value when admission | CT value when hospital discharge | Duration (days) |
|---|---|---|---|
| No.1 | 13.0 | Negative | 26 |
| No.2 | 34.5 | Negative | 15 |
| No.3 | 24.8 | Negative | 33 |
| No.4 | 25.5 | Negative | 20 |
| No.5 | 15.7 | Negative | 21 |
| No.6 | 22.7 | Negative | 43 |
| No.7 | 26.0 | 37.7 | 21 |
| No.8 | 10.8 | 36.5 | 19 |
| No.9 | 12.6 | 36.1 | 20 |
| No.10 | 18.9 | 34.0 | 21 |
| No.11 | 21.9 | 33.2 | 42 |

Note: CT: cycle threshold; COVID-19: coronavirus disease 2019.

## Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jfma.2022.01.008.

## References

1. Wang C, Wang Z, Wang G, Lau JY, Zhang K, Li W. COVID-19 in early 2021: current status and looking forward. *Signal Transduct Target Ther* 2021;**6**(1):114.
2. Wu YC, Chen CS, Chan YJ. The outbreak of COVID-19: an overview. *J Chin Med Assoc* 2020;**83**(3):217—20.
3. Summers J, Cheng HY, Lin HH, et al. Potential lessons from the Taiwan and New Zealand health responses to the COVID-19 pandemic. *Lancet Reg Health West Pac* 2020;**4**:100044.
4. Dai CY, Dai TH, Sheng WH, Ho CK. 222 days without COVID in Taiwan: what are the reasons for this success? *J Trav Med* 2021;**28**(2).
5. Lauer GM, Walker BD. Hepatitis C virus infection. *N Engl J Med* 2001;**345**(1):41—52.
6. Yu ML, Lin SM, Lee CM, et al. A simple noninvasive index for predicting long-term outcome of chronic hepatitis C after interferon-based therapy. *Hepatology* 2006;**44**(5):1086—97.
7. Hu J, Wang Y. The clinical characteristics and risk factors of severe COVID-19. *Gerontology* 2021;**67**(3):255—66.
8. Rodriguez-Guerra M, Jadhav P, Vittorio TJ. Current treatment in COVID-19 disease: a rapid review. *Drugs Context* 2021;**10**.
9. O'Dowd A. Covid-19: cases of delta variant rise by 79%, but rate of growth slows. *BMJ* 2021;**373**:n1596.
10. Lin CY, Wang WH, Urbina AN, et al. Importation of SARS-CoV-2 infection leads to major COVID-19 epidemic in Taiwan. *Int J Infect Dis* 2020;**97**:240—4.
11. Wang CJ, Ng CY, Brook RH. Response to COVID-19 in Taiwan: big data analytics, new technology, and proactive testing. *JAMA* 2020;**323**(14):1341—2.
12. Chen SC, Olsthoorn RCL, Yu CH. Structural phylogenetic analysis reveals lineage-specific RNA repetitive structural motifs in all coronaviruses and associated variations in SARS-CoV-2. *Virus Evol* 2021;**7**(1):veab021.
13. Mahase E. Covid-19: GPs urge government to clear up confusion over symptoms. *BMJ* 2021;**373**:n1654.
14. Cevik M, Tate M, Lloyd O, Maraolo AE, Schafers J, Ho A. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. *Lancet Microb* 2021;**2**(1):e13—22.
15. Wong GL, Wong VW, Thompson A, et al. Management of patients with liver derangement during the COVID-19 pandemic: an Asia-Pacific position statement. *Lancet Gastroenterol Hepatol* 2020;**5**(8):776—87.
16. Kaur SP, Gupta V. COVID-19 Vaccine: a comprehensive status report. *Virus Res* 2020;**288**:198114.
17. Sheikh A, McMenamin J, Taylor B, Robertson C, Public Health S, the EIIC. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. *Lancet* 2021;**397**(10293):2461—2.
18. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA* 2020;**324**(8):782—93.
19. Yang CJ, Wei YJ, Chang HL, et al. Remdesivir use in the coronavirus disease 2019 pandemic: a mini-review. *J Microbiol Immunol Infect* 2021;**54**(1):27—36.
20. Group RC, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with covid-19. *N Engl J Med* 2021;**384**(8):693—704.
21. Taylor PC, Adams AC, Hufford MM, de la Torre I, Winthrop K, Gottlieb RL. Neutralizing monoclonal antibodies for treatment of COVID-19. *Nat Rev Immunol* 2021;**21**(6):382—93.
22. Tardif JC, Bouabdallaoui N, L'Allier PL, et al. Colchicine for community-treated patients with COVID-19 (COLCORONA): a phase 3, randomised, double-blinded, adaptive, placebo-controlled, multicentre trial. *Lancet Respir Med* 2021;**9**(8):924—32.