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CASE REPORT

The First COVID-19 Mortality in Batu Pahat, Johor: Lesson Learnt

Shu Ann Hon[1], Lian Thai Lee[2], Qin Jian Low[1]

[1] Department of Internal Medicine, Hospital Sultanah Nora Ismail, Batu Pahat, Johor, Malaysia
[2] Department of Urology, Hospital Sultanah Aminah, Johor Bahru, Johor, Malaysia

*Corresponding author's email: honshuann@gmail.com

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ABSTRACT

COVID-19 had been declared as a global pandemic on 11 March 2020. This case report is about Severe Acute Respiratory Infection (SARI) due to COVID-19 (Corona Virus-19). A 68-year-old lady with underlying hypertension and congestive cardiac failure presented with fever and productive cough for 5 days duration. One week before her presentation, she had travelled to Kluang, Johor for a wedding gathering which was later found to have contributed to a cluster of COVID-19 cases. Otherwise, she denied any sick or known COVID-19 contact. Respiratory examination revealed left lower zone crepitations. She was tachypnoeic on a high flow mask 15 L and hypotensive (BP 90/70 mm Hg) on arrival at the hospital. Chest radiograph showed bilateral asymmetrical consolidations. There was a presence of lymphopenia while her dengue serology result was negative. She was treated as SARI secondary to pneumonia with septic shock and required mechanical ventilation due to respiratory failure. Nasopharyngeal swab for SARS CoV-2 (Severe Acute Respiratory Syndrome Corona Virus-2) was taken as positive for COVID-19 on the third day of admission. Apart from supportive and intensive care measures, she was commenced on oral hydroxychloroquine, subcutaneous Interferon Beta and syrup lopinavir/ritonavir per local guidelines during that period. Unfortunately, she developed acute respiratory distress syndrome (ARDS) on day 3 of admission and passed away due to respiratory failure. Clinicians should pay attention to the COVID-19 critical disease profile and mortality risks. By identifying high-risk patients early, medical resources can be administered in an organized way and timely way to improve the efficacy of the healthcare services.

INTRODUCTION

Since December 2019, a new cluster of pneumonia had been discovered in Wuhan, China which affected people across all continents (Chan et al, 2020). COVID-19 which was formerly known as a novel Coronavirus had spread globally within 4 months ever since its first detection in Wuhan, China. The cumulative cases increased tremendously on a day-to-day basis and it had broken the record of 153,094,318 confirmed COVID-19 cases reported worldwide up to 4 May 2021. From the figures reported, the United States of America had recorded more than 32.5 million cases which are approximately 21% of the overall cumulative cases throughout the world (National Crisis Preparedness & Response Centre, 2020).

Malaysia is currently ranked 29th globally as of 29 January 2021 (National Crisis Preparedness & Response Centre, 2020). World Health Organisation [WHO] (2020) commented that this disease even disrupted the lifesaving immunization services worldwide and putting children at risk of other diseases such as diphtheria, measles and polio. Undeniably, COVID-19 had caused devastating effects from the health to economic sectors. The rapidly increasing number of patients, especially the critical patients, took a big toll on public health. The mortality was found related closely to the healthcare resources (Chan et al, 2020).

COVID-19 has non-specific symptoms. The most common symptoms are fever, dry cough and lethargy. Other symptoms may include aches and pains, sore throat, diarrhoea, conjunctivitis, headache, anosmia and ageusia. Serious symptoms are loss of consciousness, shortness of breath and chest pain.

COVID-19 has caused a mortality rate of 2.16% worldwide up to July 12, 2021. Italy carries the highest mortality rate of 2.99% across the world as of July 12, 2021(Hannah et al., 2021). In Malaysia, the mortality rate up to July 14, 2021, is 0.75% as the latest CPRC report (Ministry of Health Malaysia, 2021).

CASE PRESENTATION

A 68-year-old lady with underlying hypertension and congestive cardiac failure presented to Hospital on 5 May 2020 with fever and productive cough with yellowish sputum for 5 days duration. She had no sore throat, gastrointestinal symptoms or any bleeding tendencies. Her fever was persistently high grade in nature, always more than 38°C.

One week before her symptoms, she had travelled to Kluang district, Johor for a wedding reception. Otherwise, she denied any sick or known COVID-19 contact. On arrival to the emergency department, she was hypotensive (blood pressure 90/70 mm Hg), tachypnoeic (respiratory rate of 30 breaths per minute), tachycardic (pulse rate was 110 beats per minute) and hypoxic (oxygen saturation of 90% on room air). Respiratory examination revealed left lower zone crepitations. Chest radiograph showed bilateral diffuse asymmetrical opacities representing acute respiratory distress syndrome (Figure 1).

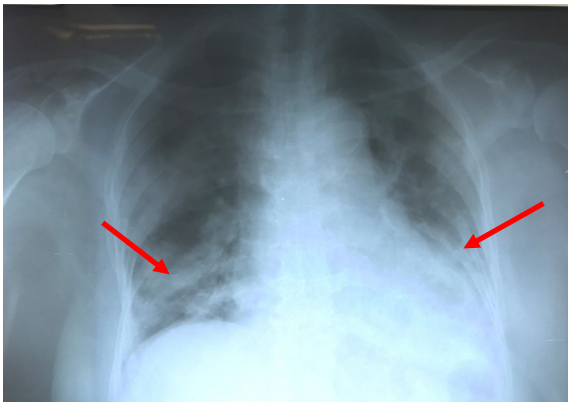

Figure 1 Chest radiograph showed diffuse bilateral coalescent opacities (red arrows) representing acute respiratory distress syndrome

There was bi-cytopenia (lymphopenia and thrombocytopenia) on full blood count with raised C-reactive protein (CRP) level while her Dengue serology was negative (Table 1). Her inflammatory markers were raised (ESR and CRP). There was also transaminitis and acute kidney injury as the serum creatinine is raised.

Table 1 Blood investigations on the day of admission

Blood investigations	Day 1 of admission	Normal range
Full blood count		
White cell count	3,300/mm^3	4,500 – 1,100/ mm^3
Lymphocyte count	1,200/mm^3	1,000 – 4,000/ mm^3
Haemoglobin	12 g/L	11.7 – 15.7g/L
Platelets	65,000/mm^3	150,000 – 410,000/ mm^3
Dengue serology	Negative	
Inflammatory markers		
Erythrocyte sedimentation rate (ESR)	90 mm/Hour	0 – 20 mm/Hour
C-reactive protein (CRP)	310 mg/L	Less than 5mg/L
Renal profile		
Urea	8.7 mmol/L	2.8 – 7.2 mmol/L
Sodium	139 mmol/L	136 – 146 mmol/L
Potassium	4.1 mmol/L	3.5 – 5.1 mmol/L
Creatinine	135 umol/L	45 – 84 mmol/L
Liver function test		
Total protein	71 g/L	66 – 83 g/L
Albumin	31 g/L	35 – 52 g/L
Globulin	40 g/L	28 – 36 g/L
Total bilirubin	13 umol/L	5 – 21 umol/L
Alkaline phosphatase (ALP)	48 U/L	30 – 120 U/L
Aspartate transaminase (AST)	157 U/L	0 – 35 U/L
Alanine Transaminase (ALT)	70 U/L	0 – 35 U/L
Lactate dehydrogenase (LDH)	508 U/L	0 – 248 U/L
Arterial blood gas on high flow mask		
pH	7.464	7.35 – 7.45
pCO_2	14.9 mmHg	32 – 45 mmHg
pO_2	128.4 mmHg	83 – 108 mmHg
HCO_3	10.6 mmol/L	22 – 26 mmol/L
Coagulation profile		
PT	10.5	9.2 – 12.6
INR	0.98	0.84 – 1.18
APTT	32.2	23.3 – 34.8

She was treated for SARI secondary to pneumonia with septic shock (clinically stage 4 on arrival). She was initially empirically treated with intravenous ceftriaxone 2 g daily and oral azithromycin 500 mg daily. Her condition deteriorated on day one of admission requiring mechanical ventilation and triple inotropic support. A nasopharyngeal swab for SARS CoV-2 was taken on the third day of admission given clinical suspicion of COVID-19 and turned out to be positive. Besides supportive measures, she was then started on oral hydroxychloroquine

400 mg OD, subcutaneous Interferon Beta II 250 mg stat and Syrup lopinavir/ritonavir (Kaletra) (400/100) 5 ml BD after confirmation of COVID-19 infection. Unfortunately, she developed acute respiratory distress syndrome and eventually succumbed after 3 days of mechanical ventilation.

DISCUSSIONS

The standard method for diagnosing SARS-Cov-2 infection is the SARS-Cov-2 virus nucleic acid RT-PCR test from nasopharyngeal swabs (Wang et al., 2020). Nucleic acid detection, gene sequencing and antibody detection are widely used in China because of limitations of the RT-PCR test due to possible interference during collection, preservation and transportation of the specimens (Wang et al., 2020). In Malaysia, both are widely available now.

In our case described above, our patient presented with a history of fever and productive cough and was admitted to the ward on 5 March 2021. She had a recent travelling history to Kluang, Johor (Kampung Dato'Ibrahim Majid. Following the detection of confirmed COVID-19 infection in our patient, contact tracing was done and found another 73 confirmed cases related to this location. Therefore, this locality was subsequently declared as a new cluster on 27 March 2020 with 74 confirmed cases of COVID-19. Her chest radiograph was consistent with pneumonia. Her laboratory results showed a low lymphocyte count and elevated CRP level, which was consistent with a viral infection. On this basis, COVID-19 was diagnosed by the positive results of the SARS-Cov-2 from her nasopharyngeal swab. She was clinical stage 4 upon admission and progressed rapidly to stage 5 upon intubation according to local guidelines.

Centers for Disease Control and Prevention [CDC] (2021) concluded that the risk factors for severe COVID-19 illness are as follows: elderly above 65 years old, institutionalized patients (those living in nursing homes or long-term care facilities), patients with chronic lung disease, patients with serious heart disease, immunocompromised persons (oncology patients on chemotherapy or radiotherapy, active smokers, people who have done bone marrow or organ transplantations, primary immune deficiencies, HIV or AIDS, prolonged steroids or immunosuppressants use), class III obesity, diabetic, chronic kidney disease or patients on dialysis or with liver disease. Based on these risk factors by CDC, our patient who had underlying congestive cardiac failure belongs to the high-risk group for severe COVID-19 illness.

A study published in April 2020 by Shaoxing Hospital, Zhejiang, China reported that males, aged over 65 and smokers have a higher tendency to develop the critical condition and the comorbidities such as cardiovascular disease hypertension, respiratory diseases, diabetes, or affect the prognosis of the COVID-19 significantly (Zhao et al., 2020). Our patient had a high-risk profile as predicted by the study above. Her long-standing diabetes and hypertension had resulted in a state of stress and low immunity. Additionally, these diseases could destroy the vasculature predisposing to severe infection (Zhao et al., 2020). Due to weakened cardiac function and low immunity state, patients with chronic heart disease are more prone to be infected. These patients develop acute cardiovascular events and progress into severe diseases when infected (Zhao et al., 2020). This study also found that aspartate transaminase (AST) of more than 40 U/L, lactate dehydrogenase (LDH) of more than 245 U/L and creatinine of more than 133 mmol/L would indicate liver and kidney dysfunction and corresponding treatments should be taken promptly to prevent further deterioration of the disease (Zhao et al., 2020). In our case, she had an AST of 157 U/L, LDH of 508 U/L and creatinine of 135 umol/L which signify liver and renal impairment. Unfortunately, she failed to respond to the adequate intensive and supportive care measures provided.

The study of Xiao et al. (2020) in Wuhan, China had identified raised CRP and lymphopenia as independent risk factors for disease severity and our patient also fulfilled these findings. On the other hand, the largest study to date in the United Kingdom reported that Asian or Black ethnicity people from deprived social backgrounds along with male gender have higher mortality with COVID-19 infection (Medical Xpress, 2020). Sequential Organ Failure Assessment (SOFA) score is a good diagnostic marker for sepsis and septic shock and reflects the state and degree of multi-organ dysfunction (Singer et al., 2016). This patient had an initial SOFA score of 10 indicating severe sepsis in septic shock and multi-organ failure. All in all, our patient had all the characteristics of severe disease profile and poor prognosis as proposed by studies worldwide.

This patient was treated with hydroxychloroquine, lopinavir/ritonavir (Kaletra) and interferon Beta. The mechanism of action of hydroxychloroquine against COVID-19 was yet to be fully understood (Pastick et al., 2020). To date, there are no adequate studies to prove that hydroxychloroquine is efficacious to treat COVID-19 (Pastick et al., 2020). In early March 2020, Chen et al. (2020) showed no significant differences ($p<0.05$) by day seven in time to the viral clearance between those who received hydroxychloroquine versus those who did not receive hydroxychloroquine. We should aim to enrol patients into clinical trials since this is a new infection and there are still many unknowns. Remdesivir had been recommended for severe COVID-19 patients. Hydroxychloroquine and chloroquine were later found to have a lack of benefit and is potentially toxic. The role of lopinavir-ritonavir was later removed due to poor outcomes. Extracorporeal membrane oxygenation (ECMO) is an option for patients as a last resort after other ventilatory strategies have failed (including prone ventilation, high positive end-expiratory pressure, recruitment manoeuvres, neuromuscular blocking agents and pulmonary vasodilators) (Chen et al., 2020).

The only drug cleared to treat COVID-19 is Remdesivir that is more beneficial on ventilated patients and also shorten the recovery time of patients (STAT, 2020). Those who received Remdesivir had a median recovery time of 11 days (95% confidence interval of 9 to 12), whereas 15 days (95% CI, 13 to 19) in those who received placebo (rate ratio for recovery, 1.32; 95% confidence interval of 1.12 to 1.55; $p<0.001$) found in a study of intravenous Remdesivir in hospitalized COVID-19 adults with lower respiratory tract involvement in European countries, Asian countries and the United States of America (John et al., 2020). Tocilizumab treatment was found to reduce the risk of invasive mechanical ventilation or death. Giovanni et al. (2020) did a study among adults more than 18 years old were compared with severe COVID-19 pneumonia cases treated with the standard treatment (i.e., supplemental oxygen, azithromycin, low molecular weight heparin, hydroxychloroquine and antiretrovirals), and the patients who also received tocilizumab. Out of 365 patients in standard treatment, 57 (16%) needed mechanical ventilation. On the other hand, out of 179 patients with tocilizumab, 33 (18%) needed mechanical ventilation. Seventy-three (20%) patients in the standard treatment group died, whereas 13 (7%; $p<0·0001$) patients died who were treated with tocilizumab (Giovanni et al., 2020). Dexamethasone, if given in ventilated COVID-19 patients who developed acute respiratory distress syndrome (ARDS) was shown to improve survival at 28 days after entry into the sickest phase (The Scientist, 2020). The Scientist (2020) pointed out that steroids reduced deaths in ventilated COVID-19 patients by one-third in the RECOVERY (Randomised Evaluation of COVid-19 thERapY) trial. Another well-known treatment in COVID-19 is interferon Beta. Sallard et al. (2020) concluded that the pharmacology of subcutaneous versus intravenous interferon Beta are the same as they produce similar anti-viral responses. However, the pharmacokinetics of subcutaneous versus intravenous interferon

Beta is completely reversed in which maximum serum concentrations and total exposure through serum concentrations are significantly higher in intravenous injections (Mager et al., 2002). The purpose of intravenous administration of interferon-Beta is to maximise the bioavailability of the drug at the lung vasculature, as well as other vascular beds (Eltzschig et al., 2020). There is another emerging drug, Favipiravir, which has been approved for the treatment of novel influenza in February 2020 in China and it is currently undergoing clinical trials in treating COVID-19. It is a new type of RNA-dependent RNA polymerase (RdRp) inhibitor (MaHTAS Malaysia, 2020). Currently, China is conducting six clinical trials involving the investigation of favipiravir's safety and efficacy for COVID-19, with some comparing favipiravir to lopinavir/ritonavir or baloxavir marboxil (Mak, 2020). Cai et al. (2020) did a pilot study of a non-randomised control trial where in terms of disease progression and viral clearance, favipiravir has shown significantly better outcomes on COVID-19. Apart from all the drugs mentioned, prophylactic anticoagulation is another essential management in COVID-19 disease. COVID-19 is a hypercoagulable state, and the risk of thromboembolic disease is higher in critically ill patients (UptoDate, 2020). Low molecular weight heparin is preferred while unfractionated heparin is chosen for a patient with renal impairment (CrCl< 15 ml/min) (UptoDate, 2020).

CONCLUSIONS

Indeed, COVID-19 pandemic effects are overwhelming. Clinicians should pay attention to the COVID-19 critical disease profile and mortality risks. By identifying high-risk patients early, medical resources can be administered in an organized way and timely way to improve the efficacy of our healthcare services. Finally, we should aim to enrol COVID-19 patients into the clinical trial which is the only way for us to contribute to the science of medicine. Together we can do better.

CONFLICT OF INTEREST AND FUNDING

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CONSENT

Written informed consent for this paper (including images, case history and data) were obtained from the patient for publication of this paper, including the accompanying figures.

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REFERENCES

Cai, Q., Yang, M., Liu, D., Chen, J., Shu, D., Xia, J., Liao, X., Gu, Y., Cai, Q., Yang, Y., Shen, C., Li, X., Peng, L., Huang, D., Zhang, J., Zhang, S., Wang, F., Liu, J., Chen, L., Chen, S., … Liu, L. (2020. Experimental treatment with favipiravir for COVID-19: An open-label control study. *Engineering (Beijing)*, *6* (10), 1192 – 1198. https://doi.org/10.1016/j.eng.2020.03.007; Epub 2020 Mar 18; PMID: 32346491; PMCID: PMC7185795.

Centers for Disease Control and Prevention (CDC). (2021). *Coronavirus Disease 2019 (COVID-19): people who need extra precautions.* Retrieved 4 May 2021, from https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html

Chan, J. S., Yuan, H., Kok, K., Kelvin, K., Chu, H., & Jin, Y. (2020). A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: A study of a family cluster. *Lancet*, *395* (10223), 514 – 523. https://doi.org/10.1016/S0140-6736(20)30154-9

Chen, J., Liu, D., Liu, L., Liu, P., Xu, Q., Xia, L., Ling, Y., Huang, D., Song, S., Zhang, D., Qian, Z., Li, T., Shen, Y., & Lu, H. (2020). A pilot study of hydroxychloroquine in treatment of patients with moderate COVID-19. *Zhejiang Da Xue Xue Bao Yi Xue Ban*, *49* (2), 215 – 219. doi: 10.3785/j.issn.1008-9292.2020.03.03. PMID: 32391667.

Eltzschig, H. K., Sitkovsky, M. V., & Robson, S. C. (2020). Purinergic signaling during inflammation. *N Engl J Med*, *367* (24), 2322 – 2333. https://doi.org/10.1056/NEJMra1205750; PMID: 23234515, PMCID: PMC3675791

Guaraldi, G., Meschiari, M., Cozzi-Lepri, A., Milic, J., Tonelli, R., Menozzi, M., Franceschini, E., Cuomo, G., Orlando, G., Borghi, V., Santoro, A., Di Gaetano, M., Puzzolante, C., Carli, F., Bedini, A., Corradi, L., Fantini, R., Castaniere, I., Tabbì, L., Girardis, M., … Mussini, C. (2020). Tocilizumab in patients with severe COVID-19: A retrospective cohort study. *Lancet Rheumatol*, *2* (8), e474 – e484. https://doi.org/10.1016/S2665-9913(20)30173-9

Hannah, R., Esteban, O. O., Diana, B., Edouard, M., Joe, H., Bobbie, M., Charlie, G., Cameron, A., Lucas, R. G., & Max, R. (2021). Coronavirus pandemic (COVID-19). Retrieved 14 July 2021, from https://ourworldindata.org/coronavirus.

John, H., Kay, M. & Lori, E. (2020). Remdesivir for the treatment of Covid-19 — preliminary report. *N Engl J Med*, *10*, 1056. https://doi.org/10.1056/NEJMoa2007764; PMID: 32445440; PMCID: PMC7262788

Lai, C. C., Wang, C. Y., Wang, Y. H., Hsueh, S. C., Ko, W. C., & Hsueh, P. R. (2020). Global epidemiology of coronavirus disease 2019 (COVID-19): disease incidence, daily cumulative index, mortality, and their association with country healthcare resources and economic status. *Int J Antimicrob Agents*, 5 (4), 105946. https://doi.org/10.1016/j.ijantimicag.2020.105946; PMID: 32199877; PMCID: PMC7156123

Liu, X., Zhou, H., Zhou, Y., Wu, X., Zhao, Y., Lu, Y., Tan, W., Yuan, M., Ding, X., Zou, J., Li, R., Liu, H., Ewing, R. M., Hu, Y., Nie, H., & Wang, Y. (2020). Risk factors associated with disease severity and length of hospital stay in COVID-19 patients. *J Infect*, *81* (1), e95 – e97. https://doi.org/10.1016/j.jinf.2020.04.008; PMID: 32305490; PMCID: PMC7162771

Mager, D. E., & Jusko, W. J. (2002). Receptor-mediated pharmacokinetic/pharmacodynamic model of interferon-beta 1a in humans. *Pharm Res*, *19* (10), 1537 – 1543. https://doi.org/10.1023/A:1020468902694; PMID: 12425473

MaHTAS Malaysia. (2020). *Favipiravir (AVIGAN®) to Treat Coronavirus Disease 2019 (COVID-19)*. Retrieved 31 May 2020, from https://www.moh.gov.my/moh/resources/penerbitan/mymahtas/MaHTAS%20COVID-19%20Rapid%20Evidence/Clinical%20Management/Favipiravir_(AVIGAN%C2%AE)_to_Treat_Coronavirus_Disease_2019_(COVID-19).pdf

Mak, E. (2020). *Sihuan starts clinical trial of Ebola drug favipiravir for COVID-19*. Retrieved 31 May 2020, from https://www.bioworld.com/articles/433502-sihuan-starts-clinical-trial-ofebola-drug-favipiravir-for-covid-19

Medical Xpress. (2020). *Risk factors for COVID-19 death revealed in world's largest analysis of patient records*. Retrieved 31 May 2020, from https://medicalxpress.com/news/2020-05-factors-covid-death-revealed-world.html

Ministry of Health Malaysia. (2021). COVID-19 Malaysia. Retrieved 14 July 2021, from http://covid-19.moh.gov.my/

National Crisis Preparedness & Response Centre. (2020). *Corona Virus Disease (COVID-19)*. Ministry of Health Malaysia. Retrieved 31 May 2020, from https://www.facebook.com/kementeriankesihatanmalaysia/photos/a.10151657414821237/10157090713431237/?type=3&theater

Pastick, K. A., Okafor, E. C., Wang, F., Lofgren, S. M., Skipper, C. P., Nicol, M. R., Pullen, M. F., Rajasingham, R., McDonald, E. G., Lee, T. C., Schwartz, I. S., Kelly, L. E., Lother, S. A., Mitjà, O., Letang, E., Abassi, M., & Boulware, D. R. (2020). Review: Hydroxychloroquine and chloroquine for treatment of SARS-CoV-2 (COVID-19). *Open Forum Infect Dis*, *7* (4), ofaa130. https://doi.org/10.1093/ofid/ofaa130; PMID: 32363212; PMCid: PMC7184359

Sallard, E., Lescure, F. X., Yazdanpanah, Y., Mentre, F., & Peiffer-Smadja, N. (2020). Type 1 interferons as a potential treatment against COVID-19. *Antiviral Res*, *178*, 104791. https://doi.org/10.1016/j.antiviral.2020.104791; PMID: 32275914; PMCID: PMC7138382

Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., Bellomo, R., Bernard, G. R., Chiche, J. D., Coopersmith, C. M., Hotchkiss, R. S., Levy, M. M., Marshall, J. C., Martin, G. S., Opal, S. M., Rubenfeld, G. D., van der Poll, T., Vincent, J. L., & Angus, D. C. (2016). The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*, *315* (8), 801 – 810. https://doi.org/10.1001/jama.2016.0287; PMID: 26903338; PMCID: PMC4968574

STAT. (2020). *Covid-19 study details benefits of treatment with remdesivir, and also its limitations.* Retrieved 31 May 2020, from https://www.statnews.com/2020/05/22/covid-19-study-details-benefits-of-treatment-with-remdesivir-and-also-its-limitations/

The Scientist. (2020). *Insight into dexamethasone's benefits in severe covid-19.* Retrieved 31 May 2020, from https://www.the-scientist.com/news-opinion/insight-into-dexamethasones-benefits-in-severe-covid-19-67647

UptoDate. (2020). *Anticoagulation in COVID-19 patients.* Retrieved 31 May 2020, from https://www.uptodate.com/contents/image?imageKey=HEME%2F128045&topicKey=ID%2F127429&source=see_link

Wang, M., Luo, L., Bu, H., & Xia, H.. (2020). One case of coronavirus disease 2019 (COVID-19) in a patient co-infected by HIV with a low CD4+ T-cell count. *Int J Infect Dis*, *96*, 148 – 150. https://doi.org/10.1016/j.ijid.2020.04.060; PMID: 32335339; PMCID: PMC7194654

World Health Organisation (WHO). (2020). *WHO, Gavi and UNICEF warn that disruption to routine vaccination leaves at least 80 million children at risk*. Retrieved 31 May 2020, from https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen

Zheng, Z., Peng, F., Xu, B., Zhao, J., Liu, H., Peng, J., Li, Q., Jiang, C., Zhou, Y., Liu, S., Ye, C., Zhang, P., Xing, Y., Guo, H., & Tang, W. (2020). Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect*, *81* (2), e16 – e25. https://doi.org/10.1016/j.jinf.2020.04.021; PMID: 32335169; PMCID: PMC7177098