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CASE REPORT

Pregnancy with COVID-19 in Malaysia: A Case Series

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ABSTRACT

This case series highlights the outcome of four pregnancies complicated with COVID-19, as the pandemic of coronavirus disease 2019 (COVID-19) poses a lot of uncertainties due to lack of scientific evidence in guiding the management of pregnancy with COVID-19. The women were between 25 and 31 years of age and of 35 - 39 weeks of gestation with no underlying medical problems. Three women were delivered via caesarean section and one woman was delivered via ventouse delivery due to poor progress during the second stage of labour. Two women were in stage 4 of the disease (having breathing difficulties and requiring oxygen support) at presentations. One of them was treated with hydroxychloroquine (HC) only while another one was treated with both HC and antiviral medications; none required assisted ventilation during their hospitalizations. There is no vertical transmission of COVID-19 disease observed in this case series.

KEYWORDS: Coronavirus, Pregnancy, Coronavirus Infection, Pandemics

INTRODUCTION

The current global pandemic began with a cluster of patients with pneumonia of unknown cause in Wuhan, China, at the end of 2019 [1, 2]. The outbreak was caused by a novel coronavirus known as Severe Acute Respiratory Syndrome-coronavirus-2 (SARS-CoV-2) and the disease is now named as coronavirus disease 2019 (COVID-19). Due to the increasing mortalities from COVID-19 globally, the World Health Organisation (WHO) has announced this highly infective disease as a global pandemic on 11th March 2020 [3].

Although pregnant women are not necessarily more susceptible to a viral illness, physiological changes of the immune system in pregnancy potentially cause pregnant women more vulnerable with more severe symptoms of COVID-19. There remain many uncertainties on the standard of care for pregnant women with COVID-19. The dilemma includes providing standard treatment of COVID-19 during pregnancy and precautions in the obstetrics management during the perinatal period. These considerations may provide a balance in minimising the risk of complications of COVID-19 and reducing the risk of vertical transmission to the fetus. The precautionary measures are also crucial to mitigate the risk of disease transmission to the healthcare provider. This case series aims to discuss on the case management and the perinatal outcomes of pregnancies with COVID-19.

CASE PRESENTATION

These cases were managed in Hospital Sungai Buloh, a tertiary hospital which has been gazetted as national COVID-19 hospital. All pregnancies in this series were confirmed positive for COVID-19 by Reverse Transcriptase – Polymerase Chain Reaction (RT-PCR) test. Other laboratory investigation results were summarised in Table 1.

Table 1 Laboratory results of the four pregnancies confirmed positive for COVID-19

	Case 1	Case 2	Case 3	Case 4
White blood cell count ($\times 10^9$ cells per L)	3.7	10	9.4	5.4
Lymphocyte count ($\times 10^9$ cells per L)	1.6	1.9→0.4	2.3	0.8
C-reactive protein (mg/L)	3.3	Not done	2.2	8.1
ALT (U/L)	22	12	32	10
AST (U/L)	35	22	76	18
LDH (U/L)	238	234	242	228
Creatinine	108	43	67	106
Total bilirubin	4.3	6	6	15→40→44→50→45→31
Hb (g/dL)	11.9	11.0	12.3	11.0

Case 1

A 31-year-old Gravida 2 Para 1 at 36 weeks gestation presented with fever, productive cough for two days and diarrhoea for one day prior to admission. She also complained of arthralgia, myalgia and shortness of breath. After tested positive for COVID-19, she was traced to have contracted it from her uncle, who was tested positive for COVID-19 one week before the onset of her symptoms. On admission, her body temperature was 37.9°C. Her chest X-ray was normal, and she was diagnosed as COVID-19 Stage 2B.

Antenatally, she had a previous lower segment caesarean section (LSCS) and was noted to have a breech presentation on admission. She was subjected for an earlier elective LSCS at 36 weeks and 4 days gestation. Intra-operatively was uneventful. She delivered a baby boy weighing 2.65kg with good Apgar Score, and she recovered well postnatally.

Case 2

The second case was a 29-year-old medical doctor, Gravida 2 Para 1, who was admitted for observation at 37 weeks gestation following a positive test for COVID-19 during an out-patient screening. She had voluntary testing because of a few potential risks of exposure which were her husband just returned from overseas' travel, her recent attendance to a wedding and potential exposure at her workplace. However, her husband and all her close contact at work were tested negative for COVID-19. At the time of writing of this manuscript, the source of infection for her remained unknown.

Antenatally, she was well with no comorbidities. She was asymptomatic initially, however, on the second day of admission, she developed mild shortness of breath and staged as COVID-19 2A. She went into spontaneous labour on the following day; therefore, an emergency LSCS was performed. The surgery was uneventful, and she delivered a healthy baby girl weighing 2.78kg with good Apgar Score. She recovered well postnatally.

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Case 3

A 27-year-old primigravida at 39 weeks gestation, who was tested positive for COVID-19, presented in labour. She contracted the disease from her husband, who was recently diagnosed with COVID-19. Antenatally, she was diagnosed to have asymmetrical intrauterine growth restriction with no other underlying maternal medical problem. Upon arrival, it was noted that cervical os was fully dilated. There was moderate meconium-stained liquor, and cardiotocograph (CTG) showed fetal bradycardia. An immediate ventouse-assisted delivery was performed. It was uneventful, and she delivered a baby boy weighing 2.0kg with good Apgar score.

Ten hours after delivery, she developed high-grade fever with the body temperature of 38.1°C. She also developed a non-productive cough and runny nose. A full septic workup was performed. There was no organism isolated, and the chest X-ray was normal. She was treated as worsening COVID-19 (Stage 2B) as other causes of puerperal pyrexia had been excluded. Hydroxychloroquine (HC) was prescribed, and symptoms resolved after one day of medication. However, HC was continued for five days as per recommendation by the national guideline. During the hospitalisation, she was also treated with daily wound dressing and antibiotics for episiotomy wound breakdown. She was discharged on day 11 postpartum following a negative COVID-19 test result.

Case 4

A 29-year-old staff nurse, Gravida 3 Para 1+1 at 35 weeks gestation without any medical problem was admitted for observation after tested positive for COVID-19. She contracted the disease from a COVID-19 positive haemodialysis patient. Antenatally, she had a history of threatened preterm contraction at 28 weeks of gestation, but otherwise was uneventful. On the day of admission, she had leaking liquor and went into labour. Otherwise, she had no symptoms of COVID-19. She was tachycardic on admission with other vital signs within the normal range. Ultrasound confirmed that she had a breech presentation. An emergency LSCS was done, and intra-operatively was uneventful. She delivered a baby girl weighing 2.74kg with good Apgar score.

Post-operatively, HC was prescribed due to persistent tachycardia which was attributed as a sign of COVID-19 after excluding other potential causes. On the second day of admission, her body temperature spiked up to 38.8° C, followed by non-productive cough and mild shortness of breath. Chest X-ray showed bilateral lower zone consolidation. She was then diagnosed as COVID-19 stage 3A. Antiviral medications Atazanavir 100mg and Ritonavir 100mg orally once a day, were added. Intravenous Unasyn 3g three times a day was also given as empirical treatment for bacterial infection. Her blood culture was later revealed as negative. In view of her prolonged fever, other blood investigations, including procalcitonin and ferritin, were taken to look for the possibility of cytokine response syndrome. Fortunately, the results were not suggestive of cytokine response syndrome. Her fever resolved after six days of treatment. The antiviral medications were stopped on day 12 of treatment because of hyperbilirubinaemia. HC was completed for 14 days. She was discharged well following a negative test for COVID-19 on day 18.

Neonatal Outcome

All babies were nursed separately in the nursery after delivery for 14 days. Neither direct breastfeeding nor giving expressed breastmilk was allowed. Breastfeeding was only commenced after repeat swab for the mothers confirmed negative for COVID-19. All babies were tested negative for COVID-19. All babies were well when discharged to their mothers after the period of isolation.

DISCUSSION

This case series of four pregnant women at advanced gestation described the case management and perinatal outcome of pregnancies with COVID-19.

Three patients in our series have been identified as close contact with COVID-19 patients. Evidence has shown that SARS-CoV-2 is transmitted by respiratory droplets, making it highly infectious to other people who are within 2 metres. It can be spread not only when they are in close proximity with COVID-19 patients, but

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also by touching contaminated surfaces or objects and subsequently touching their mouth, nose, or eyes [4, 5]. The healthcare worker (Case 4) who had close contact with an undiagnosed COVID-19 patient, illustrated the vulnerability of healthcare workers. Hence, the importance of effective screening strategies in all healthcare facilities to stratify risks of everyone attending the facilities, appropriate level of personal protective equipment (PPE) use, and compliance to hand hygiene cannot be underestimated to reduce the risk of infection towards healthcare workers.

Age is one of the risk factors of the crude fatality rate (CFR) in COVID-19. The CFR in older patients is higher than the younger patients [6]. All patients in our series were in the younger age group. Underlying comorbidities such as diabetes and hypertension are also associated with a higher risk of admission to the intensive care unit, invasive ventilation, and deaths [7]. Presence of multiple comorbidities puts a higher risk of fatality than a single medical problem. In this case series, none has comorbidities except one patient who had pre-eclampsia. However, it did not result in life-threatening complications, similarly to previously reported cases [8].

Fever and cough have been reported to be the main presenting symptom among pregnant patients [4, 9, 10]. The presenting symptoms of patients in this case series were non-productive cough, fever, shortness of breath, sore throat, malaise, and diarrhoea. Other reported presenting symptoms includes chest tightness [11], fatigue, headaches, and haemoptysis [2]. There were only two patients in this series who showed bilateral lower zone consolidation on chest X-ray. Presence of abnormal chest imaging findings in patients with COVID-19 ranging from 41.7% up to 98% [2]. This wide range possibly due to the severity of diseases among the population studied and the imaging technique used. Studies among patients with severe disease and using CT scan reported a higher incidence of abnormal findings [2]. Improvement in chest imaging was observed in patients who improved clinically [2].

The risk of intrapartum mother-to-child transmission by vaginal delivery remains a concern. Hence, caesarean section is the preferred mode of delivery for COVID-19 patients. Currently, it is our practice to deliver all COVID-19 patients via caesarean section, preferably elective, unless vaginal delivery is imminent as per local guideline [12]. The caesarean may be performed during day 1 - 4 of the illness as they may progress to the critical phase around day 5 - 7 of illness, as observed in many symptomatic COVID-19 patients. The importance of having the delivery in a planned and controlled environment should be emphasized as this allows all healthcare workers involved to be ready and allow adequate time for them to don the PPE appropriately.

However, in the situation of imminent delivery, vaginal delivery should be allowed. Nonetheless, all safety precautions must be observed strictly to reduce the chances of infection either to the baby or the healthcare workers involved. Interestingly, similar to other reported cases [9, 10], the baby delivered via ventouse-assisted delivery in this case series was tested negative for COVID-19. Even though this may suggest that vaginal delivery is potentially a safe mode of delivery for women with COVID-19, the numbers are too small for us to make any recommendation with regards to the safety of vaginal delivery in COVID-19 mothers.

Many treatments have been used to treat COVID-19 patients, which includes antiviral therapy such as oseltamivir and nebulised interferon [9, 10]. However, to date, no therapies are yet proven effective [13]. Chloroquine/Hydroxychloroquine; a longstanding anti-malarial; inhibit glycosylation of host receptors, proteolytic processing, and endosomal acidification; hence preventing viral entry to the cell. Further, they have immunomodulatory effects through attenuation of cytokine production and inhibition of autophagy and lysosomal activity in host cells [14]. Despite successfully used to treat more than a hundred COVID-19 case [15], Chloroquine has yet to have adequate quality evidence to show its effectiveness in the treatment of this disease. In this case series, both patients who were prescribed with medications improved clinically with evidence of improved radiological findings on their chest x-rays.

There were neither cases of severe pneumonia, cytokine response syndrome, nor maternal deaths in our series. It remains unclear whether maternal SARS-CoV-2 infection causes any adverse outcome to the

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newborn babies. Recently, a study found three neonatal early-onset infections with SARS-CoV-2, hence suggesting a possibility of vertical transmission of the virus [16]. However, none of the babies in our series was tested positive for COVID-19, similar to other previous reports [9, 10] Recent evidence showed no virus in breastmilk of mothers with COVID-19. However, the risk of transmission from the mother via respiratory droplets in close proximity remains. Therefore, the mothers were advice not to breastfeed and express their breast milk until they were tested negative. This policy on breastfeeding restriction will be reviewed once more scientific evidence on its safety is available.

CONCLUSION

In conclusion, there was no evidence of adverse maternal and neonatal complications in pregnant women with COVID-19. In addition, no vertical transmission of COVID-19 disease observed in this case series.

Conflict of Interest

Authors declare none.

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Authors' contribution

All authors contributed significantly to conception and design; acquisition, analysis and interpretation of the data; drafting the manuscript; revising the manuscript critically for important intellectual content and final approval of the version published.

REFERENCES

1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395(10223): 507-13. doi: 10.1016/s0140-6736(20)30211-7.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395(10223): 497-506. doi: 10.1016/s0140-6736(20)30183-5
3. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-March-2020. Accessed on 26 Jan 2021.
4. Bi Q, Wu Y, Mei S, Ye H, Zou X, Zhang Z, Liu X, Wei L, Truelove SA, Zhang T, Gao W, Cheng C, Tang X, Wu X, Wu Y, Sun B, Huang S, Sun Y, Zhang J, Ma T, Lessler J, Feng T. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. The Lancet Infect Dis. 2020; 20: 911-19. doi: 10.1016/ S1473-3099(20)30287-5.
5. Coronavirus (COVID-19) infection in Pregnancy. Royal College Obstetrician & Gynaecologists UK. 2020. https://www.rcog.org.uk/en/guidelines-research-services/guidelines/coronavirus-pregnancy/. Accessed 26 Jan 2021.
6. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, Cuomo-Dannenburg G, Thompson H, Walker P, Fu H, Dighe A, Griffin J, Baguelin M, Bhatia S, Boonyasiri A, Cori A, Cucunubá Z, FitzJohn R, Gaythorpe K, Green W, Hamlet A, Hinsley W, Laydon D, Nedjati-Gilani G, Riley S, Elsland S, Volz E, Wang H, Wang Y, Xi X, Donnelly CA, Ghani AC, Ferguson NM. Estimates of the severity of coronavirus disease 2019: a model-based analysis. The Lancet Infectious Diseases. 2020; 20(6): 669-77. doi: 10.1016/S1473-3099(20)30243-7
7. Guan W-j, Liang W-h, Zhao Y, Liang H-r, Chen Z-s, Li Y-m, Liu X-q, Chen R-c, Tang C-l, Wang T, Ou C-q, Li L, Chen P-y, Sang L, Wang W, Li J-

f, Li C-c, Ou L-m, Cheng B, Xiong S, Ni Z-y, Xiang J, Hu Y, Liu L, Shan H, Lei C-l, Peng Y-x, Wei L, Liu Y, Hu Y-h, Peng P, Wang J-m, Liu J-y, Chen Z, Li G, Zheng Z-j, Qiu S-q, Luo J, Ye C-j, Zhu S-y, Cheng L-l, Ye F, Li S-y, Zheng J-p, Zhang N-f, Zhong N-s, He J-x. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. Eur Respir J. 2020; 55(5): 2000547. doi: 10.1183/13993003.00547-2020.

8. Schwartz DA. An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes. Arch Pathol Lab Med 2020; 144(7): 799–805. doi: 10.5858/arpa.2020-0901-SA.
9. Liu W, Wang Q, Zhang Q, Chen L, Chen J, Zhang B, Lu Y, Wang S, Xia L, Huang L, Wang K, Liang L, Zhang Y, Turtle L, Lissauer D, Lan K, Feng L, Yu H, Liu Y, Sun Z. Coronavirus Disease 2019 (COVID-19) During Pregnancy: A Case Series. Preprints2020,2020020373 https://www.preprints.org/manuscript/202002.0373/v. Accessed 27 Jan 2021.
10. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, Xia S, Zhou W. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Transl Pediatr. 2020; 9(1): 51–60. doi: 10.21037/tp.2020.02.06.
11. Zhang L, Jiang Y, Wei M, Cheng BH, Zhou XC, Li J, Tian JH, Dong L, Hu RH. [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. Zhonghua Fu Chan Ke Za Zhi. 2020; 55(3): 166-171. Chinese. doi: 10.3760/cma.j.cn112141-20200218-00111.
12. Annex 23: Guidelines on Management of COVID-19 in Obstetrics & Gynaecology. 2020. http://covid-19.moh.gov.my/garis-panduan/garis-panduan kkm/Annex_23_GUIDELINES_ON_MANAGEMENT_OF_COVID19_IN_OnG_07122020.pdf. Accessed 27 Jan 2021.
13. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review. JAMA. 2020;323(18):1824–1836. doi:10.1001/jama.2020.6019.
14. Devaux CA, Rolain J-M, Colson P, Raoult D. New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19? Int J Antimicrob Agents. 2020; 55(5):105938105938.
15. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China. Clin Infect Dis. 2020; 71(15): 769-777. doi:10.1093/cid/ciaa272
16. Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, Zhou W. Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China. JAMA Pediatr. 2020;174(7):722-725. doi: 10.1001/jamapediatrics.2020.0878.