

Predictors for adverse outcomes in pregnant women with COVID-19 infection: a retrospective study

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Objectives: We aimed to identify predictors associated with adverse maternal and neonatal outcomes in women with COVID-19 infection.

Methods: Medical records of women with a singleton pregnancy who were diagnosed with COVID-19 infection at any gestational age and delivered in Tuen Mun Hospital between 1 January 2022 and 31 December 2022 were retrospectively reviewed. Pregnant women with COVID-19 infection who had or had no composite adverse outcomes were compared. Risk factors associated with COVID-19 disease severity and maternal and neonatal outcomes were determined.

Results: In total, 233 pregnant women were included in the analysis. Women with composite adverse outcomes from COVID-19 infection were more likely to have advanced maternal age (adjusted odds ratio [aOR]=4.19, $p=0.013$) and no prior COVID-19 vaccination (aOR=0.27, $p=0.019$). Women with composite adverse maternal outcomes were more likely to have advanced maternal age (aOR=2.25, $p=0.009$), an abnormal body mass index (aOR=1.76, $p=0.040$), and active COVID-19 infection at the time of delivery (aOR=1.81, $p=0.045$). Neonates with composite adverse outcomes were more likely to have been born to mothers with comorbidities (aOR=3.13, $p=0.007$).

Conclusion: Risk factors for severe COVID-19 disease and adverse maternal and neonatal outcomes include advanced maternal age, pre-existing comorbidities, abnormal body mass index, active COVID-19 infection at delivery, and no prior COVID-19 vaccination.

Keywords: COVID-19; Pregnancy outcome; Vaccination

Introduction

As of 1 September 2024, COVID-19 has caused more than seven million deaths¹. Pregnant women with COVID-19 infection are at higher risk of adverse events, compared with the general population²⁻⁵. COVID-19 infection is associated with adverse maternal and neonatal outcomes^{4,6,7}. In a systematic review of 435 studies, pregnant women with COVID-19 infection are more likely to require intensive care unit (ICU) admission, invasive ventilation, and preterm deliveries, and are at higher risk of maternal death, whereas their babies are more likely to require neonatal ICU admission⁴. Risk factors associated with severe disease in pregnant women with COVID-19 infection include older maternal age, higher body mass index (BMI), and pre-existing maternal comorbidities^{4,8-10}. We aimed to identify predictors associated with adverse maternal and neonatal outcomes in women with COVID-19 infection.

Methods

Medical records of women with a singleton pregnancy who were diagnosed with COVID-19 infection at any gestational age and delivered in Tuen Mun Hospital between 1 January 2022 and 31 December 2022 were retrospectively reviewed. The diagnosis was defined as a positive result on real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay of a nasopharyngeal swab or deep throat saliva specimen. Women were excluded if they had incomplete clinical data, a positive result from the rapid antigen test only, multiple pregnancy, or infection after delivery.

Data retrieved included maternal age at delivery,

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BMI at booking visit, ethnicity, education level, smoking and drinking habits, comorbidities (asthma, pre-existing diabetes mellitus, chronic hypertension, renal disease, cardiovascular disease, autoimmune disease, obstructive sleep apnoea, chronic lung disease, chronic liver disease, thyroid disease, and haematological disease), parity, anaemia at booking visit, COVID-19 vaccination status, pregnancy complication (anteperium haemorrhage, gestational diabetes, placenta praevia, amniotic fluid complications including oligohydramnios and polyhydramnios, and fetal growth restriction), gestational age at COVID-19 infection, presence of symptoms of COVID-19 infection, laboratory and imaging test results, length of hospitalisation, oxygen therapy, organ derangement, venous thromboembolism, ICU admission, and maternal death.

Obstetric complications recorded included hypertensive disorder of pregnancy, preterm delivery before 37 weeks of gestation, abnormal cardiotocography, placental abruption, mode of delivery, primary postpartum haemorrhage (blood loss ≥ 500 mL), and maternal ICU admission after delivery. Neonatal outcomes recorded included birthweight, neonatal ICU admission, Apgar scores, arterial umbilical cord blood pH, vertical transmission of COVID-19 infection, stillbirth, and neonatal complications (respiratory distress syndrome, hypoglycaemia, neonatal hyperbilirubinaemia requiring phototherapy, need for assisted ventilation, clinical sepsis, resuscitation at birth, hypoxic-ischaemic encephalopathy, and neonatal death). Definitions of maternal, fetal, and neonatal death and adverse birth outcomes were based on the World Health Organization definitions^{11–14}. The composite adverse outcomes from COVID-19 infection were defined by the presence of any of the following: pneumonia, need for oxygen therapy, organ derangement, venous thromboembolism, ICU admission, prolonged hospitalisation for ≥ 21 days, and maternal death. The composite adverse maternal outcomes were defined by the presence of any of the following: gestational hypertensive disorder, placental abruption, emergency Caesarean section, primary postpartum haemorrhage, and maternal ICU admission after delivery. The composite adverse neonatal outcomes were defined by the presence of any of the following: preterm birth before 37 weeks of gestation, small for gestational age, Apgar score < 7 at 5 minutes after birth, arterial cord blood pH < 7.0 , admission to neonatal ICU, hypoxic-ischaemic encephalopathy, stillbirth, and neonatal death. Small for gestational age was based on updated fetal growth curve references from the Hong Kong Chinese population¹⁵.

Risk factors for severe COVID-19 infection include the following: advanced age ≥ 35 years, abnormal BMI (< 18.5 or ≥ 23 kg/m² for the Asian population), comorbidities, parity, COVID-19 vaccination status, and infection status at the time of delivery^{16–18}. Recovery from COVID-19 infection is defined as being asymptomatic for ≥ 3 days after ≥ 10 days since the initial positive RT-PCR test¹⁹, or cycle threshold (Ct) value of ≥ 30 on two consecutive samples for RT-PCR assay, or Ct value of ≥ 30 on one sample with a positive result on immunoglobulin G assay.

Pregnant women with and without adverse outcomes were compared using the Pearson Chi-squared test or Fisher's exact test, as appropriate. Risk factors associated with COVID-19 disease severity and maternal and neonatal outcomes were determined using multivariate logistic regression analyses with adjustment for confounders (including risk factors for COVID-19 infection severity such as advanced age ≥ 35 years, abnormal BMI, comorbidities, and COVID-19 vaccination status, as well as pregnancy-related risk factors such as parity and infection status at delivery). These risk factors have been reported to affect the COVID-19 disease severity and maternal and neonatal outcomes^{4,10,16,17,20,21}. Statistical analyses were performed using SPSS (Windows version 26.0; IBM Corp, Armonk [NY], United States). A *p* value of < 0.05 was considered statistically significant.

Results

In total, 233 pregnant women (83.3% were Chinese and the rest were Southeast Asians) were included in the analysis (Table 1). The median maternal age at delivery was 32 years; 148 (63.5%) had received at least one dose of COVID-19 vaccine before infection, whereas three (1.3%) had a history of COVID-19 infection. The median Ct value at diagnosis was 23.8; 76 (32.6%) had active COVID-19 infection at delivery. Among 178 (76.4%) women with symptoms of COVID-19 infection, the most common symptoms were cough (48.1%), sore throat (43.3%), fever (35.6%), and runny nose (30.5%). Among 161 (69.1%) women hospitalised during COVID-19 infection, the median length of hospital stay was 5 days. Severe adverse events of COVID-19 infection were organ derangement (5.2%), ICU admission (1.3%), and pneumonia (0.4%). None required oxygen supplementation or had venous thromboembolism or maternal death.

Regarding maternal complications, 21 (9.0%) had hypertensive disorders of pregnancy: gestational hypertension (*n*=11), pre-eclampsia (*n*=7), gestational

Table 1. Baseline characteristics of women diagnosed with COVID-19 infection during pregnancy (n=233)

Characteristic	Value*
Maternal age, y	32 (28-35)
Advanced maternal age (≥ 35 y)	69 (29.6)
Ethnicity	
Chinese	194 (83.3)
Southeast Asian	39 (16.7)
Education level	
Primary	7 (3.0)
Secondary	140 (60.1)
Tertiary	86 (36.9)
Multiparity	141 (60.5)
Previous Caesarean section	49 (21.0)
Smoking	7 (3.0)
Drinking	2 (0.9)
Body mass index, kg/m ²	22.6 (20.5-25.5)
≥ 23 (overweight/obesity)	103 (44.2)
< 18.5 (underweight)	14 (6.0)
Comorbidities	32 (13.7)
Asthma	13 (5.6)
Chronic hypertension	5 (2.1)
Pre-existing diabetes	2 (0.9)
Thyroid disease	5 (2.1)
Cardiac disease	3 (1.3)
Autoimmune disease	3 (1.3)
Haematological disease	2 (0.9)
Liver disease	3 (1.3)
Natural conception	227 (97.4)
Prior COVID-19 vaccination	148 (63.5)
Past COVID-19 infection	3 (1.3)
Gestational age at diagnosis, w	36 (25-38)
First trimester	43 (18.5)
Second trimester	20 (8.6)
Third trimester	170 (73.0)
Active infection at delivery	76 (32.6)
Cycle threshold value at diagnosis	23.8 (18.6-29.4)
Interval between the day with lowest cycle threshold value and delivery, d	9 (1-92)
COVID-19 infection symptom	178 (76.4)
Fever	83 (35.6)
Cough	112 (48.1)
Runny nose	71 (30.5)
Sore throat	101 (43.3)
Dyspnoea	5 (2.1)
Vomiting	20 (8.6)
Diarrhoea	8 (3.4)
Reduced fetal movement	33 (14.2)

* Data are presented as median (interquartile range) or No. (%) of participants

Table 1. (cont'd)

Characteristic	Value*
COVID-19 infection severity	
Pneumonia	1 (0.4)
Oxygen supplement	0
Intensive care unit admission	3 (1.3)
Organ derangement	12 (5.2)
Venous thromboembolism	0
Maternal mortality	0
Haemoglobin, g/dL (n=166)	11.4 (10.4-12.4)
White blood cell count, $\times 10^9/L$ (n=166)	9.1 (7.2-11.5)
Platelet count, $\times 10^9/L$ (n=166)	194 (166-234)
Abnormal liver enzymes (n=152)	9 (5.9)
C-reactive protein, mg/L (n=139)	17 (4.5-36.6)
Hospitalisation	161 (69.1)
Length of hospitalisation, d	5 (4-8)

proteinuria (n=2), and eclampsia (n=1) [Table 2]. The median gestational age at delivery was 38 weeks; 24 (10.3%) had preterm delivery before 37 weeks of gestation. 107 (45.9%) underwent Caesarean sections, of which 73.8% were in an emergency setting. The most common indications for Caesarean section were previous Caesarean section (43.0%) and abnormal cardiotocography (20.6%). Of the women, 49 (21.0%) had primary postpartum haemorrhage, whereas 2.1% required ICU admission after delivery.

Regarding neonatal outcomes, the median birthweight was 3050 g; 16 (6.9%) had low birthweight (< 2500 g), whereas 21 (9.0%) were small for their gestational age (Table 3). Only one (0.4%) neonate had hypoxic-ischaemic encephalopathy. Two (0.9%) were stillbirths (one was diagnosed with placental abruption at 32 weeks and the other was diagnosed with fetal congenital leukaemia). Two (0.9%) died within 28 days of life. One who died on the third day of life was delivered at 26 weeks secondary to maternal severe pre-eclampsia, fetal growth restriction, and fetal distress. Another who died 2 hours after birth was delivered at 36 weeks owing to hydrops fetalis. The cause of hydrops was not identified, but the mother had late latent syphilis treated in the second trimester, mild COVID-19 infection treated with antiviral medication at 32 weeks, and gestational diabetes under good control.

The rate of composite adverse outcomes from COVID-19 infection was 7.3% (n=17), whereas the rate of composite adverse maternal outcomes was 45.9% (n=107) and the rate of composite adverse neonatal outcomes was 21.5% (n=50).

Table 2. Pregnancy and delivery characteristics of women diagnosed with COVID-19 infection during pregnancy (n=233)

Characteristic	Value*
Antepartum haemorrhage	20 (8.6)
Gestational diabetes	42 (18.0)
Placenta praevia	6 (2.6)
Oligohydramnios	10 (4.3)
Polyhydramnios	3 (1.3)
Intrauterine growth restriction	4 (1.7)
Any hypertensive disorder of pregnancy	21 (9.0)
Pregnancy-induced hypertension	11 (52.4)
Gestational proteinuria	2 (9.5)
Pre-eclampsia	7 (33.3)
Eclampsia	1 (4.8)
Gestational age at delivery, w	38 (37-39)
Any preterm delivery <37 w	24 (10.3)
Preterm delivery <28 w	1 (4.2)
Preterm delivery 28+0 to 33+6 w	5 (20.8)
Preterm delivery 34+0 to 36+6 w	18 (75.0)
Preterm premature rupture of membranes	8 (3.4)
Abnormal cardiotocography	49 (21.0)
Placental abruption	1 (0.4)
Induction of labour	71 (30.5)
Mode of delivery	
Normal vaginal delivery	108 (46.4)
Instrumental delivery	18 (7.7)
Caesarean section	107 (45.9)
Elective Caesarean section	28 (26.2)
Emergency Caesarean section	79 (73.8)
Indications of Caesarean section	n=107
Previous Caesarean section	46 (43.0)
Abnormal cardiotocography	22 (20.6)
Breech	7 (6.5)
Placenta praevia	7 (6.5)
Failed induction	6 (5.6)
No progress	5 (4.7)
Severe pre-eclampsia	4 (3.7)
Placental abruption	1 (0.9)
Intrauterine infection	1 (0.9)
Others	8 (7.5)
Primary postpartum haemorrhage	49 (21.0)
Need for isolation at delivery	59 (25.3)
Post-delivery maternal intensive care unit admission	5 (2.1)

* Data are presented as median (interquartile range) or No. (%) of participants

Table 3. Neonatal outcomes in women diagnosed with COVID-19 infection during pregnancy (n=233)

Neonatal outcome	Value*
Male sex	142 (60.9)
Birthweight, g	3050 (2830-3315)
Low birthweight <2500 g	16 (6.9)
Very low birthweight <1500 g	2 (0.9)
Small for gestational age	21 (9.0)
Neonatal intensive care unit admission	11 (4.7)
Apgar score at 1 minute	8 (8-8)
Apgar score at 5 minutes	9 (9-9)
Low Apgar score <7 at 5 minutes	5 (2.1)
Umbilical cord arterial pH <7.0	1 (0.4)
COVID-19 positive on nasopharyngeal swab specimen	0
Respiratory distress syndrome	21 (9)
Hypoglycaemia	2 (0.9)
Hyperbilirubinaemia requiring phototherapy	40 (17.2)
Assisted ventilation	17 (7.3)
Clinical sepsis	31 (13.3)
Resuscitation at birth	15 (6.4)
Hypoxic-ischaemic encephalopathy	1 (0.4)
Stillbirth	2 (0.9)
Neonatal death	2 (0.9)

* Data are presented as median (interquartile range) or No. (%) of participants

Women with composite adverse outcomes from COVID-19 infection were more likely to have advanced maternal age (adjusted odds ratio [aOR]=4.19, $p=0.013$) and no prior COVID-19 vaccination (aOR=0.27, $p=0.019$) [Table 4]. Women with composite adverse maternal outcomes were more likely to have advanced maternal age (aOR=2.25, $p=0.009$), an abnormal BMI (aOR=1.76, $p=0.040$), and active COVID-19 infection at the time of delivery (aOR=1.81, $p=0.045$). Neonates with composite adverse outcomes were more likely to have been born to mothers with comorbidities (aOR=3.13, $p=0.007$).

Discussion

The rate of composite adverse outcomes from COVID-19 infection among pregnant women was 7.3%, which is lower than the rate for severe COVID-19 disease of 9% reported in a systematic review of 82 studies involving 31 331 women⁴. In Hong Kong during the early times of the pandemic, the circulation of the Alpha, Beta, and Delta variants was limited²². Only eight women were

Table 4. Predictors for adverse outcomes in women diagnosed with COVID-19 infection during pregnancy

Outcome	With adverse outcome*	Without adverse outcome*	Odds ratio (95% confidence interval)	p Value	Adjusted odds ratio (95% confidence interval)	p Value
Composite adverse outcomes from COVID-19 infection	n=17	n=216				
Advanced maternal age	9 (52.9)	60 (27.8)	2.93 (1.08-7.93)	0.029	4.19 (1.36-12.94)	0.013
Abnormal body mass index	9 (52.9)	108 (50.0)	1.13 (0.42-3.03)	0.815	0.95 (0.33-2.73)	0.925
Multiparity	8 (47.1)	133 (61.6)	0.56 (0.21-1.49)	0.238	0.37 (0.12-1.12)	0.079
Prior COVID-19 vaccination	7 (41.2)	141 (65.3)	0.37 (0.14-1.02)	0.047	0.27 (0.09-0.81)	0.019
Comorbidities	4 (23.5)	28 (13.0)	2.07 (0.63-6.78)	0.264	2.34 (0.62-8.89)	0.211
Composite adverse maternal outcomes	n=107	n=126				
Advanced maternal age	40 (37.4)	29 (23.0)	2.00 (1.13-3.53)	0.017	2.25 (1.23-4.14)	0.009
Abnormal body mass index	62 (57.9)	55 (43.7)	1.78 (1.06-2.99)	0.030	1.76 (1.03-3.03)	0.040
Multiparity	61 (57.0)	80 (63.5)	0.76 (0.45-1.29)	0.313	0.60 (0.34-1.06)	0.077
Prior COVID-19 vaccination	66 (61.7)	82 (65.1)	0.86 (0.51-1.48)	0.591	0.90 (0.51-1.59)	0.711
Comorbidities	17 (15.9)	15 (11.9)	1.40 (0.66-2.95)	0.379	1.16 (0.52-2.59)	0.714
Active COVID-19 infection at delivery	42 (39.3)	34 (27.0)	1.75 (1.01-3.04)	0.047	1.81 (1.01-3.23)	0.045
Composite adverse neonatal outcome	n=50	n=183				
Advanced maternal age	16 (32.0)	53 (29.0)	1.15 (0.59-2.27)	0.677	1.06 (0.52-2.17)	0.864
Abnormal body mass index	27 (54.0)	90 (49.2)	1.21 (0.65-2.27)	0.546	1.09 (0.57-2.09)	0.788
Multiparity	29 (58.0)	112 (61.2)	0.88 (0.46-1.65)	0.681	0.84 (0.43-1.62)	0.593
Prior COVID-19 vaccination	32 (64.0)	116 (63.4)	1.03 (0.54-1.97)	0.936	0.87 (0.44-1.72)	0.681
Comorbidities	13 (26.0)	19 (10.4)	3.03 (1.38-6.69)	0.004	3.13 (1.37-7.14)	0.007
Active COVID-infection at delivery	15 (30.0)	61 (33.3)	0.86 (0.44-1.69)	0.656	0.80 (0.40-1.62)	0.544

* Data are presented as No. (%) of participants

diagnosed with COVID-19 infection during pregnancy in our institution between 2020 and 2021. The transmission became rapid in December 2021 after the outbreaks of the Omicron variant, leading to the fifth wave in Hong Kong²³. The difference in the rate of adverse outcomes from COVID-19 infection may be partly due to different predominant strains at the time of the study, because the Delta variant is associated with more severe disease, compared with the Omicron variant²⁴⁻²⁷.

Advanced maternal age was a predictor for adverse events from COVID-19 infection and adverse maternal outcomes, similar to the findings reported in a review¹⁰, which found that advanced maternal age was associated with increased risks of ICU admission, mechanical ventilation, pneumonia, placental abruption, and Caesarean delivery. Our findings also concurred with findings from

other studies for pregnant women^{4,9} and the general population^{16,17,28}.

Vaccination is associated with lower risks of severe or critical COVID-19 infection^{20,29}. Pregnant women with at least one dose of COVID-19 vaccine were less likely to have adverse outcomes from COVID-19 infection. Vaccination generates robust humoral immunity^{30,31}. Severe COVID-19 infection increases the risks of adverse maternal and neonatal outcomes including Caesarean delivery, preterm birth, and neonatal ICU admission^{8,32,33}. Vaccination is associated with lower risks of stillbirth, very or extremely preterm birth, and small for gestational age among term babies³⁴. Nevertheless, pregnant women commonly have safety concerns and thus vaccine hesitancy. The main adverse effects of vaccination are local reactogenicity events (such as pain, redness, and swelling)

and systemic reactogenicities (such as tiredness, headache, and fever)³⁵. In general, symptoms in vaccinated individuals are usually mild to moderate and self-limiting³⁶. There is growing evidence that COVID-19 vaccine causes no safety concerns on pregnancy outcomes³⁷⁻³⁹. In our study, only 63.5% of the pregnant women received at least one dose of COVID-19 vaccine. This rate is significantly lower than the vaccination rate of 83.7% among pregnant women reported in a study in Hong Kong⁴⁰. The World Health Organization, the Hong Kong College of Obstetricians and Gynaecologists, the Royal College of Obstetricians and Gynaecologists, and the American College of Obstetricians and Gynaecologists all recommend pregnant women staying up to date with COVID-19 vaccines⁴¹⁻⁴³. Therefore, pregnant women should be educated on the efficacy and safety of COVID-19 vaccines and advised to be vaccinated.

Increased BMI is a risk factor for severe COVID-19 complications^{4,9,10,44,45}. Pre-pregnancy underweight status is also a risk factor for adverse outcomes from COVID-19 infection in pregnancy¹⁰. However, we did not find any association between abnormal BMI and adverse outcomes from COVID-19 infection, probably because of the small sample size. However, we found that pregnant women with abnormal BMI were at higher risks of adverse maternal outcomes. This finding is consistent with those reported in a study in Serbia, which showed that overweight and obese pregnant women were more likely to have gestational hypertension⁴⁶.

Pre-existing comorbidities are risk factors for severe COVID-19 disease in pregnancy^{4,8,10} and adverse neonatal outcomes such as preterm birth⁴⁷, consistent with our findings.

The literature shows conflicting results with regard to the association between active COVID-19 infection at delivery and pregnancy outcomes. In our study, active COVID-19 infection at delivery was associated with adverse maternal outcomes including hypertensive disorders and emergency Caesarean delivery. This is in keeping with the findings from a population-based cohort study in England (n=342080), which showed that active COVID-19 infection at delivery was associated with higher rates of fetal death, preterm birth, pre-eclampsia, and emergency Caesarean delivery²¹. On the contrary, studies in Israel and South Africa demonstrated no associations between active COVID-19 infection at delivery and rates of emergency Caesarean delivery, fetal death, preterm birth, low birthweight, or other pregnancy-induced complications^{19,48}. In our study, no association was

found between active COVID-19 infection at delivery and adverse neonatal outcomes.

According to our hospital policy, pregnant women with active COVID-19 infection were admitted to a single room with negative pressure or the isolation ward for vaginal delivery, or were transferred to an operating theatre with negative pressure for Caesarean section. Management of labour and delivery was based on standard obstetric indications. However, the operating theatre with negative pressure is far away from the labour ward, so timely delivery in an emergency setting (eg, fetal distress during labour) might become difficult. The prolonged decision-to-delivery interval might have decreased the frontline obstetrician's threshold for arranging emergency Caesarean delivery for fetal wellbeing. Furthermore, some women changed their minds on the mode of delivery and declined a trial of vaginal birth after a previous Caesarean delivery when they were admitted for labour with active COVID-19 infection. This might result in the increased likelihood of adverse maternal outcomes in women with active COVID-19 infection at delivery. Therefore, labour wards and operating rooms with isolation facilities should be set up to facilitate intrapartum care and minimise delay in case an airborne precaution during delivery is required in future pandemics⁴⁹.

To the best of our knowledge, this is the first study in Hong Kong to identify predictors of adverse outcomes in pregnant women with COVID-19 infection. There are several limitations to our study. The study design is retrospective and the sample size is small. Analyses for each adverse outcome were not performed because of the small sample size. Sampling frames varied, depending on the time of COVID-19 diagnosis, ranging from universal COVID-19 testing for all pregnant women admitted to hospital in early 2022 to symptom-based testing in late 2022. Pregnant women with COVID-19 infection diagnosed by rapid antigen tests only were excluded. Therefore, the true sample size was probably underestimated, potentially introducing selection bias.

Conclusion

Risk factors for severe COVID-19 disease and adverse maternal and neonatal outcomes include advanced maternal age, pre-existing comorbidities, abnormal BMI, active COVID-19 infection at delivery, and no prior COVID-19 vaccination. COVID-19 vaccine can reduce adverse outcomes and is beneficial to pregnant women. Isolation facilities in labour wards should be set up in preparation for future pandemics.

Contributors

YCN, LTK, and PLS designed the study. YCN, YYL, SYL, and PLS acquired and analysed the data. YCN drafted the manuscript. All authors critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have no conflicts of interest to disclose.

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sectors.

Data availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

Ethics approval

The study was approved by the Central Institutional Review Board of Hospital Authority (reference: CIRB-2023-056-1). The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatments and procedures and for publication.

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