Obstetrics and Gynecology Reports

Research Article ISSN: 2515-2955

Convalescent plasma therapy for pregnant patients with COVID-19: Case series

Mariam Ayed[1*], Farah Alshammari[2], Amal Ayed[3], Ibrahim Gadalla[3], Fawaz Aldoohan[2] and Sondos Alsharidah[4]

[1]Neonatal Department, Farwaniya Hospital, Kuwait

[2]Department of Internal Medicine, New Jahra Hospital, Kuwait

[3]Obstetric and Gynecology Department, Farwaniya Hospital, Kuwait

[4]Sondos Alsharidah, Stem Cell Transplant Unit, Pediatric Hematology Oncology Department National Bank Kuwait Specilized Children Hospital, Kuwait

Abstract

Aim: The objective of this study is to report the effect of COVID-19 convalescent plasma (CCP) therapy in pregnant women with moderate or severe COVID-19 infection.

Methods: This study is a case series of 9 pregnant women with moderate or severe COVID-19 infection. All the patients (N = 9) received two doses (400 mL) of ABO compatible CCP. The median gestational age at the time of confirmed COVID-19 diagnosis was 31 weeks (range: 16-39 weeks).

Results: No adverse events with CCP were reported. On day 3 post-CCP administration, there was a significant improvement in oxygen saturation (p = 0.032), decrease in the respiratory rate from baseline (p = 0.041), and improvement in the lymphocyte counts (p = 0.043). None of the patients required invasive ventilatory support or extracorporeal membrane oxygenation and all were discharged home (median time from CCP administration to discharge was 6 days). All the patients gave birth to healthy new-borns. The new-borns had negative SARS-CoV-2 PCR on days 2 and 5 of ages.

Conclusion: Our case series demonstrated CCP therapy to be safe with improved clinical outcomes during moderate and severe COVID-19 infection in pregnancy. However, extensive studies are still needed to recommend the routine use of CCP in the pregnant population with COVID-19 disease.

Trial Registration: Clinicaltrials.gov NCT04474340.

Introduction

The World Health Organisation (WHO) has termed the global spread of the viral pandemic in the year 2020-21 as coronavirus disease-2019 (COVID-19) [1]. COVID-19 is known to cause by a novel coronavirus and is named the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) because of its genetic similarity to the coronavirus (SARS-CoV-1) that lead to the outbreak of the SARS epidemic in 2002-2003 [2]. To date, 114,315,846 confirmed cases of COVID-19 and 2,539,427 deaths had occurred globally [3]. Approximately 2 billion women of childbearing age [4] and other pregnant women [5,6] worldwide are estimated to be at a higher risk of catching COVID-19 infection. Recently, a study by the Centers for Disease Control and Prevention (CDC) reported 2% of cases in pregnant women out of a total of 7162 COVID-19 patients in the United States [7]. Furthermore, increased maternal age (>35 years) and comorbidities such as hypertension, chronic cardiovascular diseases, diabetes, pulmonary disease, and other malignancies may further increase the complications due to COVID-19 in pregnant women [8].

Pregnant females infected with COVID-19 present with symptoms similar to those in non-pregnant adults with COVID-19. The clinical features include fever, cough, breathlessness, loss of taste and smell, headache, and also pneumonia in a few complicated cases [9,10]. Although most of the cases with SARS-CoV-2 infection during pregnancy (85%-90%) are associated with no or only mild symptoms, 5%-10% of patients may have severe symptoms, enough to authorize hospitalization or oxygen therapy while 1%-2% may become critical requiring assisted ventilation or may even die [11]. However, till now, no significant data is available on fetal infection or intrauterine transmission of COVID-19. Nonetheless, COVID-19 during pregnancy is reported to increase the threat of preeclampsia, premature delivery, cesarean section, low weight baby, fetal distress, abortion, neonatal asphyxia, and neonatal death [12,13].

Several therapeutic options, including antiviral drugs such as remdesivir, favipiravir, and other medications as chloroquine, azithromycin, tocilizumab, and bamlanivimab plus etesevimab combination, have been suggested for patients with COVID-19 (Treatment guidelines, NIH). However, due to the lack of clear evidence regarding the efficacy and safety of these treatments, the therapeutic armamentarium for COVID-19 is currently limited. Considering the systemic hyper-inflammatory impact of SARS-CoV-2 infection, adjunctive treatments such as the passive immunization with the convalescent plasma obtained from recently cured COVID-19 patients are also being explored for the management of moderate to seriously ill COVID-19 patients [14]. In the past, convalescent plasma therapy

Correspondence to: Mariam Ayed, Neonatal Department, Farwaniya Hospital, Subah An Nasser, Kuwait City, Postal code-81400, Kuwait, Tel: 965-98880553; E-mail: Mariam.ayed@hsc.edu.kw

Keywords: *Convalescent plasma, COVID-19, Case series, Pregnancy, SARS-CoV-2*

Received: November 11, 2021; **Accepted:** November 16, 2021; **Published:** November 22, 2021

has already proven safe in fighting against various viral diseases such as poliomyelitis, measles, mumps, Spanish influenza, and SARS [15-17]. Additionally, clinical data from a systematic study has found convalescent plasma to be effective in treating COVID-19 patients [18]. The Food and Drug Administration (FDA) has authorized the emergency application of COVID-19 convalescent plasma (CCP) treatment for severe COVID-19 patients [19].

At the same time, it is also urgent to establish effective and safe alternatives for treating pregnant women with COVID-19, as are available for the general or non-pregnant population. Given the initial positive clinical outcomes related to safety and efficacy features of CCP in COVID-19 patients, this treatment is gaining interest among the investigators for its considerable use in pregnant women as well. However, the data is still insufficient and mostly includes case reports, case series, or cohort studies [20-23]. Moreover, out of a total of 91 COVID-19 interventional clinical trials on convalescent plasma studies, currently, in progress, 44 (~48%) trials have excluded pregnant and breastfeeding women due to safety concerns for the mother and to avoid any potential teratogenic effects [23].

Therefore, we report here the case series of 9 pregnant women with moderate and severe COVID-19 infection who were successfully managed with CCP therapy.

Materials and Methods

Research Design and Subjects

This is a case series study on pregnant women with SARS-CoV-2 infection who were hospitalized to New-Jahra hospital, Kuwait, from 1st September 2020 to 14th November 2020. The inclusion/exclusion criteria for the selection of patients are provided and have also been described in our earlier published paper [24]. The written informed consent was taken from each patient. The Ethics Committee of the Ministry of Health of Kuwait (2020/1417&1420) approved the present study (and is registered at Clinicaltrials.gov NCT04474340).

Inclusion and exclusion criteria for patients' selection

Inclusion Criteria

If the patients had moderate or severe COVID-19 (per WHO classification) at admission, as determined by the physician.

WHO classification [25]

1. Moderate COVID-19: Defined as the presence of clinical signs of pneumonia (fever, cough, dyspnea) and oxygen saturation (SpO_2) of more than 90% in room air.
2. Severe COVID-19: Defined as clinical signs of pneumonia plus SpO_2 less than 90% in room air or admission to intensive care unit (ICU) for respiratory support (i.e., high flow nasal cannula, non-invasive mechanical ventilation, and intubation).

Exclusion Criteria

1. Contraindication to blood transfusion (volume overload, history of anaphylaxis to blood products)
2. Acute multiple organ failure
3. Hemodynamic instability
4. Severe disseminated intravascular coagulopathy (DIC)
5. Septic shock
6. Expected survival of less than 48 hours

Collection of COVID-19 Convalescent plasma (CCP)

The inclusion/exclusion criteria for the selection of donor patients for CCP collection have been provided.24 All the donors tested negative for human leukocyte antigen (HLA) antibodies. CCP was only collected from individuals who met all donor eligibility requirements according to the United States Code of Federal Regulations (21 CFR 630.10 and 21 CFR 630.15). All donors had been tested negative respiratory viruses, as well as for hepatitis B virus, hepatitis C virus, HIV, and syphilis at the time of blood donation. Neutralizing antibodies were not measured.All the enrolled pregnant patients (N = 9) received 2 doses of ABO compatible CCP (each unit contains 200 mL) 12 hours apart as described previously [24].

Inclusion and exclusion criteria for selecting donor patients for collection of CCP

Inclusion Criteria

1. Convalesced from confirmed COVID-19 disease and
2. Positive against SARS-CoV-2.
3. Asymptomatic for at least 10 days

Exclusion Criteria

1. Tested positive for only IgM and negative for IgG antibodies against SARS-CoV-2

Data Collection

The following data were collected from 9 eligible pregnant women (who received CCP from the eligible donors, as described above) by reviewing the hospital's electronic medical record. Patients were followed up until hospital discharge or giving birth whichever comes later.

1. Demographic data: Included presenting symptoms, gestational age at the time of confirmation of COVID-19, and co-existing medical conditions.
2. Details on personalized therapies: Antenatal corticosteroids for fetal lung maturation, antibiotics, antivirals, and prophylaxis for thrombosis (such as low-molecular weight heparin).
3. Clinical and laboratory findings (pre-and post- CCP transfusion in the patients): Respiratory rate, oxygen saturation, lymphocyte count, white blood cell count, levels of C-reactive protein (CRP), D-dimer, and lactate dehydrogenase (LDH).
4. Neonatal data: Gestational age at the time of delivery, type of delivery method, weight of baby at birth, 5-minutes Apgar score, COVID-19 PCR test results (at 48 hours of age), and hospitalization to neonatal intensive care unit (NICU; if yes/no).

Statistical analysis

Data were analysed using STATA/IC 14 software (STATA Corp, College Station, Texas). Continuous variables were summarized as median and range, while categorical variables were summarized as numbers and percentages. Clinical characteristics and laboratory values before and after CCP treatment were compared by Wilcoxon signed-rank test. A p value of < 0.05 was considered statistically significant.

Results

A total of 9 eligible pregnant women with confirmed COVID-19 who received CCP were enrolled in the study.

Table 1. Demographic and clinical features of pregnant patients enrolled in the study (N = 9)

Patient	Age (years)	Parity	Gestational age at diagnosis of COVID-19	Co-existing chronic condition	Presenting symptoms	WHO classification
1	30	2	31 weeks	None	Cough, fatigue	Moderate
2	29	1	30 weeks	None	Cough	Moderate
3	29	0	22 weeks	None	Fever, cough, shortness of breath	Moderate
4	23	0	36 weeks	None	Fever, cough, shortness of breath	Severe
5	37	4	16 weeks	None	Cough, shortness of breath, fatigue	Moderate
6	29	1	23 weeks	Bronchial asthma	Headache, fever	Moderate
7	36	2	39 weeks	None	Cough, fever, diarrhoea	Moderate
8	39	3	34 weeks	None	Fever, shortness of breath, headache	Severe
9	28	2	34 weeks	None	Cough, fatigue, sore throat	Severe

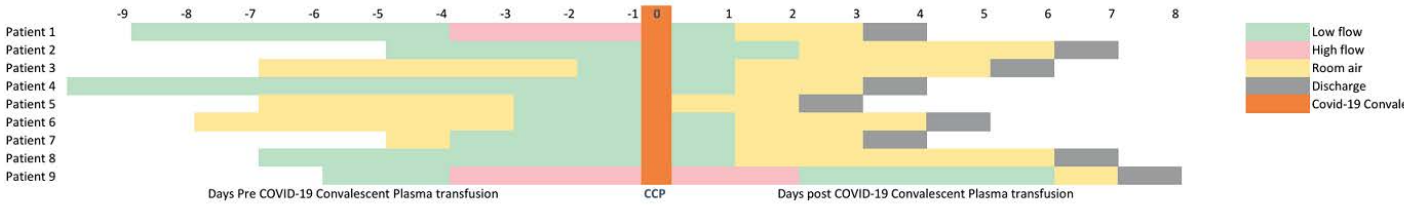

Figure 1. Clinical course of the patients (N = 9) receiving CCP

Patients' demographic and clinical characteristics

The median age of the patients was 29 years (range 23-39 years). The median gestational age at the time of confirmation of COVID-19 was 31 weeks (range 16-39 weeks). Three patients had severe COVID-19, while 6 had a moderate disease. The most common symptoms at presentation were cough (n = 7), fever (n = 5), and shortness of breath (n = 4). Other symptoms seen were headache (n = 2) and diarrhoea (n = 1). The demographic and clinical features of these patients have been given in Table 1.

Patient-specific therapies

Each patient (N = 9) was given low molecular weight heparin and antibiotics (ceftriaxone and azithromycin) to avoid possible superimposed bacterial infection. The majority of the patients (n = 7) received dexamethasone for fetal lung maturation. None of the patients received antiviral treatment or hydroxychloroquine.

The median days of receiving CCP from the date of diagnosis of COVID-19 were 5 days (range 3-7 days). No adverse events were observed in none of the 9 patients after CCP transfusion.

Study Outcomes

I. Maternal outcomes

Clinical course of the patients

The trajectory of oxygen and ventilator support overtime for all 9 patients has been shown in Figure 1.

At the time of CCP transfusion, 7 patients were on supplemental oxygen via low flow nasal cannula while 2 patients were on high flow nasal cannula. A marked improvement in oxygen requirement was observed after CCP transfusion in the patients. Seven patients showed rapid weaning to room air within 24 hours and 1 patient within 48 hours. Finally, 1 patient on high flow nasal cannula was weaned to low flow nasal cannula after 48 hours of CCP transfusion and to room air after day 6. None of the patients required invasive ventilatory support or extracorporeal membrane oxygenation (ECMO).

Clinical and laboratory findings

Various clinical and laboratory findings before and 3 days after giving convalescent plasma infusion to the patients were compared and analysed (Table 2). On day 3 post-CCP, there was a significant increase in oxygen saturation ($p = 0.032$) while a significant decrease in the respiratory rate from baseline ($p = 0.041$). In addition, there was a significant improvement in the lymphocyte counts ($p = 0.043$). However, no significant change in the neutrophil counts, CRP, D-dimer, and LDH was observed.

All the patients showed no signs of complications and were discharged home. The median length of stay in the hospital for these patients was 10 days (range 6-14 days). The median time between CCP administration and discharge was 6 days (range 3-9 days).

II. Neonatal outcomes

All the women (N = 9) gave birth to healthy new-borns. The median duration from CCP administration to giving birth was 7 weeks (range 0-23 weeks). Only 2 new-borns needed admission to the neonatal unit due to either hyperbilirubinemia secondary to blood group incompatibility (n = 1) or low birth weight and late prematurity care (n=1). All the neonates had a negative SARS-CoV-2 PCR test at 48 hours of age. The neonatal outcomes have been provided in Table 3.

Discussion

Pregnant women are more prone to severe infections, including COVID-19 and related complications. This may be attributable to the changes in maternal physical stature and the natural pro-inflammatory immune response, especially during the third trimester of pregnancy [26,27]. Besides, increased oxygen consumption, decreased functional residual capacity, high basal metabolic rate, an elevated diaphragm, airway edema, and hypercoagulable state during the respiratory

diseases, including the present COVID-19, may worsen the clinical state of a pregnant woman [28,29]. Pneumonia, a significant complication of COVID-19 infection, has also been observed as a remarkable contributing factor to mortality and morbidity in pregnancy [10].

However, as a result of limited evidence on investigating the effects of COVID-19 in pregnant patients and on the babies born to infected mothers, the clinical course or manifestation of COVID-19 is highly unpredictable [30]. Vertical transmission of the SARS-CoV-2 infection through the placenta rarely occurs, as suggested by the published data [31-33]. In contrast, a systematic review identified 41 neonates with possible COVID-19 infection but with an overall survival rate of 99%. A case study on 9 women infected with COVID-19 during the third trimester of pregnancy demonstrated an improvement in the clinical course during hospitalization with no complications [31]. On the contrary, another study showed pregnancy complications such as fetal distress, premature rupture of the membrane, or stillbirth in 10 out of a total of 13 pregnant patients x (11 patients in the third trimester and 2 in less than 28 weeks of gestation) with SARS-CoV-2 infection. Six patients (46%) between 32-36 weeks of gestation had preterm labor. The condition of 1 patient got deteriorated due to multiple organ dysfunction syndromes (MODS), thereby requiring transfer to ICU on intubation and mechanical ventilation. The investigators of the study suggested that it could be the result of the release of a cascade of pro-inflammatory cytokines, also called the 'cytokine storm', in response to the viral load due to COVID-19 infection in these patients [34].

Table 2. Clinical and laboratory findings before and after CCP

	Before CCP (baseline)	Day 1 post-CCP	Day 3 post-CCP
Clinical findings			
Oxygen saturation (%)	92 (89-95)	97 (95-100)	97 (96-98)*
Respiratory rate per minute	30 (24-30)	24 (22-30)	22 (22-26)*
Laboratory findings			
Lymphocytes x 10^9/L (normal range 1.1-3.2)	0.9 (0.3-1.3)	1.2 (0.71-2.7)	1.8 (1-2.5)*
Neutrophils x 10^9/L (normal range 1.8-6)	4.1 (3.2-4.1)	6.7 (3.1-15.8)	5.1 (3.7-11.1)
CRP, mg/L (normal value <8)	7.4 (1.8-10.8)	3.6 (1.1-7.9)	1.5 (1-55.7)
D-dimer	407 (230-1762)	379 (226-1467)	889 (185-1287)
LDH	251 (138-317)	222 (168-331)	275 (103-339)
CCP: COVID-19 convalescent plasma; CRP: C-reactive protein, LDH: lactate dehydrogenase			
*indicates p value <0.05			

Additionally, a significant proportion of women (~10%) with COVID-19 infection in pregnancy require respiratory support during pandemic, there hospitalization [35,36]. Since this number is expected to augment with the spread of the is an urgent need to provide early diagnosis of COVID-19 and appropriate therapeutic management to pregnant women. This would help prevent the mother's condition from worsening, avoid a possible premature delivery or caesarean section, and reduce any potential issues requiring critical care or respiratory support and probable maternal and fetal risk.

For the management of COVID-19, the WHO mainly focuses on preventing infection, providing early detection, monitoring the disease, optimal supportive care, and recommending non-specific treatment against SARS-CoV-2 available to-date (WHO.int). Two monoclonal antibody treatments, bamlanivimab and etesevimab (to be administered in combination), have received emergency use authorization for non-hospitalized COVID-19 patients with mild-moderate symptoms [37]. Dexamethasone and other corticosteroids recommended by NIH showed benefit in severe COVID-19 patients hospitalized on ventilator support [38]. Based on the findings of the Solidarity Trial, it is suggested that the drugs remdesivir, hydroxychloroquine, lopinavir/ritonavir, and interferon show almost no reduction in the 28-day mortality rate or any improvement in the clinical course of COVID-19 hospitalized patients [39]. Besides, encouraging data regarding the safety of convalescent plasma therapy and its use in preventing disease in high-risk cases (with comorbidities, front-line workers including health care providers, and people exposed to confirmed cases) of COVID-19 are rapidly growing. A single dose of CCP resulted in positive clinical and radiological outcomes after 3 and 7 days of the administration, respectively in 10 adults with severe COVID-19 [40]. The studies by Hartman et al. (2020), Liu et al. (2020), and Salazar et al. (2020) have demonstrated a greater clinical benefit of early CCP administration than that of delayed immunization in severe COVID-19 patients [34,41,42].

CCP transfusion is based on first collecting large pools of blood plasma from several donors or individuals who were successful in completely recovering from COVID-19 infection. Then, this plasma containing disease-specific antibodies, developed by the individuals' immune system, is infused into the COVID-19 patient to combat the infection [43]. Pregnancy is not considered a contraindication to blood plasma transfusion. In the absence of definitive therapy for COVID-19, CCP may prove useful in pregnant patients infected with SARS-CoV-2 because of several reasons: It provides short-term immunity against the disease as the antibodies produced help in neutralizing the virus through complement activation via classical pathway, cellular

Table 3. Neonatal Outcomes

Patient	Gestational age at the time of birth	Type of delivery method	Birth weight (grams)	Apgar score (5-minutes)	Neonatal COVID-19 PCR (48 hrs)	Neonatal hospitalization
1	39^{+4} weeks	Vaginal	3250	8	Negative	No
2	37^{+3} weeks	Cesarean section	2940	9	Negative	No
3	37^{+5} weeks	Vaginal	2750	9	Negative	Yes -Hyperbilirubinemia (blood group incompatibility)
4	38 weeks	Cesarean section	3120	9	Negative	No
5	33^{+4} weeks	Vaginal	1900	8	Negative	Yes - Low birth weight and late prematurity care
6	39 weeks	Vaginal	3050	10	Negative	No
7	39^{+2} weeks	Cesarean section	2980	9	Negative	No
8	37 weeks	Cesarean section	2750	9	Negative	No
9	38^{+3} weeks	Vaginal	3100	9	Negative	No

toxicity, and agglutination; Immunoglobulin G (IgG) passes through the placenta, thus providing the fetus with passive immunity; It has immune-modulatory and anti-inflammatory properties that can suppress the exaggerated production of cytokines, responsible for acute respiratory disease syndrome (ARDS) or multiple-organ failure. Other advantages of using CCP for a novel disease viz. COVID-19 includes its easy availability, lower cost of production, and antibody specificity against the virus.

In view of the safety concerns for both mother and baby, only a few studies have reported the use of different experimental treatments, including CCP therapy in pregnancy [44-46]. The results of several ongoing clinical trials reporting the inclusion of pregnant or breastfeeding women infected with COVID-19 are, however, highly awaited to confirm the safety and efficacy of CCP therapy in this patient population.

We, therefore, undertook the present study with an objective to investigate the clinical course, maternal and neonatal outcomes in those pregnant women (n = 9) who received CCP therapy for moderate-to-severe COVID-19 infection (per the WHO classification). The most typical presenting symptoms of these patients enrolled in our study were fever, cough, and shortness of breath. The median gestational age of the patients was 31 weeks. All the patients received 2 doses (within 24 hours) of CCP on the median day 5; from the date of a confirmed diagnosis of COVID-19. None of them received any antiviral treatment or hydroxychloroquine. After the CCP transfusion, a marked improvement was observed in oxygen requirement in these patients. Seven of them gradually weaned from supplemental oxygen (via high-flow/low-flow cannula) to normal room air within 24 hrs. While treating pregnant patients clinically, doctors usually aim at maintaining the oxygen saturation levels at a minimum of 95%. Conforming to this, in our study, the oxygen saturation levels were significantly increased to 97%, and the respiratory rate was significantly decreased on day 3 after the CCP treatment. The lymphocyte count was also significantly increased to 1.8×109/L. The median duration from CCP administration to giving birth was 7 weeks, and all the babies were born healthy with a mean 5-min Apgar score of 8.88. Only 2 neonates required hospitalization in the neonatal unit either because of blood group incompatibility (n = 1) or premature low birth weight (n = 1). None of the mothers or their new-born babies showed any signs of complications, and they were discharged from the hospital between 3-9 days of CCP administration. All the new-borns had negative SARS-CoV-2 PCR test results on days 2 and 5 of age.

Our findings are consistent with the other few published reports available currently. In another similar case study, administration of CCP without antiviral drugs in a pregnant COVID-19 patient at about 24 weeks of gestation depicted a promising clinical outcome for both mother and new-born. Another case of a 26-year-old pregnant woman infected with COVID-19 pneumonia gave birth to healthy twins (with no COVID-19 symptoms and negative PCR test) at 36 weeks after given a combination of favipiravir and CCP treatment. Successful management of maternal and perinatal clinical course was reported after using prone positioning and hyperimmune plasma therapy in a case of a 27.4 weeks pregnant severe COVID-19 patient [47]. Three other case reports showed the beneficial use of convalescent plasma therapy when combined with antiviral drugs (remdesivir, lopinavir/ritonavir) at a very early gestational age in critically ill obstetric patients.

However, our case series has several limitations. In addition, to the small sample size, there is an absence of a control cohort to reach any conclusive benefits with convalescent plasma treatment in COVID-19 in pregnancy. Moreover, the neutralizing antibodies in CCP were not measured. Multiple confounders that could contribute to the changes in the clinical and laboratory findings of the study were also not investigated.

Conclusion

Our findings demonstrated that CCP therapy is safe and may lead to improved clinical consequences in COVID-19 pregnant patients. Despite the initial positive results regarding the safety and efficacy of CCP treatment, further investigations with a larger sample size are required to make a clear recommendation regarding the routine use of CCP in pregnant women with moderate and severe COVID-19. Multidisciplinary management of critically ill COVID-19 pregnant patients and relevant combination therapies are essential to warrant the most appropriate maternal and fetal care. Possible side effects or adverse reactions of CCP therapy in patients should be considered well.

Declarations

Ethics approval and consent to participate: The Ethics Committee of the Ministry of Health of Kuwait (2020/1417&1420) approved the present study (and is registered at Clinicaltrials.gov NCT04474340).

Consent for Publication

Not Applicable.

Availability of data and Materials

The data used to support the findings of this study are available from the corresponding author upon request.

Conflict of interest

None.

Funding/Support

None.

Author Contribution

MA conceptualized and planned the study design, planned data collection, oversaw data collection with FA, literature review, performed the text mining analysis, drafted and revised the final version of the manuscript. MA also performed the statistical analysis. AA and SA conducted the literature review, contributed to the writing and reviewing of the manuscript. All other co-authors contributed to data collection and oversaw the manuscript.

Acknowledgement

None.

References

1. World Health Organization. Coronavirus disease (COVID-19) pandemic. 2021.
2. Wells HL, Letko M, Lasso G, Ssebide B, Nziza J, et al. (2021) The evolutionary history of ACE2 usage within the coronavirus subgenus Sarbecovirus. *Virus Evolution* 2021. [Crossref]
3. World Health Organization. Geneva (Switzerland): World Health Organization, 2020. WHO Director-General's remarks at the media briefing on 2019-nCoV. 2020.
4. World Health Organization. Women of reproductive age (15–49 years) population (thousands). 2020.
5. Dashraath P, Wong JLJ, Lim MXK, Lim LM, Li S, et al. (2020) Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *Am J Obstet Gynecol* 222: 521-531. [Crossref]

6. Pierce-Williams RAM, Burd J, Felder L, Khoury R, Bernstein PS, et al. (2020) Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. *Am J Obstet Gynecol MFM* 2: 100134. [Crossref]

7. CDC. Data on COVID-19 during Pregnancy | CDC 2020. 2020.

8. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, et al. (2020) Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 370: m3320. [Crossref]

9. Novoa RH, Quintana W, Llancarí P, Urbina-Quispe K, Guevara-Ríos E, et al. (2021) Maternal clinical characteristics and perinatal outcomes among pregnant women with coronavirus disease 2019. A systematic review. *Travel Med Infect Dis* 39: 101919. [Crossref]

10. Stumpfe FM, Titzmann A, Schneider MO, Stelzl P, Kehl S, et al. (2020) SARS-CoV-2 Infection in Pregnancy - a Review of the Current Literature and Possible Impact on Maternal and Neonatal Outcome. *Geburtshilfe Frauenheilkd* 80: 380-390. [Crossref]

11. CDC COVID-19 Response Team (2020) Preliminary estimates of the prevalence of selected underlying health conditions among patients with Coronavirus Disease 2019 - United States, February 12-March 28, 2020. *MMWR Morb Mortal Wkly Rep* 69: 382-386.

12. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, et al. (2020) Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM* 2: 100107. [Crossref]

13. Yang Z, Wang M, Zhu Z, Liu Y (2020) Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. *J Matern Fetal Neonatal Med* 30: 1-4. [Crossref]

14. Wang X, Guo X, Xin Q, Pan Y, Hu Y, et al. (2020) Neutralizing antibodies responses to SARS-CoV-2 in COVID-19 inpatients and convalescent patients. *Clin Infect Dis* 71: 2688-2694. [Crossref]

15. Casadevall A, Pirofski LA (2020) The convalescent sera option for containing COVID-19. *J Clin Invest* 130: 1545-1548. [Crossref]

16. Cheng Y, Wong R, Soo YO, Wong WS, Lee CK, et al. (2005) Use of convalescent plasma therapy in SARS patients in Hong Kong. *Eur J Clin Microbiol Infect Dis* 24: 44-46. [Crossref]

17. Luke TC, Kilbane EM, Jackson JL, Hoffman SL (2006) Meta-analysis: convalescent blood products for Spanish influenza pneumonia: a future H5N1 treatment? *Ann Intern Med* 145: 599-609. [Crossref]

18. Sarkar S, Soni KD, Khanna P (2021) Convalescent plasma is a clutch at straws in COVID-19 management! A systematic review and meta-analysis. *J Med Virol* 93: 1111-1118. [Crossref]

19. Tanne JH (2020) Covid-19: FDA approves use of convalescent plasma to treat critically ill patients. *BMJ* 368: m1256. [Crossref]

20. Anderson J, Schauer J, Bryant S, Graves CR (2020) The use of convalescent plasma therapy and remdesivir in the successful management of a critically ill obstetric patient with novel coronavirus 2019 infection: a case report. *Case Rep Womens Health* 27: e00221. [Crossref]

21. Grisolia G, Franchini M, Glingani C, Inglese F, Garuti M, et al. (2020) Convalescent plasma for coronavirus disease 2019 in pregnancy: a case report and review. *Am J Obstet Gynecol MFM* 2: 100174. [Crossref]

22. Jafari R, Jonaidi-Jafari N, Dehghanpoor F, Saburi A (2020) Convalescent plasma therapy in a pregnant COVID-19 patient with a dramatic clinical and imaging response: a case report. *World J Radiol* 12: 137-141. [Crossref]

23. Pastick KA, Nicol MR, Smyth E, Zash R, Boulware DR, et al. (2020) A Systematic Review of Treatment and Outcomes of Pregnant Women With COVID-19 - A Call for Clinical Trials. *Open Forum Infect Dis* 7: ofaa350. [Crossref]

24. Alsharidah S, Ayed M, Ameen RM, Alhuraish F, Rouheldeen NA, et al. (2021) COVID-19 convalescent plasma treatment of moderate and severe cases of SARS-CoV-2 infection: A multicenter interventional study. *Int J Infect Dis* 103: 439-446. [Crossref]

25. Integrated Management of Adolescent and Adult Illness (IMAI) District Clinician Manual: Hospital Care for Adolescents and Adults. Guidelines for the management of common illnesses with limited resources. Geneva, Switzerland: World Health Organization; 2011.

26. Liu H, Wang LL, Zhao SJ, Kwak-Kim J, Mor G, et al. (2020) Why are pregnant women susceptible to COVID19? An immunological viewpoint. *J Reprod Immunol* 139: 103122. [Crossref]

27. Abbas AM, Fawzy AT, Fathy SK (2020) Use of Convalescent Plasma for COVID-19 in Pregnancy: Lessons from other Viruses. *Am J Biomed Sci Res* 9: 427-433.

28. Louie JK, Acosta M, Jamieson DJ, Honein MA (2010) Severe 2009 H1N1 influenza in pregnant and postpartum women in California. *N Engl J Med* 362: 27-35. [Crossref]

29. Vlachodimitropoulou Koumoutsea E, Vivanti AJ, Shehata N, Benachi A, Gouez AL, et al. (2020) COVID-19 and acute coagulopathy in pregnancy. *J Thromb Haemost* 18: 1648-1652. [Crossref]

30. Zaigham M, Andersson O (2020) Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand* 99: 823-829. [Crossref]

31. Chen H, Guo J, Wang C, Luo F, Yu X, et al. (2020) Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 395: 809-815. [Crossref]

32. Liu STH, Lin HM, Baine I, Wajnberg A, Gumprecht JP, et al. (2020) Convalescent plasma treatment of severe COVID-19: a matched control study. *Nat Med* 26: 1708-1713. [Crossref]

33. Mimouni F, Lakshminrusimha S, Pearlman SA, Raju T, Gallagher PG, et al. (2020) Perinatal aspects on the covid-19 pandemic: a practical resource for perinatal-neonatal specialists. *J Perinatol* 40: 820-826.

34. Liu Y, Chen H, Tang K, Guo Y (2020) Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *J Infect* 20: 30109-30112. [Crossref]

35. Center for Disease Control and Prevention. Data on COVID-19 during pregnancy. 2020.

36. Knight M, Bunch K, Vousden N, Morris E, Simpson N, et al. (2020) Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population-based cohort study. *BMJ* 369: m2107. [Crossref]

37. Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19 | FDA. 2020.

38. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, et al. (2021) Dexamethasone in Hospitalized Patients with Covid-19. *N Engl J Med* 384: 693-704. [Crossref]

39. WHO Solidarity trial consortium (15 October 2020). Repurposed antiviral drugs for COVID-19–interim WHO SOLIDARITY trial results. *MedRxiv* 222373329.

40. Duan K, Liu B, Li C, Zhang H, Yu T, et al. (2020) Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *Proc Natl Acad Sci USA* 117: 9490-9496. [Crossref]

41. Hartman W, Hess AS, Connor JP (2020) Hospitalized COVID-19 patients treated with Convalescent Plasma in a mid-size city in the Midwest. *medRxiv* 2020. [Crossref]

42. Salazara E, Christensena PA, Gravissa EA, Nguyen DT, Castillo B, et al. (2020) Treatment of COVID-19 Patients with Convalescent Plasma Reveals a Signal of Significantly Decreased Mortality. *Am J Pathol* 190: 2290-2303. [Crossref]

43. Burnouf T, Seghatchian J (2014) Ebola virus convalescent blood products: where we are now and where we may need to go. *Transfus Apher Sci* 51: 120-125. [Crossref]

44. Zhang B, Liu S, Tan T, Huang W, Dong Y, et al. (2020) Treatment with convalescent plasma for critically ill patients with severe acute respiratory syndrome coronavirus 2 infection. *Chest* 158: e9-e13. [Crossref]

45. Magallanes-Garza GI, Valdez-Alatorre C, Dávila-González D, Martínez-Reséndez MF, Sánchez-Salazar SS, et al. (2021) Rapid improvement of a critically ill obstetric patient with SARS-CoV-2 infection after administration of convalescent plasma. *Int J Gynaecol Obstet* 152: 439-441. [Crossref]

46. Soleimani Z, Soleimani A (2020) ADRS due to COVID-19 in midterm pregnancy: successful management with plasma transfusion and corticosteroids. *J Matern Fetal Neonatal Med* 26: 1-4. [Crossref]

47. Donzelli M, Ippolito M, Catalisano G, Renda B, Tarantino F, et al. (2020) Prone positioning and convalescent plasma therapy in a critically ill pregnant woman with COVID-19. *Clin Case Rep* 8: 3352-3358. [Crossref]

Copyright: ©2021 Ayed M. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.