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OUTCOMES OF COVID-19 DURING PREGNANCY: A SYSTEMATIC REVIEW

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ABSTRACT

Objective: This paper presents specific pregnancy outcomes of COVID-19 during pregnancy, based on the literature available until August 2020. **Methods:** A systematic review was conducted in PubMed, Scopus, Google Scholar, Springer, Science Direct, and the EMBASE database of publications regarding coronavirus disease (COVID-19) following the PRISMA checklist. The search terms used include: "pregnancy"; "pregnant"; "neonatal"; "neonate"; "COVID-19"; "coronavirus disease 2019" "pregnancy", "pregnant", "neonatal" and "neonate". All studies exploring the maternal and fetal outcomes among pregnant women with COVID-19 were considered for this review. **Results:** A total of 11 case reports on 17 pregnant women and 12 retrospective reviews of the medical records of 795 pregnant women meeting the inclusion criteria were included in the review. Of 362 deliveries, 59.3% involved caesarean sections [CS] while 40.6% were vaginal deliveries. Of the 362 deliveries, 22.37% were preterm. Of 51 neonates, 20% were found to have low birth weight and one tested positive for SARS-CoV-2. A total of nine neonatal deaths were reported, which were not associated with the viral infection, and 15 neonates were found to be COVID-19 positive, although no indication of vertical transmission of infection was established. **Conclusions:** Pregnancy does not increase the risk of COVID-19 and prospective mothers should follow the same recommendations as applicable to the general population, to limit the transmission of COVID-19. Information compiled in this systematic review of COVID-19-related pregnancy outcomes may help in planning the best care in future.

Keywords: COVID-19; Pregnancy Outcome;Maternal Outcome; Foetal

INTRODUCTION

Coronavirus disease or COVID-19 is the most pressing global health issue today, affecting all sectors of society irrespective of caste, creed, ethnicity or economical differences. Although COVID-19 can affect anyone, its impact is greater on people with lower immunological status, a category that includes pregnant women (Bouaziz *et al.*, 2020).

Pregnant women and their fetuses remain at high risk during any infectious disease breakdown. (Dashraath *et al.,* 2020) Knowledge gained from previous SARS coronavirus (SARS-CoV) and MERS coronavirus (MERS-CoV) suggests that pregnant status increases the risk of poor outcomes (Zaigham &Andersson, 2020). Prevention and control of COVID-19 among pregnant women and the risk of its vertical transmission are growing concerns (Qiao, 2020).

Aims and Objectives of the Review:

COVID-19 is infecting many people globally and the numbers of infections and deaths per day are rapidly evolving. Yet there is limited data available on its impact upon pregnant women, and the maternal and fetal outcome (Rasmussen *et al.*, 2020). The clinical pneumonia associated with COVID-19 were similar in pregnant women and non-pregnant adults (Rasmussen *et al.*, 2020). The physiological changes during pregnancy, such as decreased lung capacity and other immunological adaptations, pose an increased risk of complications from respiratory illness among pregnant women (Schwartz, 2020).

Studies have shown that COVID-19 may result in fetal distress, abortion, preterm labor, and respiratory

distress in women during pregnancy (Panahi, Amiri & Pouy, 2020) Since a smaller number of cases are involved in the published studies, the research is inconclusive as to whether these maternal and fetal outcomes are exclusively due to COVID-19 related pneumonia or other pre-existing maternal conditions. A systematic review of the available literature as of August 2020 is therefore necessary to understand the effect of COVID-19 on pregnancy outcome among COVID-19-positive pregnant women.

METHODOLOGY

Study Design

Two reviewers conducted a comprehensive examination of relevant literature independently. The databases searched included Google Scholar, Springer, ScienceDirect, PubMed, Scopus and EMBASE. The search terms used include: "pregnancy"; "pregnant"; "neonatal"; "neonate"; "COVID-19"; "coronavirus disease 2019" "pregnancy", "pregnant", "neonatal" and "neonate". The search criteria sought studies that explore the impact of COVID-19 on maternal or foetal outcome among pregnant women, published in English and available as a free, full-text download. Unpublished reports, existing systematic reviews on similar topics and comments to the editor are excluded from this review.

The initial search revealed 500 studies and after removing 200 duplicates, a title-and-abstract screening of the remaining 300 studies was carried out. A further 200 studies were removed as the full text was either unavailable for free download or unavailable in English. After full-text screening, 77 studies were removed either because they lacked full information or did not mention specific maternal or foetal outcomes. The remaining 23 studies met the eligibility criteria and are included in this review. They comprise 11 case reports and 12 retrospective clinical data reviews. Twelve studies are from China, two from both the UK and USA and one from each of Australia, Brazil, France, Iran, Italy, and Sweden. One study does not mention its country of origin.

Data Extraction: Two reviewers independently of one another conducted the screening of the studies and care was taken to ensure that no study was counted twice. Since only a handful of studies with small sample sizes are available, the researchers did not undertake quality appraisal of the studies included. The data extracted from the studies includes study ID, research method, and place of study, sample, and mode of delivery, week of gestation at delivery, maternal outcome and foetal outcome.

Quality Analysis: Case reports and case series designs have poor methodological controls and are known to increase the risk of bias, but they continue to contribute to the body of medical knowledge. Both reviewers to ensure the quality of the included studies, used methodological quality and synthesis of case series along with case reports independently

Risk of Bias: The CARE checklist (Consensus-based Clinical Case Reporting Guideline Development), consisting of 30 items, was used to assess the quality of case reports retrieved (Gagnier *et al.*, 2013). The STROBE checklist (Strengthening the Reporting of Observational Studies in Epidemiology), comprising 34 items, was used to assess the reliability of cohort reports (Cevallos, Egger & Moher, 2014).

Reporting: This article followed the PRISMA checklist (Preferred Reporting Items for Systematic Review and Meta-analysis) for reporting (Moher *et al.*, 2009).

The search strategy is displayed in Figure: 1

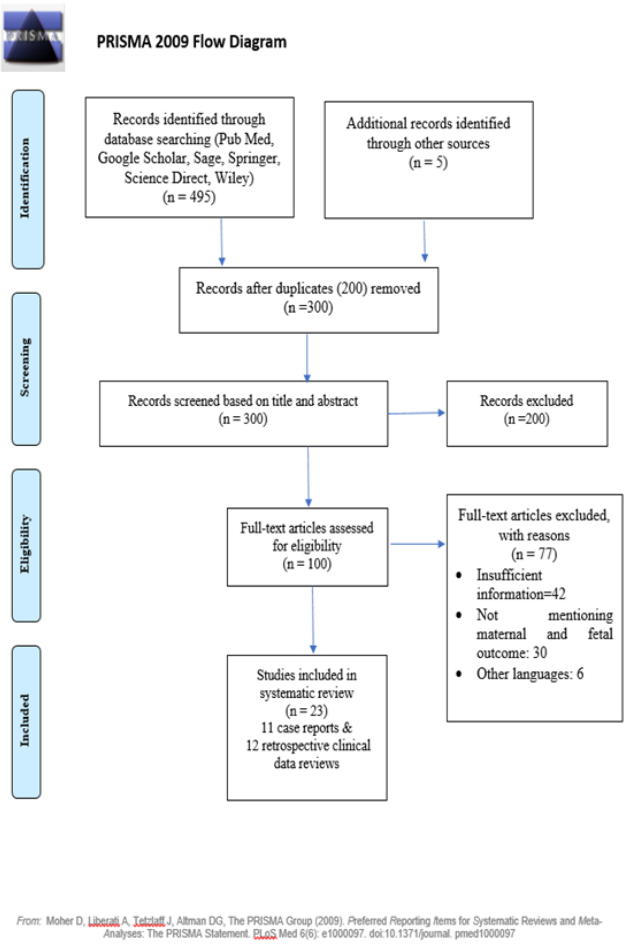

Figure: 1 PRISMA Showing the Search Strategy

RESULTS

Though the majority of reviews were from China; studies from Australia, Brazil, France, Iran, Italy, Sweden, UK and USA make this a good database for review. We made an overview and refined review to ensure a satisfactory quality of study included in the review. The researchers tried to review all available case reports to ensure maximum domain coverage of the content reviewed. The cases described and the medical record-related articles that were retrospectively reviewed were described in sufficient detail to ensure the appropriate reporting of the content under review.

The information on following items was individually collected by the researchers from the original reports: authors' names, country, study design, number of pregnant women as sample in each study, maternal characteristics (maternal age, gestational age at admission), and mode of confirmation of COVID-19 diagnosis in terms of laboratory diagnosis and clinical diagnosis. Maternal, obstetric and neonatal outcomes were also extracted from the reviewed literature.

A total of 23 studies including a sample of 812 COVID-19 pregnant women were identified as per eligibility criteria and included in this review. The results from 11 case reports with details of 17 patients are summarized together to facilitate interpretation. These were published from January 2020 to July 2020.

Among the included studies, a laboratory-confirmed case of COVID-19 was defined as a positive result on quantitative reverse transcriptase polymerase chain reaction (RT-PCR) assay of maternal pharyngeal swab specimens. Radiological and chest CT findings to supplement diagnosis were considered to be a clinical diagnosis of COVID-19.

Maternal outcomes included information about any reported complications related to pregnancy and outcomes of pregnancy, which included mode of delivery, pregnancy loss and the number of women still pregnant at the end of the study, and other possible outcomes of pregnancy, like maternal death, IUD etc. Outcomes in Neonatal reviewed were, Apgar scores, presence of neonatal asphyxia, neonatal death, neonatal positive COVID-19 tests and other types of pneumonia requiring neonatal intensive care unit (NICU) admission and care. A worksheet was prepared to summarize the data extracted from the studies reviewed. Data entry and processing were performed with Microsoft® Office Excel 365®. Data analysis consisted of the calculation of means and percentages.

Table 1: Study Characteristics n=812

Sl No	Study ID	(n)	Research Method	Country	Lab diagnosis	Clinical diagnosis	GA at diagnosis
1	Koumoutsea EV *et al* (2020)	2	Case Study Review	China	RT PCR	Chest x ray normal; NO CT; Respiratory parameters normal	35+3 WOG
2	Alzamora MC *et al* (2020)	1	Case Study Review	china	RT PCR	Not done	33 WOG
3	Liu W (2020)	3	Case Study Review	CHina	RT PCR	Not done	38+ WOG
4	Khan. S *et al* (2020)	3	Case Study Review	china	RT PCR	Not Done	33 WOG;39 WOG;38+2 WOG
5	Zambrano *et al* (2020)	1	Case Study Review	Central America	RT PCR	Not done	31WOG
6	Kolkova Z *et al* (2020)	1	Case Study Review	Sweden	RT PCR	CT scan	32 WOG
7	Celso T *et al* (2020)	2	Case Study Review	Brazil	RT PCR	Chest X ray; CT scan(2)	32WOG; 28WOG
8	Yu Y *et al*.	1	Case Study Review	China	RT PCR	Chest CT	34 WOG
9	Andrew *et al* (2020)	1	Case Study Review	Australia	RT PCR	Not done	39+3 WOG
10	Hansen *et al* (2020)	1	Case Study Review	USA	RT PCR	Not done	34WOG
11	Gonzailez *et al* (2020)	1	Case Study Review	NA	RT PCR	Chest X Ray	29+3 WOG

12	Xu L *et al* (2020)	5	Retrospective Medical records review	China	RT-PCR	X ray	34+ WOG
13	Cao D *et al* (2020)	10	Retrospective Medical records review	China	RT-PCR	Pulmonary CT	33+6 to 40+5
14	Zeng Y *et al* (2020)	16	Retrospective Medical records review	China	RT-PCR	Pulmonary CT	37+5 WOG
15	Antoun L *et al* (2020)	23	Retrospective Medical records review	UK	RT-PCR	Chest Radiography	19= 3rd trimester; 04= 2nd trimester
16	Nan Yu *et al* (2020)	7	Retrospective Medical records review	CHina	RT-PCR	CT on admission	39+1 WOG
17	Nie R, *et al* (2020)	33	Retrospective Medical records review	China	RT-PCR	Not done	3=17-26WOG; 28=<37 WOG; 2=>38 WOG
18	HantoushzadeH S, *et al* (2020)	9	Retrospective Medical records review	Iran	RT-PCR	Not done	Gestational age (wk) c1: 30 3/7 c2: 38 3/7 c3: 30 5/7 c4: 24 0/7 (undelivered) c5: 36 0/7 c6: 24 0/7 (undelivered) c7: 28 0/7
19	Liu D.*et al* (2020)	15	Retrospective Medical records review	China	RT-PCR	CT scan	12-38 WOG
20	Govind a *et al* (2020)	9	Retrospective Medical records review	London	RT-PCR	Chest X Ray (2)	mean 39WOG
21	Chen H *et al* (2020)	9	Retrospective Medical records review	China	RT-PCR	CT scan;	33-36 weeks
22	Ferrazi E *et al*. (2020)	42	Retrospective Medical records review	Northern Italy	RT-PCR	Not done	10=36+WOG;Intranatal = 27 cases; Postpartum=5 cases
23	Kayem G *et al* (2020)	617	Retrospective Medical records review	France	RT-PCR	CT scan (51);	14−21 wk 105; 22-31 wk=238;32-36 wk=142; more

Data related to the average gestational age at diagnosis and mode of confirmation of COVID-19 is presented in Table1of 17 pregnant women reported in the case reports, 31.25% (Kolkova *et al.*, 2020; Tutiya *et al.*, 2020; Romero *et al.*, 2020) were in the gestation period of 28–32 weeks, and 43.75% (Liu *et al.*, 2020; Khan *et al.*, 2020; Walczak *et al.*, 2020) were in 37–40 weeks of gestation at the time of being diagnosed with COVID-19. All 17 (100%) (Kolkova *et al.*, 2020; Tutiya *et al.*, 2020; Romero *et al.*, 2020. Liu *et al.*, 2020. Khan *et al.*, 2020; Walczak *et al.*, 2020; Koumoutsea *et al.*, 2020. Yu *et al.*, 2020, Alzamora *et al.*, 2020; Hansen, Hine & Strout, 2020) of the pregnant women were diagnosed with laboratory RT-PCR tests at the time of reporting symptoms. Chest X-ray was performed as a confirmatory assessment to rule out further lung-field involvement in 25% (Tutiya *et al.*, 2020; Romero *et al.*, 2020; Koumoutsea *et al.*, 2020) of the samples, whereas respiratory CT scans confirmed the clinical diagnosis in four out of 16 (25%) (Kolkova *et al.*, 2020; Tutiya, *et al.*, 2020; Yu *et al.*, 2020) pregnant women. No other test than RT-PCR was performed for the remaining patients and they were treated according to initial laboratory findings.

The remaining data, related to 11 retrospective clinical data reviews and one prospective review of medical records discussing 795 patients, are described in cohorts. Average gestational age of samples reviewed and the mode of clinical confirmation of COVID-19 is presented in Table 2.

Out of 795 COVID-positive pregnant women in 11 reviews, 30.4% (Kayem *et al.*, 2020) presented at 22 or more weeks of gestational age at the time of hospital admission. Only 4.2% (Zeng *et al.*, 2020, Antoun *et al.*, 2020; Yu *et al.*, 2020; Nie *et al.*, 2020; Hantoushzadeh *et*

al., 2020., Liu *et al.*, (2020); Govind *et al.*, 2020. Ferrazzi *et al.*, 2020; Kayem *et al.*, C., 2020) of women reported at term, whereas 3.4% were diagnosed as COVID-positive during the intranatal period and 0.6% (Ferrazzi *et al.*, 2020) were identified during a hospital stay in the postnatal period. All patients (Zeng *et al.*, 2020; Antoun *et al.*, 2020; Yu *et al.*, 2020., Nie *et al.*, 2020; Hantoushzadeh *et al.*, 2020., Liu, *et al.*, 2020, Govind *et al.*, 2020. Ferrazzi, *et al.*, 2020; Kayem *et al.*, 2020. Xu *et al.*, 2020).

Cao *et al.*, (2020) confirmed SARS COVID positive using RT-PCR laboratory confirmation. For 108 (Zeng, *et al.*, 2020, Yu *et al.*, 2020., Liu *et al.*, 2020, Kayem *et al.*, 2020, Cao *et al.*, 2020; Chen *et al.*, 2020) patients, confirmation of diagnosis and respiratory involvement was confirmed with a chest CT scan after hospital admission. Chest X-ray was performed for 30 (Govind, 2020; Xu *et al.*, 2020) patients to clinically diagnose COVID-19 after hospital admission. For remaining patients, no clinical confirmation of diagnosis was performed and they were treated only on the basis of laboratory diagnosis of COVID-19.

Table 2: Pregnancy Outcome during COVID 19 n=812

Sl No	Study ID	(n)	Country	Research Method	Mode of Delivery	Reason for Cs	Maternal Outcome	Fetal Outcome
1	Koumoutsea EV *et al* (2020)	2	China	case study reviews	CS	1st patient: Multidisciplinary team decision to manage COVID 19 and prevent vertical transmission. 2nd patient: Non reassuring fetal heart rate.	1st patient: PPH	1st baby=Healthy male infant Apgar 9/9 2nd baby: Non reassuring fetal heart rate Apgar: 4,2,7 at 1, 5 and 10 min
2	Alzamora MC *et al* (2020)	1	China	case study reviews	CS	Respiratory failure	Respiratory failure leading to mechanical ventilation and preterm delivery	APGAR 6 and 8 at 1 and 5 min Reported COVID 19 Positive 16 and 48 hours after birth
3	Liu W (2020)	3	China	case study reviews	2 CS; 1SVD	Not mentioned	Normal Intranatal and postnatal events	Normal. No abnormalities reported.
4	Khan. S *et al* (2020)	3	China	case study reviews	3 SVD		Normal Intranatal and postnatal events	1 Preterm APGAR 8/9 APGAR 9/10
5	Zambrano *et al* (2020)	1	Central America	case study reviews	SVD		Preterm	Normal; LBW; NICU admission for preterm care

6	Kolkova Z *et al* (2020)	1	Sweden	case study reviews	CS	Respiratory distress and mechanical ventilation	Acute respiratory Failure, Renal failure, Rhabdomyolysis, 30 days ICU care with mechanical ventilation	APGAR: 3/5/8 at1/5/10 min required manual ventilation COVID negative
7	Celso T *et al* (2020)	2	Brazil	case study reviews	CS	1 st patient: CS due to cardiovascular instability 2nd patient: CS due to respiratory failure, intubation and mechanical ventilation	1st patient: Pulmonary Microthrombi; discharged stable 15 days after ICU care 2nd patient clinically stable with 7 days of ICU care, discharged stable after 15 days	1st baby: APGAR 1/2 at 1/5min Neonatal death after 9 hrs 2nd Baby: APGAR 7/9 at 1/5 min NICU care, COVID negative. Neonate discharged from hospital after 67 days
8	Yu Y *et al*.(2020)	1	China	case study reviews	SVD		Preterm Labour: Rapidly developed respiratory distress after SVD	Healthy Newborn, SARS negative;
9	Andrew *et al* 9(2020)	1	Australia	case study reviews	SVD		Uneventful; Discharged after 10 days; COVID negative	APGAR 9/9; COVID Negative
10	Hansen *et al* (2020)	1	USA	case study reviews	CS	Uncontrolled Hypertension	Endometriosis treated with antibiotics for 7 days; Acute renal injury; ICU on day 10 for worsening hypoxia; Discharge after 17 days after COVID negative results	Normal. No data presented
11	Gonzaile z *et al* (2020)	1	NA	**case study reviews**	CS	Respiratory distress	Preterm; Normal Postnatal period; Lymphopenia	Preterm, NICU care, COVID negative
12	Liu D.*et al* (2020)	15	China	Retrospective medical records reviews	10 CS 1 SVD 4 patients still pregnant	Reason for CS not mentioned	12 patients: Lymphopenia	No neonatal abnormality reported

13	Chen H *et al* (2020)	China	9	Retrospective medical records reviews	CS	COVID 19 as reason in all; PROM: 02; Previous CS:01; Pre-eclampsia: 01; Fetal distress 01	5 patients had lymphopenia 4 preterm labour at 36-39 weeks of gestation. 1 pregnancy complicated with preeclampsia	2 patients Fetal distress 2 preterm neonates with lower birth weight
14	Ferrazi E *et al*.(2020)	42	Northern Italy	Retrospective medical records reviews	24 SVD Elective CS 18	8 Non COVID reason 10: Respiratory Distress due to COVID 19	1- Severe PPH 2 cases preterm delivery Admission to critical care unit due to respiratory distress 04 Oxygen support 07	2 newborns tested positive for COVID 19 due to breastfeeding without mask 1 Newborn Positive related to vaginal operative delivery
								3 admitted to NICU for respiratory distress
15	Kayem G *et al* (2020)	617	France	Retrospective medical records reviews	Delivered= 181; CS =83/181; SVD = 98	CS=45 for COVID 19 Other obstetrical reason =38	Fetal loss at 14-21 weeks =5/181 Preterm =50/181 IUD=7/181 Maternal death =01 8 multiple pregnancy with 03 triplets	COVID 19 Positive 02/190 NICU admission 37/190 Neonatal death 01/190
16	Antoun L *et al*(2020)	23	UK	Retrospective medical records reviews	CS=16 SVD=03 MISCARRIAGE =01 NOT DELIVERED AT TIME OF DATA COLLECTION 03	3 Elective CS, 13 Emergency CS (2 Fetal distress, 4 delay and failure to progress in labour, 7 maternal request/PPROM/sepsis	Preterm delivery (7), Reduced Fetal Movement (6), Pre term Premature ROM (4), preeclampsia (2), HELLP (2), DIC (2), OC (1), fetal distress (1) Meconium (2) Miscarriage (1) PPH (1), ECMO (1), death (1)	Infected Bacterial pneumonia (1), fetal asphyxia (Resuscitated using positive pressure/endotracheal tube) (1)
17	Nan Yu *et al* (2020)	7	China	Retrospective medical records reviews	CS	COVID 19	3 patients had Uterine scarring; NO ICU admissions	3 tested positive; kept in NICU. Discharged at 2 weeks and COVID negative

18	Xu L *et al* (2020)	5	China	Retrospective medical records reviews	4 CS 1 SVD	4 CS due to Viral pneumonia;	Lymphopenia in all patients Uneventful	Normal; all COVID negative;
19	Cao D *et al* (2020)	10	China	Retrospective medical records reviews	2 Emergency CS; 6 Elective CS; 2 SVD	2 CS: Placental separation 03: Preterm 03: COVID 19	3 preterm ;4 PROM; 1 Placental separation;2 postpartum fever; 06 Lymphopenia; 06 Mycoplasma infection	03 Premature; all COVID negative
20	Zeng Y *et al* (2020)	16	China	Retrospective medical records reviews	CS12; SVD: 04;	CS for non COVID reason; 3 CS for Preterm; 01 CS for Cardiac disorder in Pregnancy	PROM 03; Preterm 03; Polyhydramnios 01; IUGR 01	Fetal Macrosomia 01; All COVID negative
21	Nie R, *et al* (2020)	33	China	Retrospective medical records reviews	22 CS 5 SVD 5 Pregnancy ongoing at the time of manuscript writing 01 Induced Abortion	Hypertension 02; GDM=02; Preterm 01; Fetal distress :04	10: preterm labour and 3: PROM	10 Preterm, 1 tested positive for SARSCOVID-19 4: fetal distress
22	Hantoush Zadeh S, *et al* (2020)	9	Iran	Retrospective medical records reviews	06CS 1SVD 02 Not delivered	05 CS due to ARDS related to COVID; 01 CS due to twins	07 Maternal death; 02 ARDS and mechanical ventilation; improved after treatment	Fetal Death =05 02: Neonatal death All COVID Negative
23	Govinda *et al* (2020)	9	London	Retrospective medical records reviews	1 SVD; 08 CS	2 Emergency CS Respiratory distress; 1 Emergency CS for Non-reassuring CTG; 01 Elective CS for Breech; 04 Elective CS for previous CS and maternal request	patient 1= Lymphopenia, ECMO; Patient 2= Mechanical ventilation required for 4 days postnatal; others stable and managed well	1=COVID positive 1= ICU admission

The pregnancy outcomes identified from the reviews is analyzed as maternal and foetal outcomes separately and is given below. An overall summary of outcomes in mother and fetus among pregnant women who tested COVID-19 positive is presented in the case reports in table 2.

Among 17 patients, 59% (Kolkova, *et al.*, 2020., Tutiya *et al.*, 2020; Romero *et al.*, 2020, Koumoutsea *et al.*, 2020, Yu *et al.*, 2020, Alzamora *et al.*, 2020) had CS as the mode of delivery, and 41% (Liu *et al.*, 2020; Walczak, *et al.*, 2020.,Yu *et al.*, 2020; Zambrano *et al.*, 2020) underwent spontaneous vaginal delivery (SVD). Five out of 10 patients underwent CS due to respiratory failure related to their COVID-19-positive status; (Kolkova, *et al.*, 2020., Tutiya *et al.*, 2020., Koumoutsea *et al.*, 2020; Alzamora *et al.*, 2020) three out of ten patients underwent CS for obstetrical/non-COVID reasons, while no data was presented for the remaining two patients (Liu *et al.*, 2020).

In terms of maternal outcomes; five of the 17 (Romero *et al.*, 2020., Alzamora, *et al.*, 2020; Zambrano *et al.*, 2020) patients had a preterm delivery, four (Liu *et al.*, 2020. Khan *et al.*, 2020.,Walczak *et al.*, 2020) had a normal, uneventful labour process; two (Koumoutsea *et al.*, 2020., Hansen, Hine, & Strout, 2020) patients reported PPH, two more reported endometriosis; while postnatal rhabdomyolysis, lymphopenia and respiratory microthrombi were each reported by one (Kolkova *et al.*, 2020., Romero *et al.*, 2020) patient. All patients were treated and discharged healthy, after confirmation of COVID-19-negative status.

Neonatal outcomes are explained in terms of one-min and five-min Apgar scores, as well as COVID-19 status after birth. Thirty percent (Kolkova *et al.*, 2020; Tutiya *et al.*, 2020; Koumoutsea *et al.*, 2020) and 10% (Kolkova *et al.*, 2020., Tutiya *et al.*, 2020) of neonates presented with an Apgar score below five at one min and five min respectively, while an Apgar score above seven was observed in 60% (Tutiya *et al.*, 2020., Liu *et al.*, 2020, Walczak *et al.*, 2020; Koumoutsea, *et al.*, 2020) of neonates at one min and 80% (Kolkova *et al.*, 2020; Tutiya *et al* 2020; Khan et al., 2020; Walczak *et al.*, 2020. Koumoutsea *et al.*, 2020; Alzamora *et al.*, 2020) of neonates at five mins. Apgar details were not presented for three infants, whereas one (Tutiya *et al.*, 2020) neonatal deaths were reported, nine hours after birth, which was related to preterm status and respiratory failure. Out of 13 new-borns, only one baby born by CS was reported COVID-19 positive, 16 and 48 hours after birth (Alzamora *et al.*, 2020).

Among the 795 reviewed reports, 25.78% (Zeng *et al.*, 2020; Antoun *et al.*, 2020; Yu *et al.*, 2020., Nie *et al.*, 2020; Hantoushzadeh *et al.*, 2020., Liu *et al.*, 2020; Govind *et al.*, 2020; Ferrazzi *et al.*, 2020; Kayem *et al.*, 2020. Xu *et al.*, 2020; Caob *et al.*, 2020., Xu *et al.*, 2020; Cao *et al.*, 2020) of patients underwent CS; 56.6% (Antoun *et al.*, 2020; Nie *et al.*, 2020; Hantoushzadeh *et al.*, 2020; Liu *et al.*, 2020) were still pregnant at the time of review and 17.6% (Zeng et al., 2020, Antoun *et al.*, 2020., Nie *et al.*, 2020; Hantoushzadeh *et al.*, 2020; Liu *et al.*, 2020; Govind *et al.*, 2020; Ferrazzi *et al.*, 2020, Kayem *et al.*, 2020; Xu *et al.*, 2020; Cao *et al.*, 2020) had SVD. Forty-six per cent (90 of 194 patients) (Zeng *et al.*, 2020; Yu *et al.*, 2020; Hantoushzadeh *et al.*, 2020; Govind *et al.*, 2020; Ferrazzi *et al.*, 2020; Kayem *et al.*, 2020; Cao *et al.*, 2020) underwent CS for reasons connected to COVID-19, whereas 48.5% (94 of the 194) (Zeng *et al.*, 2020; Nie *et al.*, 2020. Hantoushzadeh *et al.*, 2020; Liu *et al.*,2020; Ferrazzi *et al.*, 2020; Kayem *et al.*, 2020; Xu, *et al.*, 2020; Cao *et al.*, 2020) had CS for non-COVID, obstetrical reasons. For 10 patients, the reason for CS was not presented in the report (Liu *et al.*, 2020; Govind, *et al.*, 2020).

Twenty-nine patients reported lymphopenia in the postnatal period (Liu, *et al.*, 2020; Govind, *et al.*, 2020; Xu, *et al.*, 2020; Cao, *et al.*, 2020; Chen *et al.*, 2020) 76 (Zeng, *et al.*, 2020; Antoun, *et al.*, 2020; Nie, *et al.*, 2020; Ferrazzi, *et al.*, 2020; Kayem *et al.*, 2020; Cao *et al.*, 2020) had preterm labour, two (Antoun, *et al.*, 2020; Ferrazzi *et al.*, 2020) reported severe PPH, eight (Antoun *et al.*, 2020; Hantoushzadeh *et al.*, 2020; Kayem, *et al.*, 2020) suffered maternal death related to acute respiratory distress syndrome and postnatal complications, and three patients had uterine scarring in the postnatal period (Yu, *et al.*, 2020).

A total of 14 new-born tested COVID-19 positive (Yu, *et al.*, 2020; Ferrazzi *et al.*, 2020; Kayem, *et al.*, 2020). Eight patient cases reported foetal/neonatal death (Hantoushzadeh *et al.*, 2020; Kayem, *et al.*, 2020) and 42 neonates were admitted to NICU with clinical manifestations of foetal distress (Antoun *et al.*, 2020; Nie, *et al.*, 2020; Ferrazzi, *et al.,* 2020; Chen *et al.*, 2020)

DISCUSSION

This systematic review showed a moderate effect of COVID-19 in pregnancy on outcomes in mother and

newborn. COVID-19 is a highly infectious disease with maximum incidence being reported among people with weak immune status as well as multiple comorbidities (Lipsitch, *et al.*, 2020; Zhou *et al.*, 2020; Jordan, Adab & Cheng, 2020). As the COVID-19 pandemic continues to have worldwide effects, the most affected group seems to involve a majority of pregnant women.

Cases of COVID-19 infection in pregnant women have been described in multiple reports and reviews from around the world. Obstetricians and health care workers globally have raised concerns over expected risk of severe disease, viral transmission through vertical route and complications in mother, fetus and newborn (Dong *et al.*, 2020). Primary aim of this systematic review was to describe the current scientific evidence relating to COVID-19 in pregnancy and newborn period.

Lack of mandatory testing for SARS-CoV-2 during pregnancy (understanding that most of pregnant women infected with SARS-CoV-2 were tested only after reporting symptoms while in hospital), and minimal availability of standardized antenatal surveillance, management, timing and type of delivery among women with COVID-19 was observed in all the reports reviewed. The recent updates and modifications in maternity care services worldwide may have an impact upon COVID-19's effect on outcomes in maternal and perinatal period during pregnancy, which are unmeasured in this review. A significant number of pregnant women presented in the third trimester with COVID-19 symptoms and then delivered, so we were unable to measure meaningfully the maternal and fetal outcome in terms of the association between COVID-19 infection and different gestational ages.

As shown by the studies included in this review, among 362 neonates, 22.37% of were preterm newborn and 1.3% of patients reported pregnancy loss at different initial trimesters. Of the 362 women who had delivered by the time of review completion, 215 had a CS delivery and 147 had a vaginal delivery. According to some previous reviews of similar data regarding the maternal outcome, there is some similarity between the proportion of C-section deliveries in patients with COVID-19 was 45% almost closer to that reported here of 59.3%, with both presenting an average proportion of C-section deliveries. However, a 23% rate of preterm delivery was described in a parturient with COVID-19, a similar frequency as presented 22.37% and 1.35 pregnancy loss of patients with COVID-19 included in this review (Capobianco *et al.*, 2020).

Case reports from China (Liu, *et al.*, 2020; Khan *et al.,* 2020), Australia (Walczak *et al.*, 2020) reported no adverse outcomes concerning COVID-19 and pregnancy, which was similar to report presented where few case reports reviewed from around the world showed no adverse pregnancy outcomes (Dubey *et al.*, 2020). Our review report found 4.14% COVID-19 infection rates among newborn, based on review of case study as well as in review of medical records done retrospectively. One neonate was reported with COVID-19 in the case studies review and 14 more were reported in the retrospective review of medical records. The majority of mothers of these neonates were shifted to an intensive care unit for respiratory distress in the postnatal period. Although it is insufficient to validate vertical transmission of infection, it is concomitant with the review findings presented by Dubey et al, in which 1% of neonates were found to be COVID-19 positive. However, more research is required to establish the relationship between COVID-19 and vertical transmission.

CONCLUSION

The coronavirus pandemic has had a major impact on health worldwide. Knowledge and associated facts about this illness have been discussed and presented faster than the rate of globalization in the past decade. Although there is a lack of substantial evidence of the infection affecting maternal and neonatal outcomes, studies prove that pregnant women and newborn children are at high risk of developing adverse outcomes. COVID-19 is highly contagious and must be considered when planning antenatal, Intranatal, postnatal, and newborn care. Pregnancy does not increase the risk of infection and pregnant women should follow the same recommendations as the rest of the general population to limit the transmission of COVID-19. However, pregnancy might increase the severity of respiratory distress in cases involving severe infection and may necessitate preterm labor and CS. The appropriate screening of pregnant mothers for COVID-19 at different trimesters is therefore essential, especially when there are comorbid medical illnesses and the presence of flu-like symptoms. This can reduce the maternal and fetal complications for a pregnant woman who is COVID-19 positive. As the disease is, continually evolving, healthcare providers should update themselves with recent developments in the vertical transmission of COVID-19 and other developments in the disease

process to ensure that the best maternal and fetal health care is available to pregnant women who are COVID-19 positive.

Conflict of Interests

The authors declare that they have no conflict of interest.

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