

Terminations of pregnancy/Mode of delivery and complications.

Fetal outcomes.

All titles and abstracts were reviewed independently by three researchers for relevance and inclusion in the current review. In case of disagreement, consensus was developed by discussion. Required data about COVID-19 symptoms, maternal outcomes and perinatal outcomes was extracted by the same researchers [8].

At first, general health of confirmed COVID-19 pregnant women were analyzed to assesses different parameters such as; sign/symptoms, development of COVID Pneumonia, ICU admission and mechanical ventilation and death. Secondly, maternal outcomes in terms of terminations of pregnancy/mode of delivery and complications in COVID-19 positive patients were assessed [9]. Maternal outcomes included were; Abortions, Pre-term birth, Premature rupture of membranes (PROM), Cesarean delivery and Pregnancy related complications. Finally fetal outcomes (abortions, IUD, Pre-term birth, peri-natal and neonatal deaths) were assessed. The perinatal outcomes included were; Apgar score at 1 and 5 minutes, Fetal distress, Asphyxia, perinatal death (stillbirth or

neonatal death), development of COVID Pneumonia, Neonatal Intensive Care Unit (NICU) admission, mechanical ventilation and death. Maternal COVID-19 symptoms at presentation and symptoms of SARS-CoV-2 RT-PCR and/or IgM antibodies positive newborns at birth were also included in the present review [11-15].

Data analysis

Data were entered and analyzed by using IBM-SPSS Statistics 20 software for calculation of median and percentages. MedCalc Statistical Software version 16.4.3 was used for calculation of pooled proportions. The percentages shown in of the results section are pooled proportions and the rest are reported as frequency and percentages.

Results

General characteristics of included articles are detailed. Four studies were retrospective studies, two were case series and two case reports in the selected criteria, and as a result 181 pregnant women were included in all selected studies. In some studies some or other information was missing, therefore mentioned in tables as “not reported” (Table 1) [16-20].

Table1: Characteristics of studies included in the current review.

Author	Study location	Duration	Number of pregnant women	Study design	Maternal age (years) (median)	Vertical transmission	Vertical transmission evaluated by	Test kit used
Liu Y et al[21]	China	December 8, 2019 to February 25, 2020	13	Retrospective study	30 (22-36)	No	SARS-CoV-2 Quantitative RT-PCR	not reported
ZENG et al[25]	Wuhan, China	January 2020 to February 2020	33	Case series	not reported	12114 -0.09	SARS-CoV-2 Quantitative RT-PCR	(Coronavirus PCR Fluorescence Diagnostic Kit [BGI])
Chen H et al[22]	Wuhan, China	Jan 20 to Jan 31, 2020	9	Retrospective study	28 (26-40)	No	SARS-CoV-2 Quantitative RT-PCR	(COVID-19 Kit (Bio Germ, Shanghai, China)
Hui Zeng[23]	Wuhan, China	February 16 to March 6, 2020	6	Retrospective study	not reported	44349 -0.333	SARS-CoV-2-IgM antibodies	(CLIA assays kit YHLO)
Lan Dong[27]	Wuhan, China	43831	1	Case report	29	Yes	SARS-CoV-2-IgM antibodies	not reported
Maria Claudia Alzamora[28]	Peru	43891	1	Case report	41	Yes	SARS-CoV-2 Quantitative RT-PCR	not reported
Jie YAN[24]	China	January 20 to March 24, 2020	116	Retrospective study	30.8 (24-41)	No	SARS-CoV-2 Quantitative RT-PCR	not reported
Cuifang Fan[26]	Wuhan, China	43831	2	Ca se series	34/ 29	No	SARS-CoV-2 Quantitative RT-PCR	(Bioperfectus Technologies, China)

Description of Maternal symptoms at presentation and progression of disease severity of each study. Fever seems to be the most common symptom followed by cough, sore throat, dyspnea, pneumonia, admission in intensive care unit and

patients on mechanical ventilators were also reported in most of the studies (Table 2) [29].

Table2: Clinical features of SARS-CoV-2 positive pregnant women.

Author (Study location) [Duration]	Fever	Cough	Sore throat	Dyspnea	Pneumonia per computed tomography diagnosis	Intensive care unit admission		Mechanical ventilation
Liu Y et al (China) [December 8, 2019 to February 25, 2020][21]	10/13 (77.0%)	02/13 (15.3%)	01/13 (7.70%)	03/13 (23.0%)	01/13 (7.70% ^s)	01/13 (7.70% ^s)		01/13 (7.70% ^s)
ZENG et al (Wuhan, China) [January 2020 to February 2020] [25]	08/33 (24.2%)	10/33 (30.3%)	No	No	33/33 (100%)	No		No
Chen H et al (Wuhan, China) [Jan 20 to Jan 31, 2020][22]	07/09 (77.7%)	04/09 (44.4%)	02/09 (22.2%)	01/09 (11.1%)	08/09 (88.8%)	Not reported		No
Hui Zeng (Wuhan, China) [February 16 to March 6, 2020] [23]	not reported	not reported	not reported	not reported	not reported	not reported		not reported
Lan Dong (Wuhan, China) [Jan 2020][27]	Yes	No	No	No	Yes	No		No
Maria Claudia Alzamora (Peru) [March 2020] [28]	Yes	No	No	Yes	Yes	Yes		Yes
Jie YAN (China) [January 20 to March 24, 2020] [24]	59/116 (50.9%)	33/116 (28.4%)	not reported	not reported	8/116 (6.9%)	8/116 (6.9%)		8/116 (6.9%)
Cuifang Fan (Wuhan, China) [Jan 2020][26]	02/02 (100%)	No	1/2 (50.0%)	No	02/02 (100%)	No	No	

Detail of maternal and fetal outcomes are reported and pooled proportions are reported. The age range of 181 pregnant women with COVID-19 infection from selected 8 articles was 22 to 41 years. Gestational age at the onset of COVID-19 symptoms ranged from 25 to 39 weeks. Out of 181 pregnant women, 155 newborns survived, there was 01 spontaneous

abortion, 01 still birth, 01 neonatal death. Whereas, 17 women were still pregnant till the end of study while fetal outcome of 06 pregnant women was not reported (Table 3) [30].

Table3: Pregnancy outcomes of SARS-CoV-2 positive pregnant women.

Author (Study location) [Duration]	Number of pregnant women	Gestational age at onset of illness (weeks)	Maternal outcome	Fetal outcome	Premature rupture of membranes (PROM)	Premature deliveries	Cesarean deliveries
Liu Y et al	13	35	All survived	01 still birth	01/13	6/13	10/13

Citation: Rahat T, Naz F, Saima N. Pregnancy outcomes of pregnant women with confirmed SARS-CoV-2 infection: A review. *J Pregnant Neon Med* 2021;5(4):1-8.

(China) [December 8, 2019 to February 25, 2020][21]		(25-38)			(7.70%)	(46.1%)	(76.9%)
ZENG et al (Wuhan, China) [January 2020 to February 2020][25]	33	not reported	All survived	All survived	03/33 (%)	4/33 (12.1%)	26/33 (78.8%)
Chen H et al (Wuhan, China) [Jan 20 to Jan 31, 2020][22]	09	37 (36-39)	All survived	All survived	02/09 (22.2%)	4/9 (44.4%)	9/9 (100%)
Hui Zeng (Wuhan, China) [February 16 to March 6, 2020][23]	06	3rd trimester	not reported	not reported	not reported	not reported	6/6 (100%)
Lan Dong (Wuhan, China) [Jan 2020][27]	01	34	survived	survived	No	Yes	Yes
Maria Claudia Alzamora (Peru) [March 2020][28]	01	33	survived	survived	No	Yes	Yes
Jie YAN (China) [January 20 to March 24, 2020][24]	116	38 (36-39)	All survived	01 spontaneous abortion 01 neonatal death	6/114 (5.26%)	21/99 (21.2%)	85/99* (85.9%)
	02	37	survived	survived	No	No	Yes
Cuifang Fan (Wuhan, China) [26] [Jan 2020]		36	survived	survived	No	Yes	Yes
*99 patients delivered whereas, pregnancy of rest of the patients was continued.							

On the basis of pooled proportion of reported symptoms, the most common symptom of COVID-19 among pregnant women was fever 50.77% (88/175), followed by cough 28.43% (49/174), dyspnea 23.05% (5/58) and sore throat 18.69% (4/58). COVID-19 Pneumonia was developed in almost one third, 30.90%, (54/175) of the pregnant women, 8.3% (10/132) were admitted to ICU and 8.3% (10/132) required mechanical ventilation [31]. The most common outcome observed in

84.98% (140/164) of the women was cesarean deliveries followed by premature deliveries 24.67% (38/158) and premature rupture of membranes 7.64% (12/174). No maternal death was reported by any of the included studies. Vertical transmission was observed in about 2.95% (7/164) of newborns (Table 4).

Table 4: Pooled proportion of various maternal parameters infected with Covid-19.

Parameters	Studies	Pregnancies (n/N)	I ² , (95%CI)	Pooled Proportion (95%CI)
Symptoms and severity				
Fever	7	88/175	71.67 (38.53 - 86.94)	50.777 (43.278 to 58.249)
Cough	6	49/174	0.00 (0.00 - 61.70)	28.431 (21.970 to 35.619)
Sore throat	4	21276	0.00 (0.00 - 83.86)	18.691 (6.728 to 37.453)
Dyspnea	4	21306	34.94 (0.00 - 77.28)	23.051 (9.557 to 42.351)

Pneumonia	7	54/175	96.75 (95.04 - 97.87)	30.905 (24.279 to 38.166)
ICU admission	4	10/132	54.08 (0.00 - 84.81)	8.324 (4.278 to 14.299)
Mechanical Ventilation	4	10/132	54.08 (0.00 - 84.81)	8.324 (4.278 to 14.299)
Outcome				
PROM	6	12/174	0.00 (0.00 - 66.71)	7.646 (4.218 to 12.547)
Premature deliveries	7	38/158	62.81 (15.56 - 83.62)	24.672 (18.302 to 31.975)
Cesarean deliveries	8	140/164	0.00 (0.00 - 59.35)	84.980 (78.749 to 89.963)
Maternal death	7	0/175	0	0
Vertical transmission	8	7/164	77.96 (56.54 -88.83)	2.952 (0.976 to 6.714)

Out of 7 newborns that tested positive for COVID-19, 02 developed fever, 02 had dyspnea, 01 had asphyxia, 01 had respiratory distress syndrome, 01 had cyanosis, 03 developed COVID pneumonia, 04 required NICU admission and 02 required mechanical ventilation. APGAR score at 1 and 5 minutes was reported for only five newborns. One neonate had APGAR score of 03 and 04 at 1 and 5 minutes, respectively. Another neonate had APGAR score of 06 at 1 minute and 08 at

5 minutes. Rest of the neonates had APGAR scores ranging from 8-10 at 1 and 5 minutes [32]. Since the most commonly observed pregnancy outcome was caesarean section, therefore indication of cesarean section is also given according to the reported cases. The most common indication reported is COVID-19 Pneumonia 46% (45/98), followed by previous C-section 18% (17/89) and fetal distress 13% (14/104) (Table 5) [33].

Table5: Indication for cesarean delivery.

Indications	No. of Studies	n/N	%
COVID-19 Pneumonia	5	45/98	45.92
Previous C-Sec	2	17/94	18.09
Fetal Distress	3	14/104	13.46
Failure to progress	1	31/68	5.88
Preeclampsia	2	34/455	5.32
Abnormal Fetal Growth	1	31/1079	2.35
Placenta Previa	1	31/107	3.53
Others	4	18/106	16.98

Discussion

In the current study, review was done on the available data till 15th July 2020; however published studies after 15th July 2020 are also included in discussion section for the better comparisons on the wider range of currently available data. Majority of our review findings are consistent with other reviews conducted worldwide. Age range of COVID positive pregnant women observed in current review was from 22 to 41 years, almost same age range is seen in most of the articles; National university hospital Singapore study stated age range from 23-40 years, another review on 324 pregnant women shows maternal age ranged from 20 to 44 years [34].

Gestational age reported in our study at the onset of COVID-19 symptoms ranged from 25 to 39 weeks, most of the studies are in line that pregnant women are infected with said infection during second and third trimester. On the other hand

gestational age at the time admission ranged from 5 to 41 weeks [35].

The most common symptom of COVID-19 among pregnant women was fever followed by cough, dyspnea and sore throat whereas; COVID-19 Pneumonia was developed in almost one third of the pregnant women. These types of findings are similar in most of the individual studies, case series as well as in reviews. For example a systematic review reveals the same sequence of events regarding fever, cough and dyspnea. They reported severe pneumonia from 0% to 14% among the case series [36].

With reference to the mode of delivery, the most common outcome of pregnant women observed in current study in about 85% was cesarean deliveries followed by premature deliveries (24.67%) and premature rupture of membranes (7.64%), respectively. As it was observed in the reviewed articles around 85% COVID-19 pregnancies were landed up in caesarian

section, and in almost half of the cases COVID-19 Pneumonia was the main indication for C-section.

In a review conducted on pregnancy outcome of 108 pregnant women revealed that 91% of them were delivered by C-section. In another study, out of 48 deliveries, 46 were delivered through C-section and only 02 were delivered vaginally [37]. In the review on 324 pregnant women 78% had C-section. In most cases of available literature the indication for the c-section was not clearly stated, and it is certainly possible that the decision was influenced by the understandable anxiety towards the potential consequences of a new viral infection.

Further studies are recommended in this regard to clarify whether c-section shall be opted or not if COVID Pneumonia develops in infected pregnant women. Whereas pneumonia followed by admission in ICU having mechanical ventilators observed in current review were also reported in almost same severity in other published data, however no adverse maternal outcome was seen; findings are in same line with current review [38].

It was seen that as compared to COVID positive non-pregnant women, pregnant women were more prone to be admitted in ICU (aRR=1.5 at 95% CI) and landed up with mechanical ventilation (aRR=1.7 at 95% CI). It is postulated that there is a risk of severe COVID-19 disease in pregnant women.

In 13 states of USA data was collected by hospital surveillance network in COVID-19 associated hospitals called COVID-NET on 598 hospitalized pregnant women from 1st March to 22 August 2020, it revealed that 54.5% were asymptomatic while from 272 symptomatic patients 16.2% were shifted to ICU and 8.5% were given invasive mechanical ventilation.

On the contrary a retrospective case series study conducted in China on 21 full term pregnancies reported no admission in ICU, while findings of that study are debatable since study was conducted on only 21 cases. Similarly, another study conducted in China reveals that neither pregnancy nor child birth aggravate the symptoms of COVID-19 [39].

Same is seen with other possibilities of outcomes in current review such as; miscarriages, still births, fetal distress, PROM, preterm deliveries. About 25% women had preterm delivery, however a study conducted in China on few COVID-19 pregnant women found that no newborn was preterm or had any postpartum complications. Whereas, some studies shows both maternal and fetal complications including fetal distress, preterm delivery and even death of mother, on the contrary no serious consequence in the form of maternal death is observed in pregnant women in the current review.

According to another study, the rate of miscarriage and preterm delivery cannot be solely attributed to COVID infection since no comparison group is included and further prospective research is recommended to provide evidence. On the other hand COVID-NET surveillance revealed that about 97.8% of patients gave live births while 2.2% had lost their pregnancies.

Vertical transmission of COVID-19 from mother to her fetus is highly debatable in the available literature. In our review

vertical transmission was observed in about 2.95% of newborns and out of 7 newborns that tested positive for COVID-19, 03 developed COVID pneumonia, 04 required NICU admissions and 02 neonates' required mechanical ventilation.

In comparison with a systematic search on 1316 pregnant women 11.3% neonates were admitted to ICU with 2.2% perinatal death. Moreover, no vertical transmission was observed in that review. Similarly, a vast number of studies showed no evidence of vertical transmission.

Although limited knowledge is available on giving evidence on vertical transmission of COVID-19, however current literature is providing some solid reasons in the favour of vertical transmission; perhaps prospective studies are strongly recommended to add the evidence [40].

Limitations

Mostly case reports/series and retrospective studies are available in literature and the same were included in the current review.

Conclusion

Study findings concluded that although maternal death is not very common, however, adverse maternal and fetal outcomes are associated with COVID-19 in the form of severe illness and worse birth outcomes. Moreover, unusual increase in the rates of caesarian sections is also noticed. Evidence of vertical transmission of COVID-19 infection from pregnant mothers to their fetuses is also observed, yet debatable until proved otherwise on the studies/trials to be conducted on the larger scale.

Funding

These findings emphasize the importance of preventive measure to be taken by pregnant women from COVID-19 infection.

Recommendations

More studies with larger sample size and age and time matched control group shall be done encompassing complete information regarding maternal and perinatal outcomes. All data available till now is on smaller scale and mostly retrospective therefore, provision of facts require a larger scale data on prospective studies.

References

1. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *J Med Virol.* 2020;92:401-2.
2. Hui DS, Azhar EI, Madani TA, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health. The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis.* 2020;91:264-6.

3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395:497-506.
4. Favre G, Pomar L, Musso D, et al. 2019-nCoV epidemic: What about pregnancies? *Lancet*. 2020;395:40.
5. Louie JK, Acosta M, Jamieson D, et al. California Pandemic (H1N1) Working Group. Factors associated with death or hospitalization due to pandemic. 2009:1896-902.
6. Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol*. 2004;191:292-97.
7. Clinical management of Severe Acute Respiratory Infection (SARI) when COVID-19 disease is suspected: World Health Organization. 2020.
8. Rasmussen SA, Smulian JC, Lednicky JA, et al. Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know? *Am J Obst Gynecol*. 2020.
9. Rolling updates on coronavirus disease (covid-19): World Health Organization. 2020.
10. Ma K, Chen T, Han M, et al. Management and clinical thinking of Coronavirus Disease 2019. *Chin J Hepatol*. 2020;28:E002-E.
11. World Health Organization. Coronavirus disease (COVID-19) outbreak. 2020.
12. Chen Y, Li Z, Zhang YY, et al. Maternal health care management during the outbreak of coronavirus disease 2019. *J Med Virol*. 2020.
13. Investigators AI. Australasian maternity outcomes surveillance system: Critical illness due to 2009 A/H1N1 influenza in pregnant and postpartum women: Population based cohort study. *BMJ*. 2010;340:1279.
14. Jamieson D, Honein M, Rasmussen S. The Novel Influenza A (H1N1) pregnancy working group. H1N1. 2009.
15. Siston AM, Rasmussen SA, Honein MA, et al. Pandemic 2009 influenza A (H1N1) virus illness among pregnant women in the United States. *Jama*. 2010;303:1517-25.
16. Mullins E, Evans D, Viner R. Original: Coronavirus in pregnancy and delivery: Rapid review. 2020.
17. Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection during pregnancy: Report of two cases and review of the literature. 2019.
18. Smith V, Seo D, Warty R, et al. Maternal and neonatal outcomes associated with COVID-19 infection: A systematic review. *Plos one*. 2020;15:e0234187.
19. Visscher HC, Visscher RD. Indirect obstetric deaths in the state of Michigan 1960-1968. *Am J Obst Gynecol*. 1971;109:1187-93.
20. Liu Y, Chen H, Tang K, et al. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *J Infect*. 2020.
21. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*. 2020;395:809-15.
22. Zeng H, Xu C, Fan J, et al. Antibodies in infants born to mothers with COVID-19 pneumonia. *Jama*. 2020;323:1848-9.
23. Yan J, Guo J, Fan C, et al. Coronavirus disease 2019 (COVID-19) in pregnant women: A report based on 116 cases. *Am J Obst Gynecol*. 2020.
24. Zeng L, Xia S, Yuan W. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA Pediatr*. 2020.
25. Fan C, Lei D, Fang C, et al. Perinatal transmission of COVID-19 associated SARS-CoV-2: Should we worry? *Clin Infect Dis*. 2020.
26. Dong L, Tian J, He S, et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. *Jama*. 2020;323:1846-8.
27. Alzamora MC, Paredes T, Caceres D, et al. Severe COVID-19 during pregnancy and possible vertical transmission. *Am J Perinatol*. 2020;37:861.
28. Dashraath P, Jeslyn WJL, Karen LMX, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *Am J Obst Gynecol*. 2020.
29. Juan J, Gil MM, Rong Z, et al. Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: Systematic review. *Ultrasound Obst Gynecol*. 2020;56:15-27.
30. Liu D, Li L, Wu X, et al. Pregnancy and perinatal outcomes of women with coronavirus disease (COVID-19) pneumonia: A preliminary analysis. *Am J Roentgenol*. 2020:1-6.
31. Caparros Gonzalez RA. Maternal and neonatal consequences of coronavirus COVID-19 infection during pregnancy: A scoping review. *Revista espanola de salud publica*. 2020;94:202004033.
32. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. 2020.
33. Della Gatta A, Rizzo R, Pilu G, et al. COVID19 during pregnancy: A systematic review of reported cases. *Am J Obst Gynecol*. 2020.
34. Ellington S, Strid P, Tong VT, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status-United States, January 22-June 7, 2020. *Morbidity and Mortality Weekly Report*. 2020;69:769.
35. Delahoy MJ. Characteristics and maternal and birth outcomes of hospitalized pregnant women with laboratory-confirmed COVID-19-COVID-NET, 13 states, March 1-August 22, 2020. *MMWR Morbidity and Mortality Weekly Report*. 2020;69.
36. Chen Y, Bai J. Maternal and infant outcomes of full-term pregnancy combined with COVID-2019 in Wuhan, China: Retrospective case series. *Arch Gynecol Obst*. 2020:1-7.
37. Liu W, Wang Q, Zhang Q, et al. Coronavirus disease 2019 (COVID-19) during pregnancy: A case series. 2020.

Citation: Rahat T, Naz F, Saima N. Pregnancy outcomes of pregnant women with confirmed SARS-CoV-2 infection: A review. *J Pregnan Neon Med* 2021;5(4):1-8.

38. Wang X, Zhou Z, Zhang J, et al. A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery. *Clin Infect Dis*. 2020;10.
39. Di Mascio D, Khalil A, Saccone G, et al. Outcome of Coronavirus spectrum infections (SARS, MERS, COVID 1-19) during pregnancy: A systematic review and meta-analysis. *Am J Obst Gynecol. MFM*. 2020:100107.
40. Diriba K, Awulachew E, Getu E. The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal-fetal transmission: A systematic review and meta-analysis. *Eur J Med Res*. 2020;25:1-14.

***Correspondence to**

Dr. Tayyaba Rahat

Department of Statistical Officer

Pakistan Health Research Council

Islamabad

Pakistan

E-mail: tayyabarahat@gmail.com