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Review Article

Clinical features of neonates born to mothers with coronavirus disease-2019: a systematic review of 403 neonates

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ABSTRACT

The COVID-19 pandemic emerged and spread fast affecting countries across the world consequently becoming a public health crisis. The impact of the virus on the health of adults and children has been increasingly understood but its effects on neonates born to infected mothers remain still unclear. This study aimed to throw light on the impact of novel SARS CoV-2 on pregnant patients and to examine maternal and neonatal outcomes along with the analysis of the extent of maternal-foetal transmission. A comprehensive literature search was conducted on PubMed and Google scholar till April 3 2022 using keywords COVID-19, SARS-CoV-2 and pregnancy, neonate, newborn and infant. 8 articles were reviewed, and clinical characteristics of 400 COVID-19-infected pregnant women and 403 neonates born to them were considered. Almost half of the women (56.5%) were asymptomatic. ICU admission was required by 3.75% of mothers and 1.75% mortality was reported. Out of 257 tested neonates, the positivity rate was 4.7%. Most of the neonates were asymptomatic (87.14%) and the neonatal mortality rate was 2.97%. To conclude, current evidence suggests most neonates born to covid infected mothers are not much affected by morbidity or mortality. As samples of breast milk or amniotic fluid were not tested so chances of vertical transmission cannot be ascertained. Nevertheless, considering the positivity rate in neonates as 4.7% we suggest further study in this regard. So, such infants should receive tests for SARS-CoV-2 and appropriate treatment should be initiated when needed.

Keywords: Neonates, Pregnant women, SARS-CoV-2

INTRODUCTION

COVID-19 is an infectious condition caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first reported after an outbreak of pneumonia of unknown aetiology in Wuhan, China in December 2019.[1,2] Since then, SARS-CoV-2 infection has rapidly spread across the globe and has been reported in every country in the world. WHO declared COVID-19 as a pandemic on March 11, 2020, owing to its high rate of transmission among humans.[3] By March 2020, over 317,298 cases have been recorded worldwide across 166 countries, with over 13,642 deaths attributed to the virus.[4]

The main manifestations of COVID-19 include fever and respiratory symptoms; however, the clinical presentations are variable. Infected patients might have gastrointestinal symptoms, anosmia, hyposmia, or dysgeusia or may otherwise be asymptomatic. Thus, it is difficult to control its spread.[5] Approximately 20% of infected patients have severe disease, and the approximate case-fatality rate is 5-6%.[6] Older individuals and those with underlying diseases are at a higher risk for poor outcomes. Pregnant women being one of the most fragile components of society were thought to have adverse effects from this situation although their condition remains largely unclear.

Previously, other members of the coronavirus family were reported to be associated with severe complications during pregnancy. Mainly the high pathogenic variants such as SARS-CoV and the middle east respiratory syndrome (MERS CoV). These outbreaks caused high case mortality rates and severe complications in pregnant women and their foetuses and newborns. SARS CoV-2 being yet another high pathogenic variant thus created a sense of concern.[7]

During the SARS CoV pandemic in 2003, 50% of pregnant women with SARS CoV infection were admitted to the intensive care unit (ICU). Out of these, around 33% required mechanical ventilation and the mortality rate was about 25%. Other complications of this virus included miscarriage, fetal growth restriction, preterm birth and maternal deaths.[8] Limited data is available for MERS infection in pregnant women but still according to a study by Assiri et al, during the time November 2012 and February 2016 in Saudi Arabia all cases of pregnant women with MERS had adverse effects and received intensive care. It was also noted that 40% of cases had maternal mortality and 40% of cases showed perinatal deaths.[9] The influenza pandemic in 1918 also led to higher mortality (37%) among pregnant women as compared to the mortality rate in the overall population (2.6%).[10]

All these points towards the vulnerability of pregnant women towards these infections. The reason for their higher susceptibility could be attributed to various causes. Firstly, pregnant women are particularly sensitive to respiratory pathogens and severe pneumonia, due to physiologic changes. These include immune changes like the physiological transition to a Th2 environment which favours the expression of anti-inflammatory cytokines (IL-4 and IL-10) and other unidentified immune adaptations. Cardiopulmonary changes during pregnancy include physiologic dyspnoea which is caused by increased maternal oxygen demands from heightened metabolism, gestational anaemia, and foetal oxygen consumption. Also, there are alterations in pulmonary volumes mainly due to elevation of the diaphragm, increased oxygen consumption, oedema of respiratory tract mucosa etc.[11] Secondly during the pandemic, hospital visits enhance the chances of infections. On the contrary lack of medical care during pregnancy due to the pandemic situation may further worsen the situation.

Although studies about the effects of COVID-19 on pregnancy are expanding, there are still many unanswered questions. Data regarding COVID-19 and its effects on both mother and foetus or newborn are still scarce, and the potential risk of vertical transmission is a major concern. Thus, it is important to understand the impact of COVID-19 on pregnant women in terms of morbidity, mortality, and perinatal maternal and foetal outcome. This will further help to propose strategies for better management and prevention.

METHODS

Search strategy

A systematic search was performed in pubMed and Google Scholar databases. The following keywords were used in combination for the search- (COVID-19, severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, novel coronavirus, 2019-nCov, Wuhan pneumonia) and (pregnancy, pregnant women, mother, foetus, neonate, newborn, infant) to identify studies that reported neonates born to mothers affected by COVID-19 during pregnancy. The timeline was restricted until 3rd April 2022. No constraints were placed on the year of publication, country of study and participant characteristics to ensure a comprehensive search and identify the maximum number of potential articles.

Study selection

The studies were screened independently by the titles and abstracts for potential relevance. Later on, full-text reviews of the selected articles were conducted. The studies with clinical characteristics, as well as maternal and neonatal outcomes for mothers with confirmed COVID-19, were included. Exclusion criteria were studies where the status of children was not clearly defined, studies that did not evaluate clinical outcomes and studies where mothers were not confirmed to have COVID-19 during pregnancy. Further, the selected articles were analysed and data were extracted.

Data extraction

The selected articles were read in full and critically evaluated. The data extracted from the studies were as follows: name of the first author, date of publication, study period and country; maternal outcomes of confirmed COVID-19 cases was extracted including maternal age, delivery mode, the gestational week at delivery, the diagnostic method for COVD-19 confirmation, the number of confirmed cases by reverse transcription polymerase chain reaction (RT-PCR), specimen collection site for diagnosis, clinical signs and symptoms at presentation, radiological findings, maternal health complications (GDM, PIH etc.) and poor maternal outcomes. Information for neonates includes the number of live births, singleton and twin pregnancies, birth weight, number of male and female neonates, the diagnostic method used to document COVID-19, type of samples used for testing, the number of laboratory tests performed for SARS-CoV-2, and the number of laboratory-confirmed SARS-CoV-2 cases, the incidence of prematurity, the incidence of low birth weight (LBW, <2,500 gm), APGAR score at 1 minute and 5 minute, clinical manifestations (e.g., fever, shortness of breath), neonatal complications, poor neonatal outcome (including NICU admission, mortality), incidences of rooming-in, breastfeeding at the time of discharge, incidences of

breast milk and amniotic fluid tested for covid and incidences of vertical transmission.

RESULTS

Study selection

The search revealed 160 results. The titles and abstracts of all articles were screened and 37 relevant studies were identified for full test review. Of these 8 studies fulfilling the inclusion and exclusion criteria were included in the final systematic review. The basic features of the included studies are summarized in Table 1.

The data includes 400 pregnant women who delivered 405 neonates including 403 live births and 2 stillbirths.

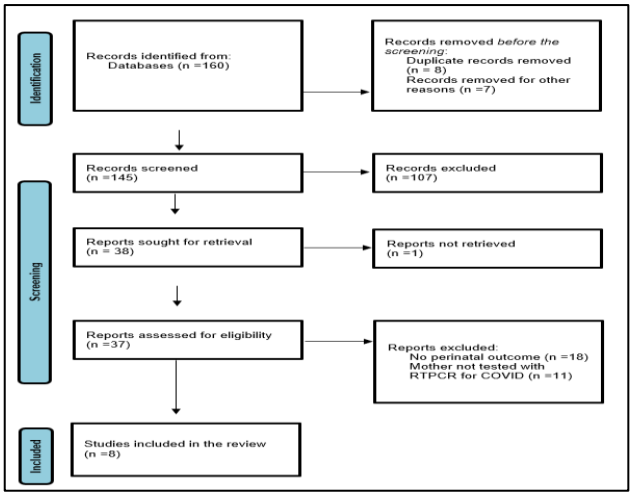

Figure 1: Flow diagram of the study selection process.

Table 1: Characteristics of the included studies.

Authors	Date	Country	Study period	Confirmed pregnant women	No. of neonates	Confirmed neonates
Kumar et al[12]	18-05-2021	India	May 2020 to October 2020	162	165	3
Antouna et al[13]	02-07-2020	UK	February 2020 to April 2020	23	20	0
Miguel et al[14]	07-07-2020	Spain	March 2020 to March 2020	42	42	0
Kumar et al[15]	30-09-2021	India	July 2020 to December 2020	47	47	4
Sadat et al[16]	31-05-2021	Iran	February to November 2020	42	44	1
Lu et al[17]	17-03-2020	Wuhan China	January to February 2020	19	19	0
Ghema et al[18]	17-03-2021	Morocco	January 2020 to December 2020.	30	30	2
El Haik et al[19]	11-11-2020	Dubai, UAE	March 2020 to August 2020	35	36	2

Maternal clinical and laboratory characteristics with pregnancy outcomes

Out of the 400 pregnant women at the time of the study 396 delivered and there were 4 ongoing pregnancies. Maternal age in studies included ranged from 16 years to 42 years. Most of the women underwent caesarean section (65.15%) and only 34.80% had a vaginal delivery. Almost all of the subjects were tested for COVID with RT-PCR (97.75% AND THE rest were clinically diagnosed. The specimen collection for RT-PCR was nasopharyngeal swabs in 86.7% and throat swabs in the rest.

Considering the maternal symptoms, more than half (56.5%) were asymptomatic. Among the 43.5% symptomatic subjects, 51.2% had a cough followed by 29% having a fever. Other symptoms observed were dyspnea in 16.7% of cases, anosmia in 11.11%, body pain in 10.7% of cases and gastrointestinal symptoms including vomiting, diarrhea etc. 7.9%. Grading of symptoms was mentioned in two studies which revealed 58.7% having mild symptoms, 10.3% having moderate symptoms and 31% with severe symptoms. Radiologically confirmed pneumonia or changes in x-ray or CT was mentioned in 3 studies which showed 36% of affected cases.

Taking into account maternal health complications PROM (premature rupture of membrane) was seen in 45 of 358 cases (12.6%), pre-eclampsia in 7 of 131 cases (5.3%), diabetes mellitus in 6 of 89 cases (6.7%), GDM (gestational diabetes mellitus in 24 of 101 cases (23.76%), hypertension/PIH (pregnancy-induced hypertension) in 8 of 124 cases (6.5%), thyroid related issues in 8 of 101 (6.10%), obesity in 5of 42 cases (11.9%). Fetal distress was seen in 20 of 131 cases (15.3%).

With regards to poor maternal outcome, 15 of 400 cases (3.75%) had ICU admission and about 30 of 400 cases (7.5%) needed respiratory assistance. There were 7 cases of mortality out of 400. Reasons for mortality included thrombo-embolism, severe sepsis, diabetic ketoacidosis etc. Only one death was presented as due to COVID complications.

Table 2: Maternal characteristics and pregnancy outcomes.

	Authors	Kumar et al[12]	Antouna et al[13]	Miguel et al[14]	Kumar et al[15]	Sadat et al[16]	Lu et al[17]	Ghema et al[18]	El Haik et al[19]	Total n/N	Percentage
	Number of confirmed pregnant women	162	23	42	47	42	19	30	35	400	
	Mean maternal age (range)	31 y (19 to 41y)	29 y (16-40 y)	33.6±4.9 y	NA	30y	31 y (27–34 y)	NA	32 y (24-42)	(16- 42 y)	
	Vaginal delivery	59	3	22	8	10	1	8	27	138/396	34.80
	Cesarean section	103	16	20	39	32	18	22	8	258/396	65.15
	Diagnostic method	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	10-RT PCR 9-clinically diagnosed	RT-PCR	RT-PCR	391/400	97.75
	Specimen collection site	NP swab	NP swab	NP swab	NP swab	Throat swab	Throat swab	NP swab	NP swab	NP swab-339/391 throat swab-52/391	NP swab-86.7% throat swab-13.3
Maternal symptoms	Symptomatic	37	23	38	6	33	15	15	7	174/396	43.50%
	Grading of symptoms	NA	Mild-13, moderate-2, severe-8	NA	Mild-4, moderate-1, severe-1	NA	NA	NA	NA	Mild-17/29 moderate-3/29 severe-9/29	Mild-58.7% moderate-10.3% severe-31
	Fever	16	17	25	NA	9	11	15	NA	93/318	29
	Cough	NA	12	28	NA	26	5	9	NA	80/156	51.20
	Dyspnea	21	8	10	NA	4	5	NA	NA	48/288	16.70
	Anosmia	NA	NA	3	NA	NA	NA	5	NA	8/72	11.11
	Body pain	NA	NA	6	NA	3	NA	NA	NA	9/84	10.70
	Gastrointestinal symptoms (vomiting, GI bleeding)	NA	4	3	NA	1	2	NA	NA	10/126	7.90
	Asymptomatic	125	0	4	41	9	4	15	28	226/ 400	56.50
	Radiologic confirmed pneumonia/ changes in x-ray or CT	NA	23	NA	NA	NA	2	1	NA	26/72	36.00
Maternal health complications	Obesity	NA	5	NA	NA	NA	0	NA	NA	5/42	11.90
	Diabetes mellitus	NA	4	NA	2	NA	0	NA	NA	6/89	6.70
	GDM	NA	NA	NA	7	NA	0	NA	13	24/101	23.76
	Hypertension/ PIH	NA	1	NA	4	NA	0	NA	3	8/124	6.50
	Pre-eclampsia	NA	2	NA	1	4	0	NA	NA	7/131	5.30
	Thyroid related issues	NA	1	NA	4	3	0	NA	NA	8/131	6.10
	Fetal distress	NA	1	NA	13	6	0	NA	NA	20/131	15.30
	PROM	25	4	NA	0	5	3	6	2	45/358	12.60
Poor maternal outcome	ICU admission	0	4	3	0	6	0	2	0	15/400	3.75
	Respiratory assistance	21	4	NA	NA	4	0	1	NA	30/400	7.50
	Mortality	1	1	1	0	2	0	1	1	7/400	1.75

n- Cases with the characteristics, N- Total available cases except for missing value in the studies considered.

Table 3: Clinical characteristics and outcomes of infants born to mothers with COVID-19.

	Authors	Kumar et al[12]	Antouna e al[13]	Miguel et al[14]	Kumar et al[15]	Sadat et al[16]	Lu et al[17]	Ghema et al[18]	El Haik et al[19]	Total n/N	%
	Number of Live births	165	20	42	47	44	19	30	36	403	_
	Singletons	157	18	42	47	40	19	30	34	387/405	96
	Twins	10	2	0	0	4	0	NA	2	18/405	4
	Mean birth weight (range)	2690 gm (700-4000 gm)	3139±437 gm (2240-4450 gm)	3082±683 gm	2776.7 gm	NA	3293± 425 gm	NA	2985 gm (1500-3845 gm)	700-4450 gm	_
	Male	87	NA	18	22	26	13	20	19	205/383	53.50
	Female	78	NA	24	25	18	6	10	17	178/383	46.50
	Diagnostic method	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR	PCR	RT-PCR	All studies had RT-PCR	_
	Specimen collection site	NP swab	NP swab	NP swab	NP swab	Throat swab	Throa t swab	NP swab	NP swab	NP swab-194/257 Throat swab-63/257	NP swab-75.5 throat swab-24.5
	Tested neonates	32	7	42	47	44	19	30	36	257/403	63.80
	Laboratory confirmed cases of SARS-CoV-2	3	0	0	4	1	0	2	2	12/257	4.70
	Inconclusive positive	NA	NA	3	NA	NA	NA	NA	1	4/257	1.60
	Premature birth	27	7	9	6	18	0	NA	12	79/373	21.20
	LBW	49	NA	0	17	NA	0	0	0	66/339	19.50
	APGAR score at 1 min	NA	8 to 9	9	NA	9 score - 31 children 8 score- 7 children <7 score-5 children	8	NA	8	Majority had APGAR between 8-9 at 1 min and 5 min	–
	APGAR score at 5 min	0-3 score-6 children 4-7 score-8 children >7 score-151 children	9 to 10	10	NA	10 score-42 children 0 score- 2 children	9	NA	9	Majority had APGAR between 8-9 at 1 min and 5 min	–
Neonatal symptoms	Fever	NA	218	0	0	0	0	0	1	1/218	0.45
	Respiratory distress	22	NA	9	2	10	0	3	4	50/383	13
	Shortness of breath	NA	NA	0	0	3	0	3	NA	6/182	3.30
	Cynosis	NA	NA	0	0	1	0	2	NA	3/182	1.60
	Gastrointestinal symptoms (vomiting, GI bleeding)	NA	NA	2	2	0	0	NA	NA	4/251	1.60
	Asymptomatic	NA	NA	NA	44	32	19	27	NA	122/140	87.14
Neonatal complications	IUGR	NA	NA	NA	NA	1	NA	NA	NA	1/403	0.20
	HIE	6	NA	NA	NA	NA	NA	NA	NA	6/165	3.60
	Birth Asphyxia	NA	1	0	2	0	0	6	NA	9/202	4.45
	Meconium-stained amniotic fluid	39	NA	NA	1	1	NA	NA	2	43/292	14.70
	Sepsis	12	NA	NA	NA	NA	NA	NA	NA	12/165	7.30
	Neonatal hyper bilirubinaemia	2	NA	4	9	NA	NA	NA	NA	15/254	5.90
Poor neonatal outcome	ICU admission	38	1	9	0	22	19	NA	9	98/373	26.30
	Assisted ventilation/ respiratory support needed	13	1	10	0	14	0	2	NA	40/367	10.90
	Mortality	5	0	0	0	5	0	2	0	12/403	2.97

Continued.

	Authors	Kumar et al[12]	Antouna e al[13]	Miguel et al[14]	Kumar et al[15]	Sadat et al[16]	Lu et al[17]	Ghema et al[18]	El Haik et al[19]	Total n/N	%
	Rooming in	138	NA	5	0	NA	0	NA	27	170/309	55
	Breast feeding at time of discharge	125	NA	6	36	NA	NA	NA	32	199/290	68.60
	Vertical transmission	Possible transmission in 9.4% cases	No vertical transmission	No vertical transmission	Occurs with low possibility	Cannot be confirmed or denied	No vertical trans-mission	Occurs with low possibility	Cannot be confirmed or denied	Yes- 3 No- 3 Indecisive-2	Yes- 37.5 No- 37.5 Indecisive-25

n- Cases with the characteristics, N- Total available cases except for missing value in the studies considered.

Clinical characteristics and outcomes of neonates born to COVID-19 infected mothers

In total there were 403 neonates out of which 387 were singletons and there were 9 pairs of twins. The birth weight ranged from 700 gm to 4450 gm. There were 205 males and 178 females. The diagnostic method used in all studies was RT-PCR and about 63.8% of neonates were tested. A nasopharyngeal swab was used in 75.55% of cases and the rest were tested by taking a throat swab. Out of tested 257, 12 were laboratory-confirmed cases of covid (4.7%) and 4 cases had inconclusive results. Incidence of prematurity was seen in 79 of 373 cases (21.25) and LBW (low birth weight) was seen in 66 of 339 cases (19.5%). Considering the APGAR score, the majority of the included studies had a score between 8-9 at both 1 minute and 5 minutes.

Taking into consideration neonatal symptoms, 122 of 140 cases (87.14%) were asymptomatic. On detailed analysis, respiratory distress was seen in 50 of 383 cases (13%), followed by shortness of breath in 6 of 182 cases (3.3%), gastrointestinal symptoms including vomiting, GI bleeding etc. in 4 of 251 cases (1.6%) and cyanosis in 3 of 182 cases (1.6%). Fever was seen only in 1 of 218 cases (0.45%).

Considering neonatal complications, meconium-stained amniotic fluid was seen in 43 of 292 cases (14.7%), followed by sepsis in 12 of 165 cases (7.3%), neonatal hyperbilirubinemia in 15 of 294 cases (5.9%), birth asphyxia in 9 of 202 cases (4.45%) and HIE in 6 of 165 cases (3.6%). IUGR was noticed in only 1 of 403 cases (0.20%).

With regards to poor neonatal outcomes, 98 of 373 cases (26.3%) had NICU admission and about 40 of 367 cases (10.9%) needed respiratory assistance. There were 12 cases of mortality out of 403 (2.97%). Reasons for mortality included severe HIE, extreme LBW, prematurity, severe sepsis etc.

More than half of neonates, 170 of 309 (55%), were roomed in with their mothers following appropriate COVID protocols and also 199 of 290 (68.6%) were breastfeeding at the time of discharge. With regards to vertical transmission, out of the 8 studies considered here, 3 concluded that there is a chance of vertical transmission. Out of these, one study showed possible transmission in 9.8% of cases while the other two studies pointed toward only slight chances. Two studies denied any chances of such transmission while two were indecisive and concluded that vertical transmission cannot be confirmed or denied

DISCUSSION

The study results revealed that the most common symptoms among pregnant women were cough, fever and dyspnoea. This is similar to non-pregnant patients according to a study by Ashraf et al.[20] In our study majority of women delivered their baby through caesarean section (65.15%). This was higher than the average cesarean section birth rate in India which was around 17.2% and also the WHO threshold which was 15%.[21] However, in a systematic review of studies all outside India, 108 SARS-CoV-2 positive pregnancies were evaluated and results showed 92% were delivered by cesarean section and the indication was fetal distress.[22] Also, in the present study, the women were discharged from the hospital with only a small portion having poor maternal outcomes (1.75% mortality). This is in contrast to pregnant women affected with SARS and MERS, the other two high pathogenic coronaviruses, which showed a mortality rate as high as 25%.[23]

In a study by Lam et al, the clinical course and results of pregnancy in women with SARS were assessed.[24] It was revealed that even though pregnancy had no influence on clinical symptoms of SARS but complications including sepsis, acute kidney injury, and disseminated intravascular coagulation (DIC) were considerably higher in pregnant women. Also, it was observed that the usage rate of mechanical ventilation and mortality were more common among pregnant women. But present analysis shows that in women with SARS-CoV-2 the maternal complications are not that severe. Similar results were obtained in a study by Mullins et al. also.[25]

Lu et al reviewed 230 children in their study with COVID-19-positive mothers and reported that most of the children had mild disease conditions and all neonates were healthy.[26] We had similar findings with 87.14% asymptomatic neonates and only 2.97% cases of neonatal mortality. Also, the rate of prematurity and LBW is 21.2% and 19.5% respectively. This is within the normal rates in India which are 40% for prematurity and 30% for LBW according to the national neonatal-perinatal

database.[27] Also, the analysis revealed that only a small portion of neonates tested positive for COVID-19 infection (4.7%). Even though neonatal death was noticed in about 12 cases, none of them was covid positive.

The main mode of transmission of this disease is by droplets, contact, aerosol, and faecal-oral route. This is revealed by many studies including one by Zhang et al.[28] Also, other studies revealed that the amniotic fluid, cord blood, neonatal throat swab, and breastmilk samples from neonates born to COVID-19-positive mothers were negative.[29] So, it seems that the possibility of vertical transmission in pregnant women with COVID-19 infection is lower than expected and the chances of a neonate getting infected are more from other modes. Also, only one study reviewed in this paper showed a 9.4% chance of vertical transmission along with two other studies revealing slight chances of vertical transmission. All others studies were either against it or indecisive. Also, these studies did not present data related to the testing of breastmilk samples or amniotic fluid samples so further conclusions cannot be made in this regard. We suggest further research should be undertaken to evaluate the chances of vertical transmission.

Nevertheless, Hantoushzadeh et al reported that among nine pregnant women in their second and third trimesters with positive SARS-CoV-2, seven patients died, one remained critically ill and ventilator-dependent, and one recovered after long-term hospitalization.[30] Their results were significantly different from the results of this study, and it means that long-term follow-up may be necessary for the evaluation of the consequences of SARS-CoV-2.

The current study had certain limitations. All the available studies were in the form of case series or case reports. There were no cohort or retrospective studies in this regard. Also, the included studies had heterogeneity, so some outcomes were missed in some of the studies.

CONCLUSION

In our review of the recent literature, the clinical outcome for mothers infected with COVID-19 and neonates born to them was mostly satisfactory. Also, there was no significant difference in the clinical characteristics of pregnant and non-pregnant COVID-19 patients. On considering the neonatal aspect 4.7% of neonates tested positive for COVID-19 infection in this review. As breast milk or amniotic fluid samples were not tested, chances of vertical transmission cannot be ascertained. Henceforth we suggested further research in this regard. To conclude infants born to infected mothers should receive tests for SARS-CoV-2 and appropriate treatment should be initiated when needed. Also, due consideration should be given regarding treatment to avert the complications associated with the comorbidities.

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REFERENCES

1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020;382:1199-207.
2. Diseases TL. COVID-19, a pandemic or not? Lancet Infect Dis. 2020;20(4):383.
3. WHO Director-General's opening remarks at the media briefing on COVID-19- 11 March 2020. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. Accessed on 6 April 2020.
4. World Health Organization: Coronavirus disease (COVID-2019) situation reports. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports. Accessed on 6 April 2020.
5. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239-42.
6. Li LQ, Huang T, Wang YQ, Wang ZP, Liang Y, Huang TB, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. J Med Virol. 2020;92(6):577-83.
7. 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. J Microbiol Immunol Infect. 2019;52:501-3.
8. Schwartz DA. An analysis of 38 pregnant women with COVID-19, their newborn infants, and maternal-fetal transmission of SARS-CoV-2: maternal coronavirus infections and pregnancy outcomes. Arch Pathol Lab Med. 2020;144(7):799-805.
9. Assiri A, Abedi GR, Al Masri M, Bin Saeed A, Gerber SI, Watson JT. Middle East respiratory syndrome coronavirus infection during pregnancy: a report of 5 cases from Saudi Arabia. Clin Infect Dis. 2016;63(7):951-3.
10. Gottfredsson M. The Spanish flu in Iceland 1918. Lessons in medicine and history. Laeknabladid. 2008;94(11):737-45.

11. Yan J, Guo J, Fan C, Juan J, Yu X, Li J, et al. Coronavirus disease 2019 in pregnant women: a report based on 116 cases. Am J Obstet Gynecol. 2020;223(1):111-e1.
12. Nayak MK, Panda SK, Panda SS, Rath S, Ghosh A, Mohakud NK. Neonatal outcomes of pregnant women with COVID-19 in a developing country setup. Pediatr Neonatol. 2021;62(5):499-505.
13. Antoun L, El Taweel N, Ahmed I, Patni S, Honest H. Maternal COVID-19 infection, clinical characteristics, pregnancy, and neonatal outcome: a prospective cohort study. Eur J Obstet Gynecol Reprod Biol. 2020;252:559-62.
14. Marín Gabriel MA, Cuadrado I, Álvarez Fernández B, González Carrasco E, Alonso Díaz C, Llana Martín I, et al. Multicentre Spanish study found no incidences of viral transmission in infants born to mothers with COVID-19. Acta Paediatr. 2020;109(11):2302-8.
15. Kumar P, Prasad A, Akhtar A, Chaudhary BK, Tiwari LK, Chaudhry N. Vertical transmission and clinical outcome of the neonates born to SARS-CoV-2-positive mothers: a tertiary care hospital-based observational study. BMJ Paediatr Open. 2021;5(1).
16. Hosseini MS, Hosseini A, Ghaffari E, Radfar M, Shirvani F, Tabatabai S, et al. Evaluation of clinical outcomes of neonates born to mothers with coronavirus (COVID-19) in Shahid Beheshti Hospitals. J Educ Health Promoti. 2021;10(1).
17. Liu W, Wang J, Li W, Zhou Z, Liu S, Rong Z. Clinical characteristics of 19 neonates born to mothers with COVID-19. Front Med. 2020;14(2):193-8.
18. Ghema K, Lehlimi M, Toumi H, Badre A, Chemsi M, Habzi A, et al. Outcomes of newborns to mothers with COVID-19. Infect Dis Now. 2021;51(5):435-9.
19. Elhalik M, Dash S, El-Atawi K, Mahfouz R, Ramzy A, Dsouza D, et al. Clinical profile of neonates delivered from mothers with confirmed COVID-19 infection: An experience from a Tertiary Perinatal Care Center in Dubai, UAE. J Pediatr Neonat Care. 2020;10:142-6.
20. Ashraf MA, Shokouhi N, Shirali E, Davari-tanha F, Memar O, Kamalipour A, et al. COVID-19 in Iran, a comprehensive investigation from exposure to treatment outcomes. MedRxiv. 2020.
21. Guilmoto CZ, Dumont A. Trends, regional variations, and socioeconomic disparities in cesarean births in India, 2010-2016. JAMA Network Open. 2019;2(3):e190526.
22. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: a systematic review of 108 pregnancies. Acta Obstet Gynecol Scandi. 2020;99(7):823-9.
23. Schwartz DA, Graham AL. Potential maternal and infant outcomes from coronavirus 2019-nCoV (SARS-CoV-2) infecting pregnant women: lessons from SARS, MERS, and other human coronavirus infections. Viruses. 2020;12(2):194.
24. Lam CM, Wong SF, Leung TN, Chow KM, Yu WC, Wong TY, et al. A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. BJOG: An Int J Obstet Gynaecol. 2004;111(8):771-4.
25. Mullins E, Evans D, Viner RM, O'Brien P, Morris E. Coronavirus in pregnancy and delivery: rapid review. Ultrasound Obstet Gynecol. 2020;55(5):586-92.
26. Lu Q, Shi Y. Coronavirus disease (COVID-19) and neonate: What neonatologist need to know. J Med Virol. 2020;92(6):564-7.
27. Lee AC, Katz J, Blencowe H, Cousens S, Kozuki N, Vogel JP, et al. National and regional estimates of term and preterm babies born small for gestational age in 138 low-income and middle-income countries in 2010. Lancet Glob Health 2013;1:e26e36.
28. Zhang W, Du RH, Li B, Zheng XS, Yang XL, Hu B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg Microb Infect. 2020;9(1):386-9.
29. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, 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(10226):809-15.
30. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, Arian SE, et al. Maternal death due to COVID-19. Am J Obstet Gynecol. 2020;223(1):109-e1.

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