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Assessment of the possibility of vertical transmission of COVID-19: A systematic review and meta-analysis protocol

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Protocol

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Abstract

Background

The novel coronavirus 2019 (COVID-19) outbreak has put a great burden on global health and healthcare systems. One of the vulnerable groups to COVID-19 infection and complications is the pregnant women. There is controversy regarding the possibility of vertical transmission of COVID-19 from mother to infant. The aim of this systematic review and meta-analysis was to assess the possibility of vertical transmission of COVID-19 based on currently published literature including observational studies. All published articles including case reports, case series,

Methods

This study will be conducted on all published observational studies, including cross-sectional studies, cohort, case-control, case reports, and case series, in peer reviewed journals in any language until the end of March 2020. Editorials, commentaries and letter to editors will be excluded from the review. Search will be conducted in international bibliographic databases including PubMed, Embase, and Web of Science based on preferred reporting items for systematic reviews and meta-analysis (PRISMA) checklist. Primary search will be performed in PubMed and Embase using the Coronavirus 2019 and vertical transmission keywords based on medical subject heading (MeSH) terms along with free text searching in combination with Boolean operations. The search strategy will be improved and finalized based on the results of the primary search. The World Health Organization (WHO) and google scholar websites will be searched as grey literature. Articles will be reviewed by two authors independently for the relevance of titles and abstracts. Data extraction of the included articles will be performed by two researchers using the Zotero and review manager (revMan) software. Heterogeneity of the articles will be assessed using DerSimonian & Laird Q test and I 2 statistic. The pooled estimated prevalence of vertical transmission of COVID-19 will be performed using the Metaprop command. Publication bias will be assessed using the Begg's rank correlation and the Egger weighted regression methods.

Discussion

The findings of this systematic review and meta-analysis will help practitioners and health care providers in decision making for the care and management of COVID-19 infected pregnant women.

Systematic review registration

In process

Background

The novel coronavirus 2019 (COVID–19) began circulating in Wuhan, Hubei province, China in December 2019. It is a highly contagious disease, and can wildly and rapidly spread by respiratory droplets of infected individuals (1). The ongoing outbreak has been declared by the World Health Organization

(WHO) as a global public health emergency. On March 8, 2020 WHO announced that 100 countries have reported COVID19 cases and the number of positive cases passed 100,000 cases worldwide and on March 11, 2020 WHO made the declared that COVID–19 can be characterized as a pandemic (2).

Based on the findings of one of the first published studies about COVID–19, the common symptoms at onset of illness included fever, cough, and myalgia or fatigue, while less common symptoms were sputum production, headache, hemoptysis, and diarrhea (1). However the symptoms may be more sever in older people, the immunosuppressed and some chronic diseases, including diabetes, cancer and lung dysfunction (3).

Since pregnancy is an immunosuppressive condition, pregnant women are at high risk of developing viral infections including COVID–19 (4). Evidence indicate that coronavirus family are responsible for poor outcomes in pregnant women and their neonates (5–7). Adverse outcomes in pregnancy may include miscarriage, fetal growth restriction, preterm labor, and maternal mortality (3, 8). Alfaraj et al (2019) estimated the incidence of neonatal adverse outcomes to be near 91%. The adverse effects included admission to the intensive care unit, prematurity and neonatal mortality (7).

Regarding the high potential of neonatal adverse outcomes, the evidence on vertical transmission of COVID–19 during pregnancy and delivery are very important. However, there is no confirmed evidence for the vertical transmission of COVID–19 during pregnancy and labor in current literature (9). Chen et al (2020) evaluated the clinical records of 9 pregnant women with COVID–19 infection in Zhongnan Hospital of Wuhan University, Wuhan, China. They reported that Amniotic fluid, cord blood, neonatal throat swab, and breastmilk samples from six patients were tested, and all samples tested negative for the COVID–19 (10). Li et al (2020) published a case repot about a woman with COVID–19 infection in her 35th weeks of gestation who delivered an infant via cesarean section. The infant was tested negative for COVID–19. They suggested that vertical transmission is unlikely for this virus (11). Wang et al (2020) reported a pregnant case of positive COVID–19 infection who gave birth to an infant who was tested negative for SARS Cov 2 based on reverse transcription polymerase chain reaction (RT-PCR) (3). On the other hand, some studies have debated no vertical transmission of COVID–19. A narrative review study pointed out due to lack of adequate data on COVID–19 during pregnancy, both the mother and the fetus should be followed up extensively (9). Favre et al (2020) insisted on the current lack of data on the consequences of COVID–19, and recommended extended follow-up for infected pregnant women and their fetuses (8).

However, confirmed evidence on the COVID–19 vertical transmission is very crucial and essential in decision-making for the management of pregnant women with COVID–19 infection. Therefore, this systematic review and met analysis protocol was designed to assess the possibility of vertical transmission of COVID–19.

Methods

Study type

All observational studies, including cross-sectional studies, cohort, case-control, case reports, and case series that were published in peer reviewed journals until the end of March 2020 will be reviewed. Editorials, commentaries and letter to editors will be excluded from the review. Articles in any language will be included.

Type of participants

The inclusion criteria for the studies include:

- Human studies
- Studies that include adult women over the age of 18 years old
- Women should have given birth to live child in the past 3 months
- Women should be tested positive for COVID–19

Type of exposure

The exposure in the studies will be infection with SARS-COV2 virus documented by positive COVID–19 RT-PCR (12). The sensitivity for RT-PCR in detecting COVID–19 infection was previously reported to be range between 95% and 100% (13, 14). All subjects that have at least two positive RT-PCR results for COVID–19 will be considered as COVID–19 infected. This diagnosis implies for both mothers and newborn infants.

The RT-PCR is not performed routinely for all pregnant mothers, and only those who present clinical signs and symptoms that make them suspicious to COVID–19 infection and have positive radiological findings for COVID–19 infection will be tested using RT PCR.

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Primary objective

To assess the possibility of vertical transmission of SARS-COV2 virus through mother to child.

Secondary objective

- To assess the association between time of infection (based on gestational age) and vertical transmission of SARS-COV 2 to new born. In case sufficient case reports are present for the assessment, the relationship between gestational age at time of test positivity and vertical transmission will be analyzed.
- To assess the association between mode of delivery (normal vaginal delivery or caesarean section) and SARS_COV 2 vertical transmission.
- To assess the association between breastfeeding and SARS-COV 2 transmission

The search method used for the study

The international bibliographic databases including PubMed, Embase, and Web of Science as well as Google scholar will be searched to identify eligible studies. The search strategy will be designed based on preferred reporting items for systematic reviews and meta-analysis (PRISMA) checklist. A PRISMA-P checklist for this protocol is shown in Additional File 1. The search terms include the following keywords based on medical subject heading (MeSH) terms along with free text searching in combination with Boolean operations (AND and OR) (Table 1).

Table 1. The keyword search for the study

Keyword	Search terms
Coronavirus 2019	covid 19
	covid 19 infection
	covid 19 outbreak
	covid 19 pneumonia
	severe acute respiratory syndrome coronavirus 2
	severe acute respiratory syndrome coronavirus infection
	severe acute respiratory syndrome coronavirus sars cov
	severe acute respiratory syndrome coronaviruses
	severe acute respiratory syndrome sars coronavirus
Vertical transmission	vertical transmission
	vertical transmission rate
	vertical transmission rates
	vertical transmission risk
	vertical transmission risks
	vertical transmission route
	vertical transmission studies
	vertical transmission study
	vertical transmissions
	vertical transovarial transmission
	vertical transplacental transmission

The primary search will be conducted on PubMed and Embase and the search will be improved based on the search results. The final keywords and search terms will be used in the search in other databases.

Searching other resources

The World Health Organization (WHO) website (www.who.int) will be searched for the keywords. Furthermore, the reference list of the identified studies will also be checked manually for similar studies and these studies will also be included in the review.

Data collection

Study selection

The Zotero reference manager (https://www.zotero.org/) will be used to merge the identified studies and remove duplicate publications as well as screening the titles and abstracts. The identified studies will be assessed by two authors independently based on title and abstracts. The articles that meet the inclusion criteria will be selected for the review. In case of discrepancies, a third reviewer will be asked to judge whether to include or exclude the study. In the next step the full text of the studies will be reviewed by the authors.

Data extraction

All authors will contribute in data extraction from identified studies. Extracted data will be summarized in a checklist which is designed by the authors of this review. Based on this checklist, the following data will be extracted:

- General characteristics of the study (author names, title, publication date, and review date)
- Type of the study
- Sample size
- Study subject characteristics (demographic characteristics, predisposing conditions, gestational age)
- Outcome measures and analyses (diagnostic test used, number of positive samples)
- Study findings

Quality assessment of the studies

The quality of the identified studies will be assessed by two authors independently. As the studies in this review include cross-sectional studies, cohort, case-control, case reports, and case series, the quality assessment will be performed using the risk of bias assessment software by Cochrane Collaboration, review manager (revMAn).

Data analysis

Heterogeneity among studies will be assessed by DerSimonian & Laird Q test and I^2 statistic which is the proportion of total variation due to between-studies heterogeneity. To calculate the pooled prevalence estimate of vertical transmission and corresponding 95% confidence intervals (CIs), we will use the Metaprop (15). a Stata-based command developed for binominal data.

To combine Risk ratio in cohort studies and odds ratio in case control studies for assessing the association of gestational age for acquiring the infected in mothers, delivery mode and breastfeeding with vertical transmission of COVID–19, we will apply random effects model in case of heterogeneity among studies. Otherwise, fixed effects model will be used. The Begg's rank correlation and the Egger weighted regression methods will be used to statistically assess the publication bias. We will also visually assess the publication bias using funnel plot. P-value<0.05 will be considered statistically significant in all tests. Stata version 12 (Stata Corp, College Station, Texas) will be used for all statistical analyses.

Discussion

This systematic review will assess the possibility of vertical transmission of SARS-COV 2 virus from infected mother to child through the transuteral, vaginal and breast milk routs. The findings of this review will also aim to identify the effect of the duration of COVID–19 infection based on gestational age and the possibility of vertical transmission of SARS-COV 2 to infant. The findings of this study will help healthcare providers and physicians to identify the risk of vertical transmission in pregnant women infected with COVID–19.

Declarations

Ethics approval and consent to participate

This study was approved and sponsored by the Research Council of Gonabad University of Medical Sciences (Grant number: A-10-1296-6).

Consent for publication

The Research Council of Gonabad University of Medical Sciences is aware of the proposal of this study and has provided written consent for publication of the protocol and the results.

Availability of data and materials

The search strategy and checklists and the list of the retrieved articles will be provided online. The full text of the articles will be provided based on the availability of the full text (only open access articles will be provided online).

Competing interests

None to declare

Funding

This study was sponsored by the research council of Gonabad University of Medical Sciences (Grant number: A-10-1296-6).subscribing journals and data bases to access the full text of articles.

Authors' contributions

All authors contributed to the development of this protocol. All authors read and approved the final manuscript. SD contributed in study design, and commented on database search strategy. TFN contributed in study design and commented on the protocol. HRT contributed in data collection and data analysis techniques. NB contributed in manuscript writing, search strategy and study correspondence.

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Abbreviations

Covid-19: Coronavirus 2019

WHO: World Health Organization

RT-PCR: Reverse transcription polymerase chain reaction

SARS-COV 2: Severe acute respiratory syndrome due to coronavirus 2

PRISMA: Preferred reporting items for systematic reviews and meta-analysis

MeSH: Medical subject heading

RevMan: Review manager

CI: Confidence interval

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B.Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5. .
2. World Health Organization. Rolling updates on coronavirus disease (COVID-19). Avalable from : https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen. [site accesse: March 11, 2020].
3. Wang X, Zhou Z, Zhang J, Zhu F, Tang Y, Shen X. A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery. Clin Infect Dis. 2020 Feb 28. pii: ciaa200. doi: 10.1093/cid/ciaa200. .

4. Meijer WJ, van Noortwijk AG, Bruinse HW, Wensing AM. Influenza virus infection in pregnancy: a review. Acta Obstet Gynecol Scand. 2015 Aug;94(8):797-819. doi: 10.1111/aogs.12680. .
5. Maxwell C, McGeer A, Tai KFY, Sermer M. No. 225-Management Guidelines for Obstetric Patients and Neonates Born to Mothers With Suspected or Probable Severe Acute Respiratory Syndrome (SARS). J Obstet Gynaecol Can. 2017 Aug;39(8):e130-e137. doi: 10.1016/j.jogc.2017.04.024.
6. Alserehi H, Wali G, Alshukairi A, Alraddadi B. Impact of Middle East Respiratory Syndrome coronavirus (MERS-CoV) on pregnancy and perinatal outcome. BMC Infect Dis. 2016 Mar 2;16:105. doi: 10.1186/s12879-016-1437-y.
7. Alfaraj SH, Al-Tawfiq JA, Memish ZA. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection during pregnancy: Report of two cases & review of the literature. J Microbiol Immunol Infect. 2019 Jun;52(3):501-503. doi: 10.1016/j.jmii.2018.04.005. Epub 2018 Jun 2.
8. Favre G, Pomar L, Musso D, Baud D. 2019-nCoV epidemic: what about pregnancies? Lancet. 2020 Feb 22;395(10224):e40. doi: 10.1016/S0140-6736(20)30311-1. .
9. Mardani M, Pourkaveh B . A Controversial Debate: Vertical Transmission of COVID-19 in pregnancy. Arch Clin Infect Dis. 2020 February; 15(1):e102286. doi: 10.5812/archcid.102286.
10. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, Li J, Zhao D, Xu D, Gong Q, Liao J, Yang H, Hou W, Zhang Y. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet. 2020 Mar 7;395(10226):809-815. doi: 10.1016/S0140-6736(20)30360-3.
11. Li Y, Zhao R, Zheng S, Chen X, Wang J, Sheng X, Zhou J, Cai H, Fang Q, Yu F, Fan J, Xu K, Chen Y, Sheng J. Lack of Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, China. Emerg Infect Dis. 2020 Jun 17;26(6). doi: 10.3201/eid2606.200287.
12. Chu DK, Pan Y, Cheng S, Hui KP, Krishnan P, Liu Y, Ng DY, Wan CK, Yang P, Wang Q, Peiris M. Molecular diagnosis of a novel coronavirus (2019-nCoV) causing an outbreak of pneumonia. Clinical chemistry. 2020 Jan 31. doi: 10.1093/clinchem/hvaa029.
13. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, Bleicker T, Brünink S, Schneider J, Schmidt ML, Mulders DG. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Eurosurveillance. 2020 Jan 23;25(3).
14. Liu YS, Zhang D, Tang S, Chen H, Chen L, He X, Tong M, Liu M, Lin Y, Zhu B, Su X. The Epidemiological and Clinical Characteristics of 2019 Novel Coronavirus Infection in Changsha, China. China (2/10/2020). 2020 Feb 10.
15. Nyaga, V. N., Arbyn, M. & Aerts, M. Metaprop: a Stata command to perform meta-analysis of binomial data. Arch Public Health.2014 Nov 10;72(1):39. doi: 10.1186/2049-3258-72-39.

Supplementary Files

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