Review Article

Manuscript title: A review of COVID-19's impact on pregnancy

Acknowledgments (if any): None

Funding information (if any): None

Ethics approval statement: Not required

A review of COVID-19's impact on pregnancy

Abstract

Background and Aim: Since the new Coronavirus started spreading in December 2019, the virus has had enormous consequences on people's health and way of life in every nation on earth has been touched. A pregnant lady is more susceptible to infection than a healthy one because she is immunocompromised throughout pregnancy. The purpose of this present paper is to review relevant published literature to determine the impact of covid-19 on pregnant women.

Method: In this narrative review all publications published in the databases PubMed, Scopus, Embase, Science Direct, and Web of Science from December 2019 to August 2022 by conducting a complete search with the required keywords, including covid-19, coronavirus illness 2019, SARS-CoV-2, and miscarriage, abortion, or pregnancy outcomes. After applying inclusion/exclusion criteria and following the PRISMA guidelines, total 25 papers were identified and thoroughly examined. There are few accessible data on the effects of covid-19 on pregnancy. Every day, new information emerges on the management of pregnancy during the covid-19 era.

Results: Pregnant women with covid-19 experienced fever, cough, dyspnea, myalgia, and exhaustion in the early stages, while headache, chest discomfort, and diarrhea were less common. Results shows that covid-19 can cause fetal distress, miscarriage, respiratory distress, and preterm delivery in pregnant women, according to the reviewed literature.

Conclusion: There is a higher risk in women who have a positive SARS-CoV-2 test result. covid-19 infection during pregnancy may cause pregnancy problems such as preterm birth, fetal distress and miscarriages. Due to the absence of adequate data regarding the effects of covid-19

on pregnancy, it is required to monitor suspected pregnant women to prevent miscarriage, fetal distress, respiratory distress and preterm delivery.

Keywords: Covid-19, pregnancy, miscarriages,

1. Introduction:

In December 2019, an unidentified pneumonia outbreak was reported in Wuhan, Hubei Province, China [1]. The World Health Organization (WHO) has officially declared the disease 2019 coronavirus disease (covid-19) as a pandemic on March 12, 2020, due to the global spread of SARS-CoV-2 and thousands of deaths caused by coronavirus illness [1].

Those who have COVID-19 typically experience viral pneumonia, with the most common symptoms being fever, cough, sore throat, myalgia, and weariness [2]. Covid-19 has afflicted over 170 million individuals globally, resulting in over 3.5 million deaths by the end of May 2021[3]. Coronaviruses are enclosed, non-segmented, single-stranded ribonucleic acid (RNA) viruses that cause illnesses ranging from simple colds to serious prenatal disorders. SARS-CoV, which causes severe acute respiratory syndrome (SARS), and MERS-CoV, which causes Middle East respiratory syndrome (MERS), are the two most well-known fetal viruses [4]. Several covid-19 vaccinations were introduced to prevent the spread of covid-19 during the pandemic, and treatment regimens were quickly established with the introduction of new pharmaceuticals, including anti-SARS-CoV-2 monoclonal antibodies and antiviral treatments [3].

Pregnant women may be highly susceptible to experiencing more severe symptoms due to the significant impact of physiological changes in the immune system, respiratory system, cardiovascular system, and coagulation changes during pregnancy [5]. These could accelerate or

halt the progression of covid-19 disease [5]. SARS-CoV-2 primarily spreads through the respiratory route, suspended on droplets or, less frequently aerosols [6]. For that reason, pregnant women may be more likely to experience more severe symptoms after contracting respiratory viruses [7]. MERS-CoV and SARS-CoV have also been linked to more serious pregnancy problems and higher case fatality rates [8]. However, there are few reports on the effect of covid-19 on pregnancy [9].

Pregnancy is thought to be a risk factor for severe sickness from covid-19, which is caused by SARS-CoV-2 infection. Furthermore, pregnant women with covid-19 may be at a greater risk of other negative outcomes, such as preterm delivery and abortion [9]. An increasing body of evidence suggest linking of COVID-19 to abortion [10]. The chance of developing a serious covid-19 related illness is increased in pregnant women. Compared to non-pregnant women, pregnant women are more likely to be referred to an intensive care unit (ICU) [11]. By conducting a systematic review that evaluated the impact of covid-19 on pregnancy, this paper is aimed to review potential maternal symptoms of covid-19 including the occurrence of miscarriages based on the findings of human studies during the pregnancy.

1.1 Impact of Covid-19 on pregnancy: Pregnancy alters the immune system, and the reaction to viral infections in general might result in more severe symptoms, especially if the virus is acquired in the third trimester of pregnancy, as is the case with covid-19 [12]. However, those who are pregnant or have recently given birth run a higher chance of developing a serious illness from covid-19. If the pregnant women have a serious sickness, they may need to be hospitalized and get critical care. Additionally, covid-19 positive pregnant women are more likely to give birth before the 37th week of pregnancy (premature birth). Furthermore, covid-19 positive pregnant women may be more likely to experience issues including stillbirth and miscarriage

[13]. Some of the main issues include whether infected pregnant women have worse outcomes in terms of morbidity and/or death compared to non-pregnant women of the same ages, whether infected pregnant women have more severe disease, or whether they have worse maternal-fetal outcomes compared with uninfected pregnant women of comparable ages [14].

Compared to their women who are not pregnant, pregnant women with COVID-19 may be at higher risk for more serious sickness, according to the data that is currently available. However, Table-1 shows some maternal symptoms which was caused in pregnant women during their gestational weeks. There hasn't been any evidence of a rise in mortality rates. Pregnant women with comorbidities like obesity and gestational diabetes may be at an even higher risk for serious illnesses than the general population with comparable comorbidities [15]. It's significant that analyses performed thus far have been constrained by a significant quantity of missing data and the fact that many publications lack an adequate comparative control group that isn't pregnant [15].

1.2 Covid-19 infection and miscarriages: A miscarriage occurs when a pregnancy ends on its own before the 20th week. The majority of miscarriages happen prior to the 12th week of pregnancy [16]. Research has revealed that the covid-19 virus adheres to a number of bodily organs. In early placental tissue, SARS-Cov-ACE2 protein is expressed, which makes the early pregnancy vulnerable to the effects of covid-infection [17].

During the periconceptional period, miscarriage and unsuccessful embryo implantation are more likely in women with covid-19. Unbalanced immune hormones causes "cytokine storm" results a hypercoagulable state that is harmful to normal fetal development [18]. In fact, anomalies in the

mother's immune system during the peri-implantation and early stages of pregnancy have been associated to repeated implantation loss and miscarriage [19].

2. Materials and Methods

A systematic literature review method was used to achieve the objectives of this study. We followed to the Preferred Reporting Items for Systematic Reviews (PRISMA) 2020 criteria [20], which emphasize a number of factors to assure transparent, reliable, and scientifically adequate systematic reviews.

2.1 Information sources and search strategy: This review intended to comprehensively analyze the risk of covid-19 in pregnancy. This review period began in June 2022, with additional updates in July and August. The popular databases like databases PubMed, Scopus, Embase, Science Direct, and Web of Science during December 2019 to August 2022 were investigated using the following search terms: covid-19, coronavirus illness 2019, SARS-CoV-2, miscarriage, abortion, or pregnancy outcomes. The search was limited to english-language academic publications. EndNote X9 (Clarivate Analytics US LLC, Philadelphia, USA) was also utilized as reference management software. Additionally, a manual search of the references included in the chosen papers and reviews was done.

2.1.1 Inclusion and Exclusion Criteria: Specific inclusion and exclusion criteria were defined in order to select and include only relevant studies for our study topic identified from databases.

Inclusion Criteria

a) Journal articles.

b) The study is written in English.

c) The study is peer-reviewed.

d) The study is not listed in another database.

e) The full text of the study is available.

f) The study includes reviews, research, or descriptions of the impact of covid-19 in pregnancy

Exclusion Criteria

a) Proceedings of congresses, conference papers, books, book chapters, and other nonpeer-reviewed publications.

b) The study is written in other languages or not written in English.

c) The study is not peer-reviewed.

d) The study is listed in another database.

e) The study is not related to the impact of covid-19 on pregnancy.

f) The full text of the study is not available.

2.2 Data extraction and quality assessment: Data were retrieved from the publications that were ultimately chosen. We reviewed all papers that reported on the effect of covid-19 on pregnancy. Data such as information about the place of origin, the number of pregnant patients with confirmed covid-19, clinical symptoms, laboratory results, outcomes, miscarriages rates and other related key findings were extracted. Two authors independently retrieved data from all included studies and developed a data extraction procedure on an excel sheet. Authors disagreements were resolved through discussions.

2.3 Ethical endorsement: Since the data included in this particular systematic review was obtained from previously published studies in the literature, ethical approval is not applicable.

2.4 Funding: This review was neither sponsored nor funded.

Results

The information's that were collected from the journals were summarized in table 1 & 2. This search approach produced an initial total of 80 potentially applicable publications, of which 50 were excluded by title and abstract evaluation, as shown in Fig 1. After applying the inclusion/exclusion criteria to the full-text papers, twenty-five (25) publications were selected. The included articles that were published because of the following reasons: Maternal symptoms and complications due to Covid-19 infection in pregnancy; Miscarriages in different gestational weeks, Miscarriages occurred in different countries pregnant women due to covid-19. Covid-19 was detected by RT-PCR test in pregnant women. All included studies were completely about pregnant patients in which miscarriages or abortion were mentioned as one of the complications of pregnancy.

The most prevalent symptoms among pregnant patients were fever and cough, while they often had other symptoms like dyspnea, chest pain, myalgia, diarrhea, and fatigue as shown in Table-1. Several studies found that, some pregnant women did not show any kind of symptoms that means they were asymptomatic[21-24]. Noelle et al.[22] studied on 43 pregnant women and among them 48% were suffering from fever and 65% were suffering from cough. This study also reported other maternal symptoms that were occurred due to covid-19 such as dyspnea, chest pain, myalgia, diarrhea and the percentages were 24%, 17%, 38% and 28% respectively. Ferrazzi et al. [25] also reported that they found fever, cough, dyspnea and myalgia as covid-19 complications in pregnant women.

For the first time, Chen et al.,[26] described miscarriage as a potential pregnancy outcome in pregnant women with covid-19. This study was conducted on total 118 pregnant women. Three spontaneous abortions, two ectopic pregnancies, and four induced abortions occurred in this group of patients in Wuhan City, China. It was impossible to quantify the miscarriage rate without knowing the number of covid-19 cases per trimester, hence the authors omitted this information. All of the losses in pregnant women with non-severe covid-19 occurred in the early half of the pregnancy. As in Table-2 indicated, the number of miscarriages that were found in different countries in pregnant women in various gestational weeks. One study was done in Italy where the number of pregnant women were 225 and among them 12 women had experienced miscarriages during the 12-13 gestational weeks approximately [27]. A study was reported by Sahin et al.,[28] in Turkey where they studied 553 pregnant women and they found 12 miscarriages in different gestational weeks. In China, 116 cases were reported and pneumonia were found in 51 cases and 1 missed abortion were occurred in the first trimester [29]. However, in other countries like Kuwait, Malaysia, France and Switzerland, pregnant women also experienced miscarriages in their second and third trimester due to covid-19 (Table-2).

3. Discussion:

Pregnancy is a distinct immunological state in which complex physiological processes occur at the maternal-fetal contact. When this delicate equilibrium is troubled by infections, the system might collapse. That's why during this fast evolving coronavirus epidemic, pregnant women's health must be taken into consideration. It is crucial to provide pregnant women the key interventions they need. Few data exist about the immunological response to SARS-CoV-2 infection during pregnancy, highlighting the significance of this review. Regarding the specific immunological features of covid-19 in pregnant women, there is still no solid publication based

on currently available scientific information. Regardless of study design, this review chose all studies pertaining to covid-19 and pregnancy. All included papers are narrative reviews devoid of methodological and technical information regarding the selection of data.

According to the World Health Organization (WHO), there is no discernible difference between non-pregnant and pregnant women of reproductive age in the chance of experiencing clinical symptoms [30]. Although some patients may be asymptomatic, most patients often appear with moderate infection-related symptoms such fever, cough, lethargy, and shortness of breath [30]. Liu et al. conducted a retrospective review and compared fifty-nine individuals, including both pregnant and non-pregnant adults. The development of the clinical symptoms of SARS-CoV-2 was not significantly different between the various groups, according to this review [31].

But also there are some case reports and case studies from the pandemic have shown that pregnant women who tested positive for SARS-CoV-2 have a higher risk of abortion, fetal distress and preterm delivery. The majority of these research discussed how the virus affects the pregnant women and causes serious impact which slows down fetal growth and may cause abortion. A case report done by Fang et al.,[32] in 2020 in USA resulted one miscarriages of a pregnant women with covid-19 [32]. In Malaysia another case report was done by Wong, T.C. and miscarriages occurred in two of the cases during the first trimester of pregnancy where both pregnant women were infected by SARS-Cov 2 [33]. A study was done in 727 women made their first prenatal visit between June 29 and September 30, 2019, and 67 of them (9.2%) experienced a miscarriage. 542 women had their first prenatal appointment during the same time period in 2020, and 64 (11.8%) of them miscarried before 12 weeks' gestation. Prior to admission, SARS-CoV-2 was tested on all women who miscarried in 2020, and 4.7 percent (3/64) of the tests were positive [34].

According to the results of the current study, further investigation into the potential for vertical transmission of covid-19 from mother to fetus is considered essential. Results from studies indicate that infected or suspected mothers should be closely monitored before and after giving birth. The recommendation is for women who believe they may have been exposed to covid-19 to hold off on nursing until they have received formal clearance [35]. A study done by Chen et al., 2020 found that COVID-19 can induce fetal discomfort in pregnant women but does not infect infants [36]. A similar study was done by Msq et al., [37] in China. They have found that there is no evidence of intrauterine covid-19 infection caused by vertical transfer to the fetus [37]. According to a study in Iran, women who are suspected or know for sure that they have covid-19 should not breastfeed their babies for at least two weeks after they are born. If covid-19 infection is confirmed while a woman is pregnant, both the mother and the fetus should be closely watched [38]. Another study in China suggest that there is no proof that covid-19 causes fetal distress or infections in babies. covid-19 can be mild or severe during pregnancy, and it can cause the baby to come early which may sometimes cause critical issues in newborn [39]. According to a 2020 Chinese study, infection with COVID-19 during pregnancy might result in adverse consequences such miscarriage, fetal development impairment, early delivery, and even maternal fatality [40]. But another study shows that there is no indication that pregnant women can transmit Covid-19 vertically [41].

A research was done in the United States in 2020, some newborns showed signs of fetal distress and preterm delivery. After birth, SARS-CoV-2 testing was negative for all children born to pregnant women with covid-19 [42]. According to a study done in China in 2020, prenatal covid-19 infection may have detrimental effects on newborns. These effects may include fetal discomfort, early labor, respiratory distress, thrombocytopenia followed by impaired liver

function, and even death [43]. As per some studies neither the mother nor the infant have shown any signs of having contracted SARSCoV-2 during pregnancy [44-46]. According to research, being affected with SARS during the perinatal period is associated with a high prevalence of potentially harmful maternal and neonatal side effects, including disseminated intravascular coagulopathy, spontaneous abortion preterm birth, intrauterine growth retardation, neonatal, intubation and the need for the newborn to be admitted to a neonatal intensive care unit (ICU) and organ failure [47]. Because of physiological, immune, and anatomical changes, pregnant women are more susceptible to respiratory diseases. Some studies point to a significant shift to a T-helper lymphocyte type 2 (Th2) immune response during pregnancy as a potential contributor to the severity of Covid-19 cases [47]. Furthermore, the cytokine storm that occurs in severe cases causes an increased inflammatory state, which may worsen the clinical prognosis in this population. As a result, pregnant women may be a vulnerable group to Covid-19 infection, owing to an immune imbalance at the maternal-fetal interface [48]. Therefore, there is a hypothesis that the hormone level and immunological condition differ at various phases of pregnancy. In early pregnancy, for instance, the author suggests that the immune balance is still unstable, which can lead to a severe immune system disorder and internal environment imbalance in the event of a viral infection, resulting in abortion or abnormal fetal growth, similar to that observed in other respiratory infections. According to this author, as the pregnancy proceeds, the mother is constantly changing this immunological balance, with presumably decreasing severity [49]. Recent research indicates that in severe cases of covid-19 infection, a cytokine-storm occurs, which is characterized by increased concentrations of plasma mediators such as IL-2, IL-7, IL-10, granulocyte-colony stimulating factor, and tumor necrosis factor alpha, most of which are associated with an inflammatory response [50]. Dashraath et al. hypothesized

that the physiological change to a Th2-anti-inflammatory environment during pregnancy and other undisclosed immune adaptations may function as the major immune response to SARS-CoV-2, resulting in a less severe manifestation of covid-19 in the pregnant women. These results are consistent with the scant literature that asserts that, despite being put in high-risk groups mostly due to preventive measures, cases of covid-19 among pregnant women may be more severe or have worse clinical outcomes than those in the general population. Due to the lack of relevant data about the effects of covid-19 on the immune response during pregnancy, a number of issues remain unresolved until the publication of adequate, case-based, evidence-based studies [51].

According to Li et al., 2020 [44] four of seven pregnant women with Covid-19 who presented in the first trimester experienced spontaneous miscarriages, while two had voluntary terminations. The sole newborn survivor was born at full term, and no birth defects were noted [52]. Yan et al. hypothesized that pregnant women with covid-19 had a higher rate of maternal mortality, intubation, and ICU hospitalization than non-pregnant women with Covid-19, but that the virus was not transmitted to the newborn. In addition, more problems such as miscarriage, premature birth, and small-for-gestational-age newborns have been documented. One study, however, found no increase in the risk of spontaneous abortion or spontaneous preterm birth among pregnant Covid-19 carriers. Numerous systemic infections and inflammatory conditions are related with premature birth, and preterm births have been observed in women infected with covid-19. However, the majority were recorded in China, which has a distinct medical system, and it is still unclear whether SARS-CoV-2 caused these premature births or whether they were iatrogenic as a result of maternal distress or other indicators [44]. In table 2, this review study

attempted to compile data on the number of miscarriages caused by covid-19 in pregnant women from various countries.

There are some limitations to our review. According to our inclusion criteria, even some small case series were included, which may have resulted in certain clinical aspects and outcomes being amplified. The included studies differed significantly in terms of study design (case series, cohorts, or universal screening), clinical treatment, and outcome reporting. This may result in significant bias in the ratio of features identified and limits the comparison between research. However, the lack of information about the epidemic among pregnant women is one of the study's inadequacies. This may be connected to pregnant mother's anxiety about receiving routine prenatal treatment in clinics during the covid-19 epidemic. Also there is little information available from the pregnant women who had abortions during the pandemic. Future work must clearly detail the actual nature of clinical characteristics, patient care, and adverse outcomes for clarity. Maternal mortality may occur in severe covid-19 instances. Given that the full outcome data for the majority of the critical cases were not confirmed, the true impact of SARS-CoV-2 infection on maternal mortality in comparison to the general population cannot be reliably ascertained at this time. Further investigation is therefore required to determine the causes of pregnancy loss in covid-19 infected mothers and whether there is any evidence that viral transmission to the fetus causes miscarriage due to the virus's direct impact on the fetal organs.

Conclusion

This review compiled previously published case series and investigations concerning pregnant women infected with SARSCoV-2 and studied the characteristics of pregnant women with covid-19 infection. According to the case reports and case studies that have been reported throughout the pandemic, fever, cough, dyspnea, myalgia, and fatigue were the first signs of

covid-19 in patients and maternal infection due to covid-19 can cause major complications such as miscarriages, premature labor, and fetal distress. Covid-19 has a great impact on pregnant women but some clinical findings were not significantly different from other patients. covid-19 has been the subject of numerous investigations. However, there are only a few case studies that look at how it affects women during pregnancy. There is insufficient evidence to establish a definitive conclusion. As the covid-19 virus spreads throughout the world, additional research on pregnant patients is required.

6. References

1. **Ciotti M, Ciccozzi M, Terrinoni A, Jiang W-C, Wang C-B, Bernardini SJCricls. The COVID-19 pandemic. 2020;57(6):365-88.**

2. **Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. 2020;395(10223):514-23.**

3. **Cavalcante MB, Cavalcante CTdMB, Cavalcante ANM, Sarno M, Barini R, Kwak-Kim JJJoRI. COVID-19 and miscarriage: From immunopathological mechanisms to actual clinical evidence. 2021;148:103382.**

4. **Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. 2020;395(10224):565-74.**

5. **Wastnedge EA, Reynolds RM, Van Boeckel SR, Stock SJ, Denison FC, Maybin JA, et al. Pregnancy and COVID-19. 2021;101(1):303-18.**

6. Meyerowitz EA, Richterman A, Gandhi RT, Sax PEJAoim. Transmission of SARS-CoV-2: a review of viral, host, and environmental factors. 2021;174(1):69-79.

7. Wang C-LJIjoms. Impact of COVID-19 on Pregnancy. 2021;18(3):763.

8. Wei SQ, Bilodeau-Bertrand M, Liu S, Auger NJC. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. 2021;193(16):E540-E8.

9. Schwartz DA, Graham ALJV. Potential maternal and infant outcomes from coronavirus 2019-nCoV (SARS-CoV-2) infecting pregnant women: lessons from SARS, MERS, and other human coronavirus infections. 2020;12(2):194.

10. Kazemi SN, Hajikhani B, Didar H, Hosseini SS, Haddadi S, Khalili F, et al. COVID-19 and cause of pregnancy loss during the pandemic: A systematic review. 2021;16(8):e0255994.

11. Pinar MH, Gibbins K, He M, Kostadinov S, Silver RJF, pathology p. Early pregnancy losses: review of nomenclature, histopathology, and possible etiologies. 2018;37(3):191-209.

12. Ortiz EI, Herrera E, De La Torre AJCM. Coronavirus (COVID 19) infection in pregnancy. 2020;51(2).

13. Figueiro-Filho EA, Yudin M, Farine DJJopm. COVID-19 during pregnancy: an overview of maternal characteristics, clinical symptoms, maternal and neonatal outcomes of 10,996 cases described in 15 countries. 2020;48(9):900-11.

14. Elsaddig M, Khalil AJBP, Obstetrics RC, Gynaecology. Effects of the COVID pandemic on pregnancy outcomes. 2021;73:125-36.

15. Mahtab NT, Chowdhury TSJBMJ. Clinical outcomes of women with COVID 19 during pregnancy: an update. 2020:93-102.

16. Mily SJ, Akter KM, Jabin N, Mitra S, Emran TB, Nandi M, et al. COVID-19 Infection in Pregnancy: A Review. 2022;22(5):12-21.

17. Overtoom EM, Rosman AN, Zwart JJ, Vogelvang TE, Schaap TP, van den Akker T, et al. SARS□CoV□2 infection in pregnancy during the first wave of COVID□19 in the Netherlands: a prospective nationwide population□based cohort study (NethOSS). 2022;129(1):91-100.

18. Sills ES, Wood SHJIJoM, Medicine C. An experimental model for Peri-conceptual COVID-19 pregnancy loss and proposed interventions to optimize outcomes. 2020;9(3):180.

19. Yang KM, Ntrivalas E, Cho HJ, Kim NY, Beaman K, Gilman□Sachs A, et al. Women with multiple implantation failures and recurrent pregnancy losses have increased peripheral blood T cell activation. 2010;63(5):370-8.

20. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. 2021;10(1):1-11.

21. Breslin N, Baptiste C, Miller R, Fuchs K, Goffman D, Gyamfi-Bannerman C, et al. Coronavirus disease 2019 in pregnancy: early lessons. American journal of obstetrics & gynecology MFM. 2020;2(2):100111.

22. Noelle B, Cynthia G-B, Russell M, Rebecca M, Kyra B, Laurence R. COVID-19 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed

presentations to an affiliated pair of New York City hospitals. Am J Obstet Gynecol MFM. 2020;100118.

23. Baergen RN, Heller DS. Placental pathology in Covid-19 positive mothers: preliminary findings. Pediatric and Developmental Pathology. 2020;23(3):177-80.

24. Gagliardi L, Danieli R, Suriano G, Vaccaro A, Tripodi G, Rusconi F, et al. Universal severe acute respiratory syndrome coronavirus 2 testing of pregnant women admitted for delivery in 2 Italian regions. American Journal of Obstetrics & Gynecology. 2020;223(2):291-2.

25. Ferrazzi E, Frigerio L, Savasi V, Vergani P, Prefumo F, Barresi S, et al. Vaginal delivery in SARS□CoV□2□infected pregnant women in Northern Italy: a retrospective analysis. BJOG: An International Journal of Obstetrics & Gynaecology. 2020;127(9):1116-21.

26. Chen L, Li Q, Zheng D, Jiang H, Wei Y, Zou L, et al. Clinical characteristics of pregnant women with Covid-19 in Wuhan, China. New England Journal of Medicine. 2020;382(25):e100.

27. Cosma S, Carosso AR, Cusato J, Borella F, Carosso M, Bovetti M, et al. Coronavirus disease 2019 and first-trimester spontaneous abortion: a case-control study of 225 pregnant patients. American journal of obstetrics and gynecology. 2021;224(4):391. e1-. e7.

28. Sahin D, Tanacan A, Erol SA, Anuk AT, Yetiskin FD, Keskin HL, et al. Updated experience of a tertiary pandemic center on 533 pregnant women with COVID□19

infection: a prospective cohort study from Turkey. International Journal of Gynecology & Obstetrics. 2021;152(3):328-34.

29. 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. American journal of obstetrics and gynecology. 2020;223(1):111. e1-. e14.

30. Aylward B, Liang WJW-CJMCD. Report of the WHO-China joint mission on coronavirus disease 2019 (COVID-19). 2020;2019:16-24.

31. Liu H, Liu F, Li J, Zhang T, Wang D, Lan WJJoi. Clinical and CT imaging features of the COVID-19 pneumonia: Focus on pregnant women and children. 2020;80(5):e7-e13.

32. Fang NZ, Castaño PM, Davis AJC. A hospital-based COVID-19 abortion case in the early phase of the pandemic. 2020;102(2):137-8.

33. Wong TC, Lee ZY, Sia TL, Chang AK, Chua HHJSccm. Miscarriage risk in COVID-19 infection. 2020;2(9):1449-52.

34. Sacinti K, Kalafat E, Sukur Y, Koc A. Increased incidence of first□trimester miscarriage during the COVID□19 pandemic. Ultrasound in Obstetrics & Gynecology. 2021;57(6):1013.

35. Panahi L, Amiri M, Pouy S. Risks of novel coronavirus disease (COVID-19) in pregnancy; a narrative review. Archives of academic emergency medicine. 2020;8(1).

36. 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. The lancet. 2020;395(10226):809-15.

37. Msq C, Jcs L, Sulaiman S, Tan H. From the frontline of COVID-19-How prepared are we as obstetricians: a commentary. https://obgyn onlinelibrary wiley com/doi/pdfdirect/101111/1471-052816192. 2020.

38. Mardani M, Pourkaveh B. Neoscriber Demo Publisher. A Controversial Debate: Vertical Transmission of COVID-19 in Pregnancy[Google Scholar]. 2020.

39. 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. Clinical infectious diseases. 2020.

40. Favre G, Pomar L, Musso D, Baud D. 2019-nCoV epidemic: what about pregnancies? Lancet (London, England). 2020;395(10224):e40.

41. Liang H, Acharya G. Novel corona virus disease (COVID-19) in pregnancy: What clinical recommendations to follow? 2020.

42. Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. American journal of obstetrics and gynecology. 2020;222(5):415-26.

43. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. New England journal of medicine. 2020.

44. Liu D, Li L, Wu X, Zheng D, Wang J, Liang B, et al. Pregnancy and perinatal outcomes of women with COVID-19 pneumonia: a preliminary analysis. Available at SSRN 3548758. 2020.

45. Lu Q, Shi Y. Coronavirus disease (COVID□19) and neonate: What neonatologist need to know. Journal of medical virology. 2020;92(6):564-7.

46. Liu W, Wang Q, Zhang Q, Chen L, Chen J, Zhang B. Coronavirus disease 2019 (COVID-19) during pregnancy: a case series. 2020. Preprint. 2020.

47. 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 International Journal of Obstetrics & Gynaecology. 2004;111(8):771-4.

48. Silva CRACd, Oliveira LVd, Lopes LP, Santos WAGd, Agra IKR. Immunological aspects of coronavirus disease during pregnancy: an integrative review. Revista da Associação Médica Brasileira. 2020;66:696-700.

49. Jiao J. Under the epidemic situation of COVID□19, should special attention to pregnant women be given? Journal of medical virology. 2020.

50. Liu H, Wang L-L, Zhao S-J, Kwak-Kim J, Mor G, Liao A-H. Why are pregnant women susceptible to COVID-19? An immunological viewpoint. Journal of reproductive immunology. 2020;139:103122.

51. Dashraath P, Wong JLJ, Lim MXK, Lim LM, Li S, Biswas A, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. American journal of obstetrics and gynecology. 2020;222(6):521-31.

52. Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, Shek CC, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. American journal of obstetrics and gynecology. 2004;191(1):292-7.

53. Fan C, Lei D, Fang C, Li C, Wang M, Liu Y, et al. Perinatal transmission of COVID-19 associated SARS-CoV-2: should we worry? Clinical infectious diseases. 2020.

54. Khan S, Jun L, Siddique R, Li Y, Han G, Xue M, et al. Association of COVID-19 with pregnancy outcomes in health-care workers and general women. Clinical microbiology and infection. 2020;26(6):788-90.

55. Cao D, Yin H, Chen J, Tang F, Peng M, Li R, et al. Clinical analysis of ten pregnant women with COVID-19 in Wuhan, China: A retrospective study. International Journal of Infectious Diseases. 2020;95:294-300.

56. Huang W, Zhao Z, He Z, Liu S, Wu Q, Zhang X, et al. Unfavorable outcomes in pregnant patients with COVID-19. Journal of Infection. 2020;81(2):e99-e101.

57. Govind A, Essien S, Karthikeyan A, Fakokunde A, Janga D, Yoong W, et al. Re: novel coronavirus COVID-19 in late pregnancy: outcomes of first nine cases in an inner city London hospital. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2020;251:272-4.

58. Ayed A, Embaireeg A, Benawadh A, Al-Fouzan W, Hammoud M, Al-Hathal M, et al. Maternal and perinatal characteristics and outcomes of pregnancies complicated with COVID-19 in Kuwait. BMC pregnancy and childbirth. 2020;20(1):1-9.

59. Wong TC, Lee ZY, Sia TL, Chang AK, Chua HH. Miscarriage risk in COVID-19 infection. SN comprehensive clinical medicine. 2020;2(9):1449-52.

60. Rana MS, Usman M, Alam MM, Khalid A, Ikram A, Salman M, et al. First trimester miscarriage in a pregnant woman infected with COVID-19 in Pakistan. Journal of Infection. 2021;82(1):e27-e8.

61. Buonsenso D, Costa S, Sanguinetti M, Cattani P, Posteraro B, Marchetti S, et al. Neonatal late onset infection with severe acute respiratory syndrome coronavirus 2. American journal of perinatology. 2020;37(08):869-72.

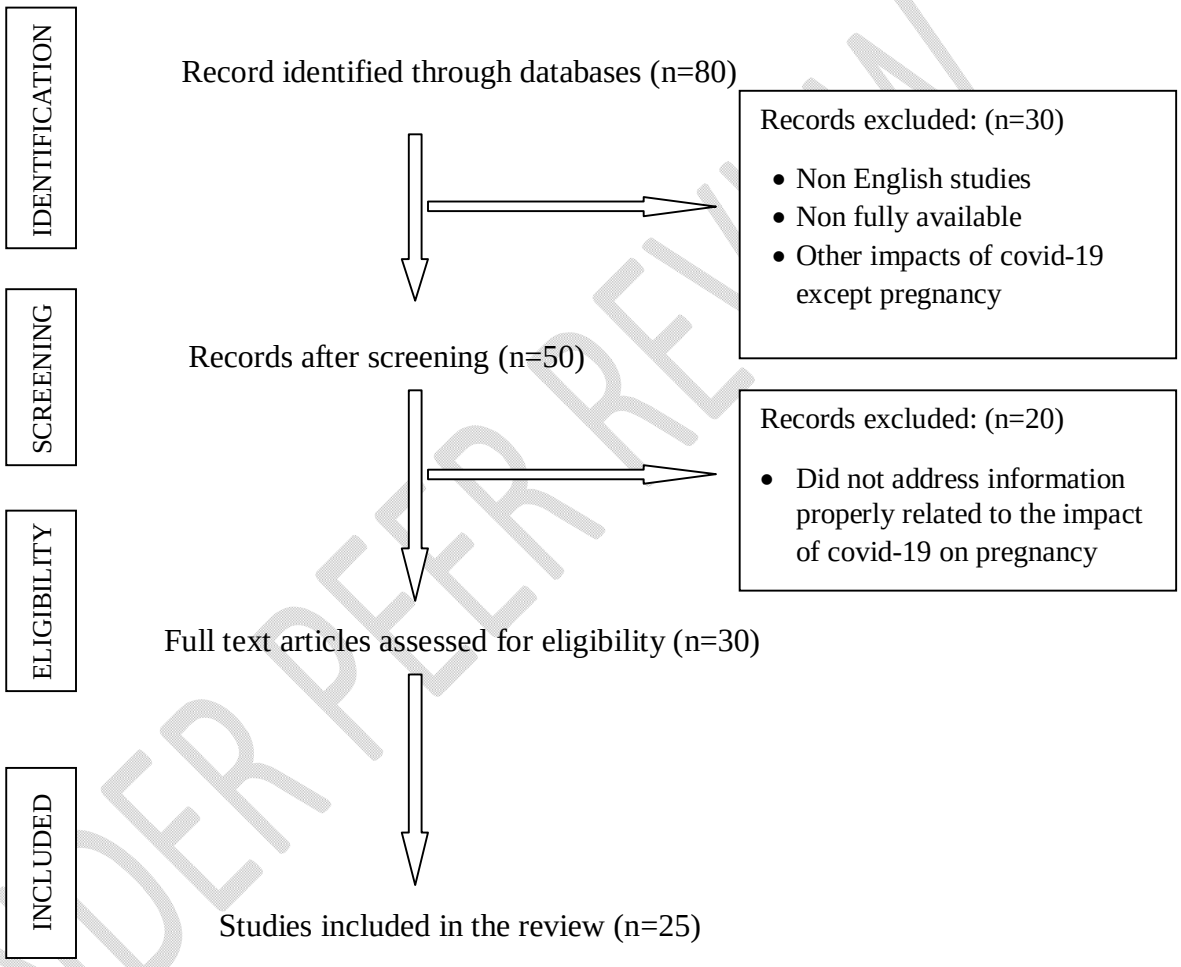
62. Sentilhes L, De Marcillac F, Jouffrieau C, Kuhn P, Thuet V, Hansmann Y, et al. Coronavirus disease 2019 in pregnancy was associated with maternal morbidity and preterm birth. American journal of obstetrics and gynecology. 2020;223(6):914. e1-. e15.

63. Di Mascio D, Sen C, Saccone G, Galindo A, Grünebaum A, Yoshimatsu J, et al. Risk factors associated with adverse fetal outcomes in pregnancies affected by Coronavirus disease 2019 (COVID-19): a secondary analysis of the WAPM study on COVID-19. Journal of perinatal medicine. 2020;48(9):950-8.

64. Baud D, Greub G, Favre G, Gengler C, Jaton K, Dubruc E, et al. Second-trimester miscarriage in a pregnant woman with SARS-CoV-2 infection. Jama. 2020;323(21):2198-200.

Figure

Figure-1: Flow chart summarizes the study search and selection process by following PRISMA 2020 for inclusion of articles on the impacts of covid-19 in pregnancy.



Tables

Table-1: Maternal symptoms during Covid-19

No. of pregnant patients	Asymptomatic (%)	Fever (%)	Cough (%)	Dyspnea (%)	Chest pain (%)	Myalgia (%)	Headache (%)	Diarrhea (%)	Fatigue (%)	References
7	28.5	28.5	43	-	28.5	43	28.5	-	-	[21]
43	33	48	65	24	17	38	28	-	-	[22]
20	80	10	-	10	-	-	-	-	-	[23]
2	-	100	-	-	-	-	-	-	-	[53]
17	-	18	35	12	-	-	-	18	-	[54]
10	-	70	10	-	10	-	-	-	10	[55]
8	-	62.5	87.5	37.5	-	37.5	-	-	37.5	[56]
42	-	48	43	19	-	17	-	5	-	[25]
9	-	44	89	44		56	-	-	67	[57]
3	67	-	-	-	-	-	-	-	33	[24]

Table-2: Number of miscarriages due to covid-19 in pregnant women from different countries

Location	No. of patients	No. of miscarriages	Gestational weeks	References
Italy	225	12	Approx. 12-13 weeks	[27]
China	116	1	38 weeks	[44]
Turkey	553	12	1st trimester (130) 2nd trimester (165), Third trimester (238)	[28]
Kuwait	185	3	29 weeks	[58]
Malaysia	2	2	10 weeks	[59]
Pakistan	1	1	10 weeks	[60]
Italy	7	1	37 Weeks	[61]
China	118	9 (3 spontaneous abortion)	Mostly 3rd trimester	[26]
France	54	1	37 weeks	[62]
22 countries	887	11	Approx. 20 weeks	[63]
Switzerland	1	1	19 weeks	[64]