REVIEW ARTICLE

A Meta-Meta-Analysis of The Impact of COVID-19 on Pregnant Women

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ABSTRACT

Background: Many studies have examined the effects of COVID-19 on pregnant women. Providing comprehensive evidence on the physical, psychological, and fetal effects, the knowledge gained can be applied to the care of pregnant women and their infants. This study aimed to conduct a meta-analysis on the impact of COVID-19 on pregnant women and their infants. **Methods:** This meta-analysis encompasses 21 meta-analyses identified via a search of electronic databases (PubMed, CINAHL). Meta-analyses have reported the effects of coronavirus disease 19 (COVID-19) on pregnant women and neonates. Analyses were based on random effects models. To combine the results, the effect estimates of the meta-analyses were transformed to SMD and weighted to correct primary study overlap, conducted by the PRISMA 2020 reporting guidelines, and the data were analyzed using the meta-analysis website. The meta-analyses sample included 21 meta-analyses (total number of studies k = 914, n = 3,936,822). **Results:** The effect of COVID-19 affected depression (EF = 21.74(95% CI 13.84 – 34.15) p <.01, I^2 = 97%, p <.01), anxiety (EF = 23.77(95% CI 14.71 – 38.42) p <.01, I^2 = 89%, p <.01. However, COVID-19 has not affected the health of pregnant women and infants. **Conclusion:** The findings of this study emphasize the importance of prioritizing the mental health of pregnant women affected by COVID-19 and offer valuable insights for public health officials regarding the necessity of addressing their mental well-being.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic was caused by a novel coronavirus (SARS-CoV-2) and was a public health emergency of international concern. SARS-CoV-2 is an RNA virus responsible for causing COVID-19. Previous studies have shown that pregnant women infected with the novel coronavirus (SARS- CoV) are at high risk of developing adverse complications, with a high mortality rate. In pregnant women infected with the virus, the mortality rate is as high as 40% (Alfaraj et al. 2019), and we should be vigilant. Thus, there is the possibility of similar serious side effects in pregnant women infected with COVID-19. However, a Swedish study found that pregnant and postpartum women infected with COVID-19 may have a higher risk of being admitted to the intensive care unit (ICU) compared to non-pregnant women of the same age (Collin et al. 2020).

The impact of the COVID-19 outbreak has psychologically affected the mental health of pregnant women (Saccone et al. 2020). Pregnant women assessed during the COVID-19 pandemic reported higher distress and psychiatric symptoms than those assessed before the pandemic, most commonly depression and anxiety (Durankus and Aksu. 2022).

In addition, the COVID-19 pandemic has affected infants, with an increase in the number of infants diagnosed as small for gestational age (SGA), 5th minute Apgar score less than 7, and infants diagnosed with hypoxic-ischemic encephalopathy (Hekimoglu and Acar. 2022).

Although there are many meta-analyses of the effects of COVID-19, there is still no meta-analysis to provide comprehensive information on the physical, mental, and infant effects; therefore, the knowledge gained can be applied to the care of pregnant women and infants. This meta-meta-analysis aimed to determine the impact of COVID-19 on pregnant women and infants.

MATERIALS AND METHODS

Study Design

This was a systematic review and meta-analysis of all studies evaluating the impact of COVID-19 on pregnant women and infants.

Eligibility criteria

To select the papers, the following inclusion criteria were

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defined: (a) articles focused on the impact of COVID-19 on pregnant women, and (b) articles with meta-analysis research papers. We excluded review studies regarding other viruses in the coronavirus family (i.e. SARS-CoV-1, MERS-CoV) and reports on the effects on the unborn child.

Information sources

PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Scholar were searched up to 15th June 2024—research published in English. The research strategy adopted included different combinations of the following terms: "SARS-CoV-2", "COVID-19", "meta-analysis", and "pregnancy".

Manual searches included scanning reference lists of relevant papers and meta-analyses during the literature analysis.

Study selection

All studies identified through electronic database searches were systematically recorded, including citation details, titles, authors, and abstracts. To ensure accuracy, duplicates were identified and removed through a manual screening process that was independently conducted by two researchers. Any discrepancies were resolved through discussion or consultation with a third party. The quality of the included reviews was assessed using an abbreviated list of quality criteria extracted from PRISMA 2020 (Tsuge et al., 2024). A PRISMA 2020 flow diagram of the selection process is shown in Figure 1.

For the eligibility process, two authors (RG and DTF) independently screened the titles and abstracts of all non-duplicated papers and excluded those not pertinent to the topic. The same two authors independently reviewed the full text of documents that passed the first screening and identified those to be included in the review. Discrepancies were resolved by consensus.

Data extraction

Two researchers conducted data extraction using a predefined form to collect details such as author, study timing, location, design, and participant demographics. Outcomes of interest were categorised into two groups: psychological health, the mental health of women and the foetus.

Statistical analysis

In this systematic review and meta-analysis, the relative risk (RR) with a 95% confidence interval (CI) was employed to measure effect sizes across all included studies. The mean effect sizes and their corresponding 95% CIs, as reported in the original meta-analyses, were illustrated using forest plots. The standardized mean difference (typically d or g) was the most frequently reported effect size, and these measures were utilized to plot the effects. Data analysis was conducted using an online meta-analysis platform (https://metaanalysisonline.com/).

RESULTS

Figure 1 shows a flowchart of the study selection process. The literature search resulted identified 545 published papers. An additional 21 publications were identified through the reference search.

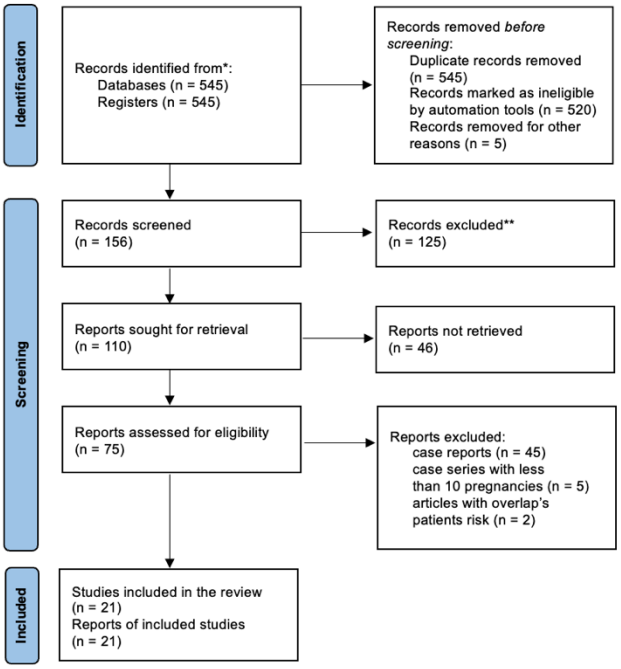

Figure 1: Flow diagram of meta-analyses

Participant Characteristics

The PRISMA 2020 flow diagram outlined the study selection process. Following the full-text screening, 21 systematic reviews were included. Our meta-analyses sample included 21 meta-analyses (total number of studies k = 914, n = 3,936,822). Fifteen studies reported physical effects and six reported psychological effects.

Study results and summary meta-analysis

The impact of COVID-19 on the health of pregnant women includes preeclampsia, gestational diabetes, lymphocytopenia, ICU admission, and death. It also affects the mental health of mothers. In addition, the effects on the infant included low birth weight, fetal distress, preterm birth, cesarean delivery, APGAR score < 7, NICU admission, and neonatal death**.**

A meta-meta-analysis of preeclampsia included seven studies on preeclampsia in women with COVID-19 (Figure 2). Heterogeneity for the two combined effect sizes was high (I^2 = 91%) and the summary effect size was not statistically significant [overall effect size = 1.71 (95% CI = 0.78, 1.76, p = 0.45)]. COVID-19 does not affect preeclampsia in pregnant women.

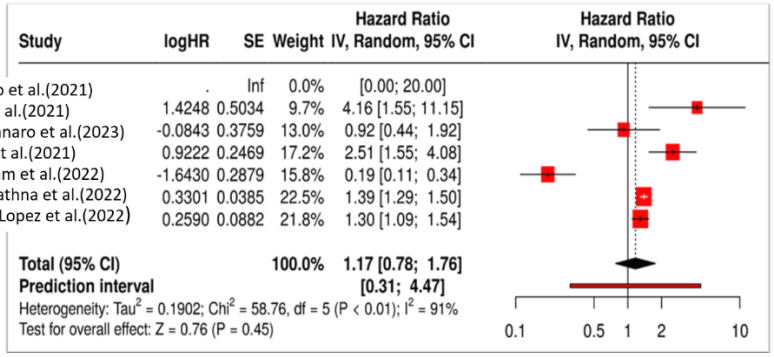

Figure 2: Meta-meta-analysis examining the association between COVID-19 and the risk of preeclampsia

Meta-meta-analysis of gestational diabetes included two studies on gestational diabetes in pregnant women with COVID-19 (Figure 3). Heterogeneity for the two combined effect sizes was high (I^2 = 81%) and the summary effect size was not statistically significant [overall effect size = 1.30 (95% CI = 0.63, 2.67, p = 0.48)]. COVID-19 does not affect gestational diabetes in pregnant women.

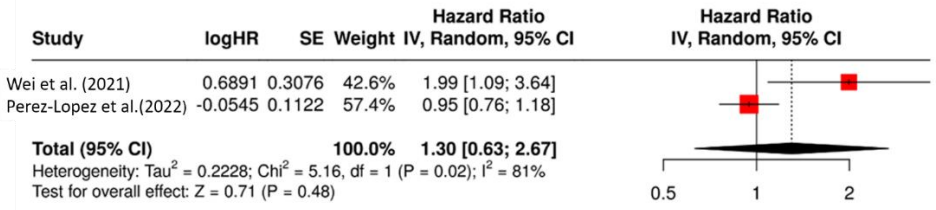

Figure 3: Meta-meta-analysis examining the association between COVID-19 and the risk of gestational diabetes

The meta-meta-analysis of lymphocytopenia included three studies on lymphocytopenia in pregnant women with COVID-19 (Figure 4). The combined effect sizes were highly heterogeneous (I^2 = 99%) and the summary effect size was not statistically significant (overall effect size = 3.48 (95% CI = 0.32, 37.30, p = 0.30)). COVID-19 does not affect lymphocytopenia in pregnant women.

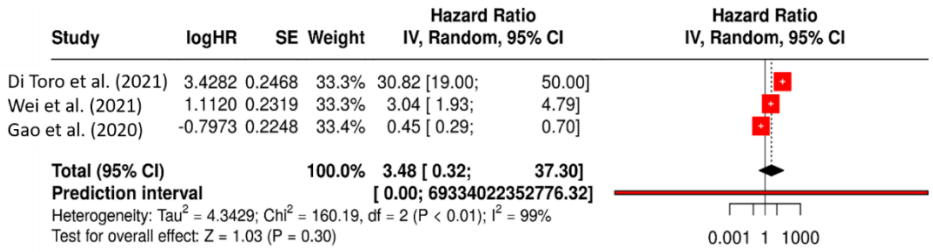

Figure 4: Meta-meta-analysis examining the association between COVID-19 and the risk of lymphocytopenia

Four studies reported ICU admissions in pregnant women with COVID-19 (Figure 5). The combined effect sizes were highly heterogeneous (I^2 = 96%) and the summary effect size was not statistically significant [overall effect size = 2.40 (95% CI = 0.66, 8.79, p = 0.19)]. COVID-19 does not affect ICU admission in pregnant women.

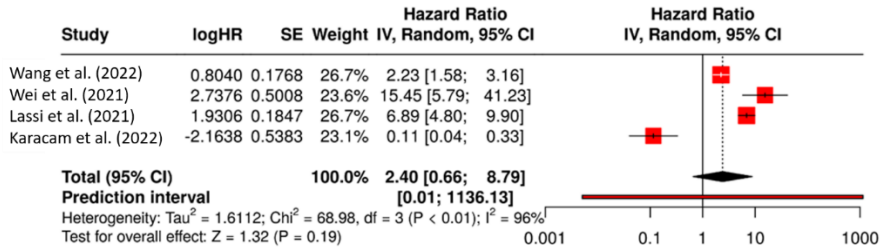

Figure 5: Meta-meta-analysis examining the association between COVID-19 and the risk of ICU admission

Nine studies reported maternal death in pregnant women with COVID-19 (Figure 6). The two combined effect sizes were highly heterogeneous (I^2 = 98%) and the summary effect size was not statistically significant [overall effect size = 0.55 (95% CI = 0.16, 1.84, p = 0.33)]. COVID-19 does not affect maternal death in pregnant women.

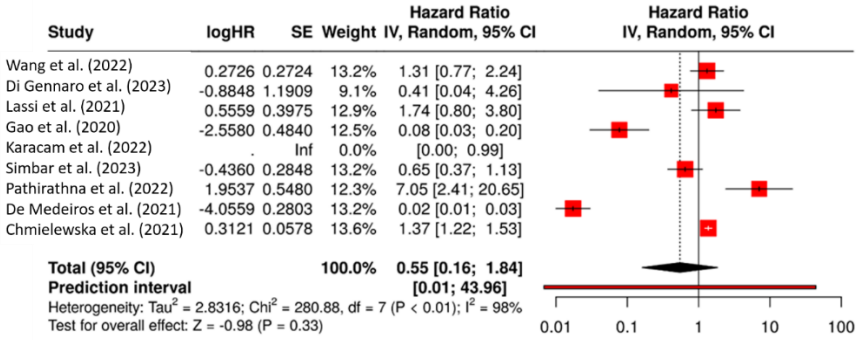

Figure 6: Meta-meta-analysis examining the association between COVID-19 and the risk of maternal death

Eleven studies reported cesarean deliveries in pregnant women with COVID-19 (Figure 7). The combined effect sizes were highly heterogeneous (I^2 = 100%) and the summary effect size was not statistically significant [overall effect size = 3.14 (95% CI = 0.82, 12.08, p = 0.10)]. COVID-19 does not affect cesarean delivery in pregnant women.

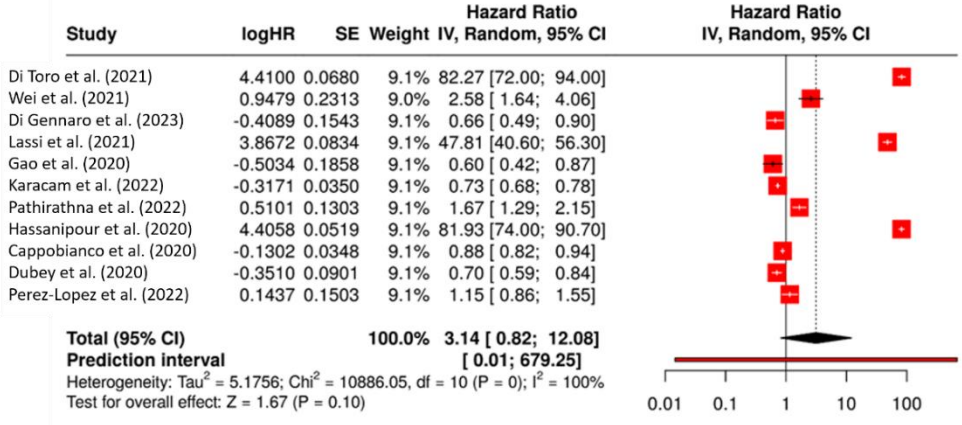

Figure 7: Meta-meta-analysis examining the association between COVID-19 and the risk of cesarean delivery

Five studies reported fetal distress in foetuses with COVID-19 (Figure 8). The combined effect sizes were highly heterogeneous (I^2 = 98%) and the summary effect size was not statistically significant (overall effect size = 0.43 (95% CI = 0.14, 1.32, p = 0.14)). COVID-19 does not affect fetal distress.

Twelve studies reported preterm births in foetuses with COVID-19 (Figure 9). The combined effect sizes were highly heterogeneous (I^2 = 99%) and the summary effect size was not statistically significant [overall effect size = 1.47 (95% CI = 0.54, 3.98, p = 0.45)]. COVID-19 does not affect preterm birth in the foetus.

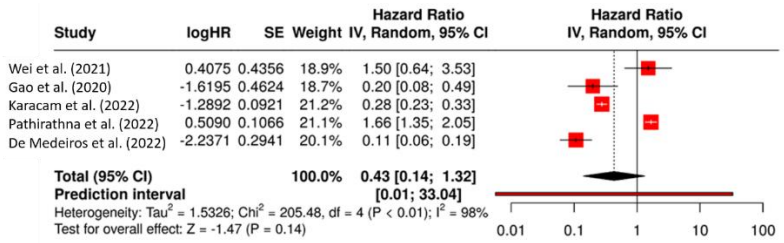

Figure 8: Meta-meta-analysis examining the association between COVID-19 and the risk of fetal distress

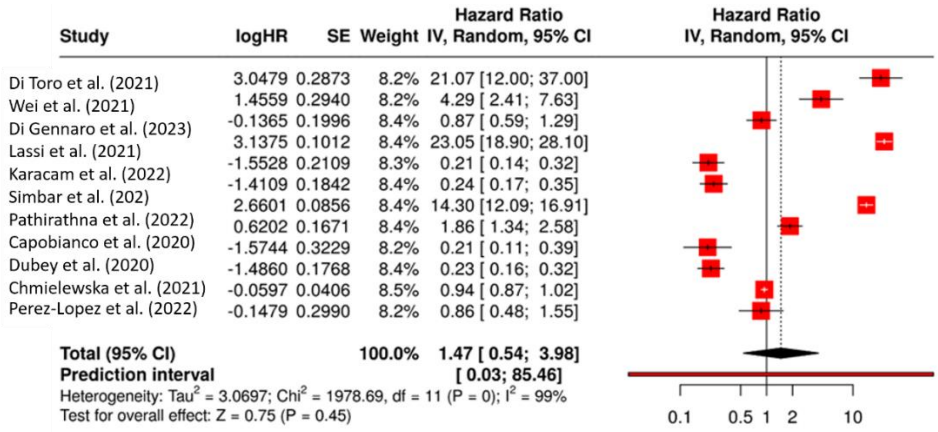

Figure 9: Meta-meta-analysis examining the association between COVID-19 and the risk of preterm birth

Six studies reported an APGAR score < 7 in foetuses with COVID-19 (Figure 10). The combined effect sizes were highly heterogeneous (I^2 = 98%) and the summary effect size was not statistically significant [overall effect size = 0.42 (95% CI = 0.11, 1.59, p = 0.20)]. COVID-19 infection did not affect the APGAR score of < 7 in the foetus.

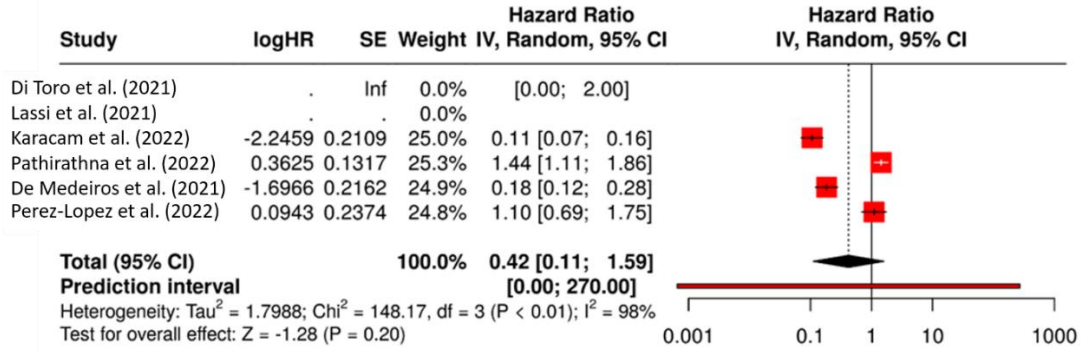

Figure 10: Meta-meta-analysis examining the association between COVID-19 and the risk of an APGAR score < 7

Birth weight < 2,500 g: Six studies reported birth weight < 2,500 g in foetuses with COVID-19 (Figure 11). The combined effect sizes were highly heterogeneous (I^2 = 99%) and the summary effect size was not statistically significant (overall effect size = 0.67 (95% CI = 0.15, 3.04, p = 0.61)). COVID-19 infection does not affect a birth weight of < 2,500 g in the foetus.

Ten studies reported NICU admission in foetuses with COVID-19 (Figure 12). The combined effect sizes were highly heterogeneous (I^2 = 98%) and the summary effect size was not statistically significant [overall effect size = 1.56 (95% CI = 0.46, 5.30, p = 0.47)]. COVID-19 does not affect NICU admission to the foetus.

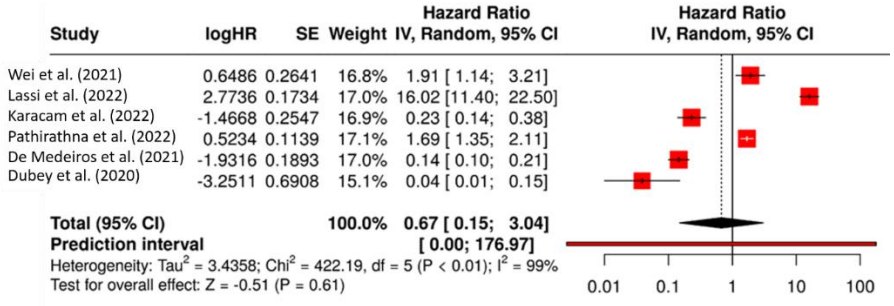

Figure 11: Meta-meta-analysis examining the association between COVID-19 and the risk of birth weight < 2,500 g

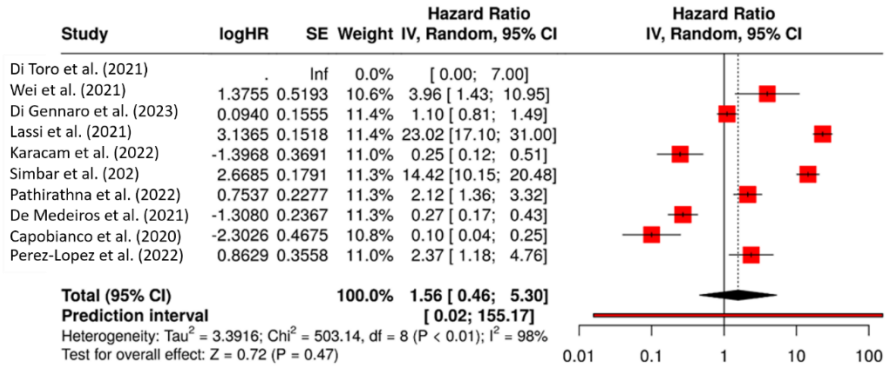

Figure 12: Meta-meta-analysis examining the association between COVID-19 and the risk of NICU admission

Ten studies reported neonatal deaths in foetuses with COVID-19 (Figure 13). The combined effect sizes were highly heterogeneous (I^2 = 95%) and the summary effect size was not statistically significant (overall effect size = 0.80 (95% CI = 0.43, 1.47, p = 0.47)). COVID-19 does not affect neonatal death in foetuses.

The impact of COVID-19 on the mental health of pregnant women included depression and anxiety. Five studies reported depression in pregnant women with COVID-19 (Figure 14). The combined effect sizes were highly heterogeneous (I^2 = 97%) and the summary effect size was statistically significant [overall effect size = 21.74 (95% CI = 13.84, 34.15, p < 0.01)]. COVID-19 affects depression in pregnant women.

Six studies reported on anxiety in women with COVID-19 (Figure 15). The combined effect sizes were highly heterogeneous (I^2 = 89%) and the summary effect size was statistically significant [overall effect size = 23.77 (95% CI = 14.71, 38.42, p < 0.01)]. COVID-19 affects anxiety in pregnant women.

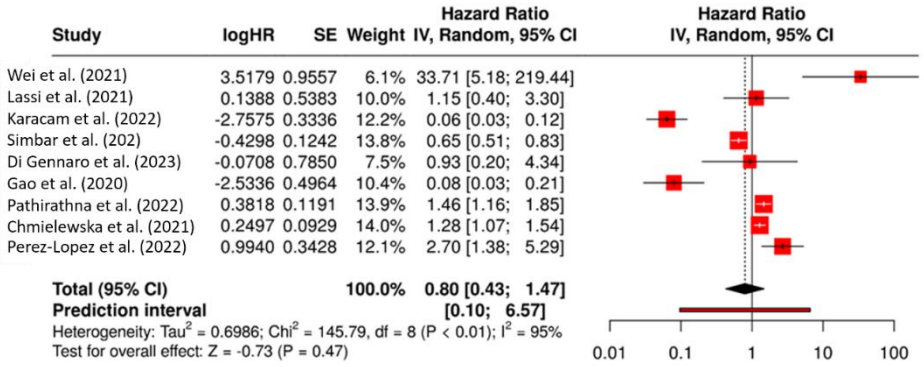

Figure 13: Meta-meta-analysis examining the association between COVID-19 and the risk of neonatal death

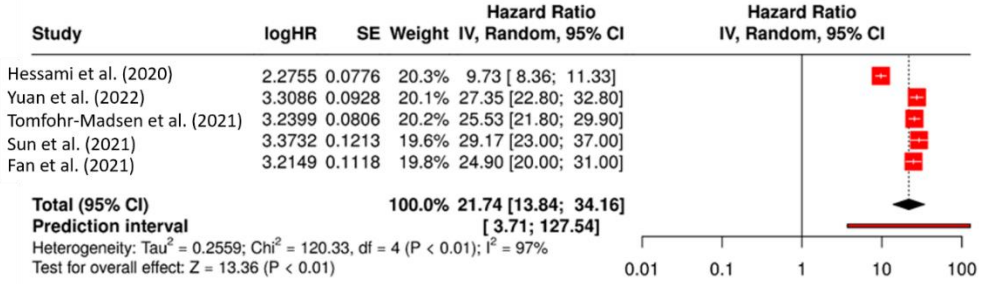

Figure 14: Meta-meta-analysis examining the association between COVID-19 and the risk of depression

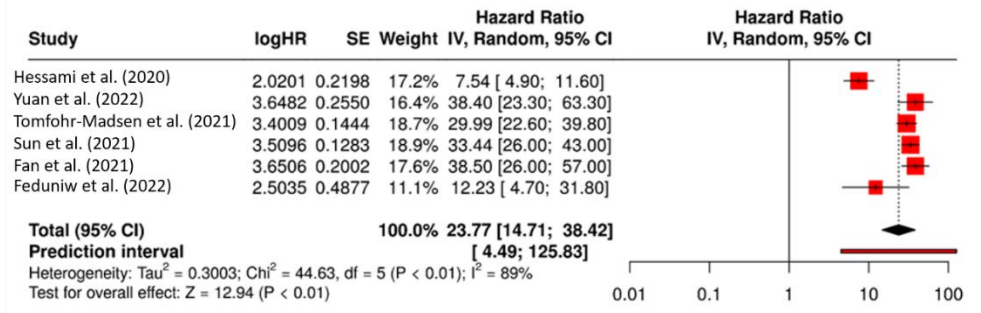

Figure 15: Meta-meta-analysis examining the association between COVID-19 and the risk of anxiety

In summary, COVID-19 infection during pregnancy was associated with anxiety and depression in pregnant women but was not associated with physical morbidity of the mother and foetus, such as ICU admission and mortality. Addressing these challenges require adapting healthcare delivery, enhancing mental health resources, and providing robust support systems to help pregnant women navigate the unprecedented period. This heightened mental health burden is often linked to fears of health risks, disruptions in prenatal care, and social isolation. Depression and anxiety in pregnant women are associated with potential adverse effects on foetal development.

This included concerns about preterm birth and low birth weight, although evidence is still emerging. Enhanced prenatal monitoring, including regular check-ups and appropriate testing, can help manage potential complications. Early identification and intervention are crucial to mitigate the risks associated with COVID-19 during pregnancy. Providing comprehensive care and support, including mental health resources and guidance on infection control, helps to address the broader impact of the pandemic on pregnant women.

DISCUSSION

This study conducted a meta-analysis on the impact of COVID-19 on pregnant women and their infants. Our results indicate that COVID-19 has a statistically significant impact on the mental health of pregnant women. This leads to stress and depression. This result is consistent with the findings of Tomfohr-Madsen et al. (2021), who found that the prevalence of anxiety was higher in studies conducted later in the pandemic. The post-pandemic period has seen an increase in anxiety, which may be linked to chronic stress exposure during the pandemic and ongoing uncertainty. Hessami et al. (2022) found that the COVID-19 pandemic significantly increases the risk of anxiety among women during pregnancy and the perinatal period. Other studies have shown that pregnant women reported increased anxiety and depressive symptoms during the pandemic, with some experiencing PTSD (Savenysheva et al., 2024; Zhou et al., 2024). Research indicates that 53% of pregnant women encounter the psychological impact as severe (Saccone et al., 2020).

Pregnant women are inherently more vulnerable to emotional distress, and the uncertainty surrounding COVID-19 intensifies these feelings (Cigăran et al., 2024). Sun et al. (2021) found a higher prevalence of depression, anxiety, and depression in pregnant and delivery women during the COVID-19 pandemic. Factors such as hospitalisation due to COVID-19 are significantly correlated with worsened mental health outcomes (Cigăran et al., 2024). Owing to the COVID-19 outbreak, pregnant women must be quarantined and separated from their families. Thinking about illness concerns about a disease and illness in an unborn child. The COVID-19 pandemic has significantly affected the mental health of pregnant women, leading to increased anxiety and depression during the perinatal period. Research indicates that lockdowns and associated stressors exacerbate preexisting vulnerabilities, necessitating targeted support measures for this high-risk population.

The psychological impact of COVID-19 on pregnant women has highlighted their vulnerability, necessitating ongoing evidence-based screening and treatment of depression and anxiety. Research indicates that the pandemic has exacerbated mental health issues in this population, with significant rates of anxiety and depression reported. The physical impact on the pregnant women and infants was not substantial. Studies have shown significantly reduced risks of severe outcomes, including hospitalization, ICU admission, oxygenation, mechanical ventilation, and mortality for Omicron compared to other variants such as Delta. Omicron's hospitalization rate was lower than that of Delta (Arabi et al., 2023). The mortality rate for Omicron infections ranges from 0.01% to 13.1%, notably lower than the 0.08% to 29.1% observed with earlier variants ("The disease severity of COVID-19 caused by Omicron variants: A brief review," 2023).

The research report was synthesized from the period when the COVID-19 vaccine was administered to pregnant women. This result is consistent with the findings of Ciapponi et al. (2024), who found low to very low certainty evidence suggesting that vaccination during pregnancy with mRNA vaccines may reduce severe cases or hospitalisations in pregnant persons with COVID-19, symptomatic COVID-19, and virologically confirmed SARS-CoV-2 infection. Hybrid immunity from vaccinations and previous infections has contributed to milder outcomes associated with Omicron (Shervani et al., 2022). Vaccination, particularly booster doses, has been shown to enhance protection against severe illnesses from Omicron (Arabi et al., 2023). Although Omicron is generally less severe, it still poses risks, especially for high-risk populations. The ongoing evolution of the virus and its variants necessitates continued monitoring and research to fully understand their implications (Parise et al., 2023). The administration of COVID-19 vaccines during pregnancy has been shown to significantly reduce the risk of severe COVID-19 and its associated adverse outcomes in both mothers and their offspring.

LIMITATION

A limitation of this study was that the data extracted from all the studies were collected retrospectively. Patient information regarding secondary outcomes was missing or unavailable in many studies. Future research should explore increased screening for depression and stress in pregnant women and develop programs to reduce depression and stress in pregnant women.

CONCLUSION

Our study underscores the critical need to prioritize the mental health of pregnant women impacted by the COVID-19 pandemic. Despite the evident importance of this issue, research remains limited, leaving significant gaps in understanding the unique psychological challenges faced by this vulnerable population and the development of effective intervention strategies. The study aims to bridge these gaps by offering valuable insights for public health officials to design targeted mental health support initiatives for pregnant women during the pandemic. It contributes to the broader understanding of mental health by illustrating its profound implications on pregnancy outcomes. Findings reveal that the COVID-19 pandemic has exacerbated anxiety symptoms among pregnant women, a group already predisposed to mental health vulnerabilities. Elevated anxiety levels during this period were primarily driven by concerns related to maternal and foetal health, restricted access to prenatal care, and heightened social isolation. These results highlight the need for healthcare systems to adopt proactive and adaptive strategies to address mental health challenges among pregnant women. Such adaptations should ensure adequate support for this population, regardless of external stressors, to mitigate the adverse effects on maternal well-being and pregnancy outcomes.

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