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COVID-19 vaccine hesitancy among pregnant women: a systematic review and meta-analysis

Oashe Bhattacharya ,[1] Bodrun Naher Siddiquea,[1] Aishwarya Shetty,[1] Afsana Afroz,[1,2] Baki Billah[1]

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[1]Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia
[2]Centre of Epidemiology and Biostatistics, School of Population and Global Health,The University of Melbourne, Melbourne, Victoria, Australia

Correspondence to
Oashe Bhattacharya;
obha0002@student.monash.edu

ABSTRACT

Objective The aim of this study was to perform a systematic review and meta-analysis to estimate the vaccines' acceptance level and to find the factors influencing pregnant women's vaccination decisions, with the goal of assisting in the development of interventions and promoting more research in this area.

Design Systematic review and meta-analysis.

Data sources MEDLINE, Embase, CINAHL and PubMed.

Eligibility criteria Studies providing any kind of quantitative assessment of overall COVID-19 vaccination acceptance among pregnant women in any country or region across the globe.

Data extraction and synthesis The pooled prevalence of COVID-19 vaccine acceptance among pregnant women was calculated using the random-effects model. Subgroup (sensitivity) analysis was performed to determine the overall COVID-19 vaccine acceptance level to understand the sources of substantial heterogeneity.

Results Out of the 375 studies identified, 17 studies from four continents assessing 25 147 participants (pregnant women) were included in this study. Among the participants, only 49% (95% CI 42% to 56%, p<0.001) had COVID-19 vaccine acceptance. High-income countries (47%; 95% CI 38% to 55%, p<0.001), participants with fewer than 12 years of education (38%; 95% CI 19% to 58%, p<0.001) and multiparous women (48%; 95% CI 31% to 66%, p<0.001) had lower COVID-19 vaccine acceptance. Overall heterogeneity was high (I^2 ≥98%), and publication bias was present (p<0.001). A very weak positive correlation between COVID-19 knowledge and COVID-19 vaccine acceptance was observed (r=0.164; 95% CI −0.946 to 0.972; p=0.8359).

Conclusion Overall, COVID-19 vaccine acceptance among pregnant women was low across the studies and considerably low among some specific subgroups of participants. These research findings have implications for the development of effective interventions that could increase the COVID-19 vaccine acceptance level among pregnant women to attain herd immunity.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review determined the pooled prevalence of COVID-19 vaccine acceptance among pregnant women across the globe.
⇒ Subgroup analyses by gravidity, parity, employment status, income level of the country, continent and study quality were conducted to identify sources of heterogeneity.
⇒ Potential participants without internet access might have been missed from studies that were conducted online.

INTRODUCTION

COVID-19, an acute respiratory infectious disease, has spread across the world and has come to be known as one of the major global public health events.[1] In December 2019, the novel coronavirus surfaced in Wuhan in China and continued to spread across neighbouring countries, resulting in a pandemic.[2] Since then, it has been the reason behind large epidemics among people of all ages around the globe. As of 1 June 2022, there have been 527 211 631 confirmed cases of COVID-19, including 6 289 371 deaths.[3] Individuals' financial difficulties, stress connected with known and, particularly, unknown knowledge and uncertainty about the effect of this pandemic are some of the negatives of this pandemic, in addition to a high prevalence of infection and death.[4 5]

To halt the spread of COVID-19 among various population groups, a global effort to create vaccines against the virus was launched based on decades of experience and previous pandemic immunisation knowledge.[6] Vaccination has long been regarded as one of the most significant breakthroughs in public health in medical history.[6] Implementing an effective immunisation strategy, which would aid in limiting the hazards, received much attention.[6 7] In December 2020, the UK became the first nation to start mass vaccination, 9 months after the WHO had originally declared COVID-19 a global pandemic.[6 7] Vaccination is a critical strategy in controlling the severity of COVID-19 disease. As of late, pregnancy has been perceived as a risk factor for COVID-19 disease. Because of the

exhibited security of COVID-19 immunisation during pregnancy, the Centers for Disease Control and Prevention in the United States suggests a COVID-19 vaccine for every pregnant woman.[8] However, to ensure the implementation of vaccination strategies effectively, a widespread acceptance of the COVID-19 vaccines is required among pregnant women.[8]

At present, 65.8% of the world's population has received at least one COVID-19 vaccine dose, with approximately 11.83 billion doses having been delivered worldwide and 5.67 million doses being administered every day.[39] However, as the vaccination campaign got underway, published research studies expressed continued concerns about the COVID-19 vaccines' safety.[4 10] It has been noted that the vaccination campaign has had a disproportionate impact on persons in various population groups and particularly on pregnant women.[10] COVID-19 susceptibility in pregnant women has prompted several concerns.[11] Despite this, one of the least discussed aspects of COVID-19 is its effect on pregnant women.[11] Women are prone to viral respiratory infection due to the physiological changes in the immune and cardiovascular systems that occur during pregnancy.[11] Although there is no evidence of vertical transmission of COVID-19 in pregnant women, there has been an increase in the rate of premature births.[11] The COVID-19 virus has the potential to change immunological responses at the maternal–foetal interface, affecting both the mother and the child.[11] Despite the large and rapidly increasing number of cases and deaths, there is a dearth of information on the clinical characteristics of pregnant women who have been affected by COVID-19.[12] This could potentially be a direct cause of vaccine hesitancy among pregnant women.[12] Details of the references (study design, eligibility, attrition and risk of bias) are in online supplemental table 1.

Vaccine hesitancy is defined by the WHO Sage Working Group as 'a delay in accepting or refusing immunisation notwithstanding the availability of vaccination services'.[13] It was considered 'one of the 10 greatest threats to global health' in 2019 and has been extensively discussed in relation to COVID-19 vaccine development and roll-out.[13] Vaccine reluctance can be influenced by the perceived necessity for vaccination, as well as by perceived dangers and benefits of immunisation.[11 13] Pregnant women have been observed to be more vaccine apprehensive than the general population based on the results of prior epidemics.[14–17] Due to the rise of autism in the last 20 years, parents are concerned that their children would get autism after receiving a vaccine.[11] It is erroneously assumed to be a vaccination causality rather than a correlation.[10 18] Despite the fact that a vaccine is one of the most efficient defences against infectious disease, pregnant women have historically been excluded from vaccine research and development, which could explain why pregnant women are wary of vaccines.[10 18] Pregnant women were not in favour of receiving a COVID-19 vaccine during pregnancy, with overall concerns regarding the vaccines' safety.[19]

Vaccine hesitancy is influenced by a variety of factors that differ between vaccines and target populations.[20] As a result, it is critical to recognise the drivers of vaccine hesitancy in pregnant women. Every day, more information is gathered, and it is critical to give healthcare providers the most up-to-date information on COVID-19 vaccination in pregnant women.[21] Thus, the aim of this study was to conduct a systematic review and meta-analysis to estimate vaccine acceptance levels and to find the factors influencing pregnant women's vaccination decisions, with the goal of assisting in the development of interventions and promoting more research in this area.

METHODS

This study was conducted in adherence to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement.[22] A PRISMA 2020 checklist, including a flow diagram, can be found in online supplemental table 2 and online supplemental figure 1. The protocol has been registered on PROSPERO with the registration number CRD42021277754.

ELIGIBILITY CRITERIA

This review covered studies that provided any kind of quantitative assessment of the overall COVID-19 vaccine acceptance level among pregnant women in any country or region across the globe. There were no constraints on the participants' age, ethnicity or current health status, nor on the duration of the study or the study's geographical location. However, only articles that had been published and had the full text available were included.

Exclusion criteria

Short reports, case reports, briefs, letters and duplicated studies.

SEARCH STRATEGY, INFORMATION SOURCES AND STUDY SELECTION

With the help of a senior medical librarian, two authors (OB and BNS) independently searched for publicly available published articles relating to COVID-19 vaccine acceptance among pregnant women using the databases MEDLINE, Embase, CINAHL and PubMed. the PRISMA-P checklist was used to make the final list of the papers.[22] The search covered published articles from December 2020 to April 2022. This review also included pre-prints, which provide a dynamic update of research papers related to COVID-19. The main keywords for the search strategy included 'vaccine acceptance', 'vaccine hesitancy', 'pregnant women' and 'COVID-19 vaccine'. The search strategy is detailed in online supplemental table 3. There were no language restrictions. EndNote was used to store, organise and manage all the citations.

This search was followed by the initial screening by the same authors (OB and BNS) of the title and abstract of

each article obtained from the literature search by the same authors (OB and BNS). When a title or abstract was not sufficient to reject the article, the full text was obtained and assessed. The reference lists of the articles selected during this meta-analysis were also manually screened for any additional studies.

STUDY OUTCOMES

As the primary outcome, the meta-analysis was to address vaccine acceptance pertaining to COVID-19 among pregnant women. The secondary outcomes included the estimated effects of parity, gravidity, comorbidity, education, employment status (unemployed vs employed), continent and income level of the country where the study was conducted (low income vs middle income vs high income).

DATA EXTRACTION

Using a data extraction template (an Excel spreadsheet), key information regarding the identification of the study (authors, publication month and country where the studies had been conducted), methodology (study setting, study design, study population, sample size, data collection tool, recruitment method and recruitment period), participants' demographics (age, education, current employment status, income and area of residence), and primary and secondary study findings (prevalence of vaccine acceptance) was extracted by the two reviewers (OB and BNS). The two data files were then verified by a third reviewer (AS). Any disagreements were resolved by a consensus meeting under the supervision of a senior investigator (BB).

QUALITY ASSESSMENT AND RISK OF BIAS IN INDIVIDUAL STUDIES

All the studies in this systematic review were found to be cross sectional. Since the National Heart, Lung and Blood Institute quality assessment tool[23] was designed for cross-sectional studies, it was used to assess the quality of the included studies by two independent reviewers (OB and AS). This tool uses 14 criteria to assess internal validity and risk of bias. Each criterion was rated as 'yes', 'no', 'cannot determine', 'not applicable' or 'not reported. The overall quality of the study was then rated as good, fair or poor (online supplemental table 4). Any discrepancies in the ratings between the two reviewers were resolved by the third author (BNS).

DATA ANALYSIS

The extracted quantitative data (eg, overall COVID-19 vaccine acceptance levels, and acceptance by parity, gravidity, current employment status, educational level, comorbidity of the participants, continent and Europe vs other continents) from each study were analysed using the statistical software package Stata V.16. A p value of 0.05 or less was considered to be of statistical significance. The pooled proportion of vaccine acceptance of COVID-19 was calculated as a data synthesis of primary as well as secondary outcomes and was presented in forest plots. This analysis was performed using the random-effects model, as this method demonstrates better properties in the presence of heterogeneity (if any), accounting for both within-study and between-study variances.[24]

The χ^2 test on Cochran's Q statistic, which was obtained using H and I^2 indices, was used to assess heterogeneity among the included studies.[24] The I^2 index is a measure of overall heterogeneity across research that is based on genuine differences across studies rather than chance. Low heterogeneity was indicated by I^2 values of 0%–25%, moderate heterogeneity was indicated by I^2 values of 26%–75% and substantial heterogeneity was indicated by I^2 values of 76%–100%.[24 25] Egger's regression analysis was performed to examine for publication bias by evaluating the symmetry of the funnel plots.[26]

To further understand the sources of substantial heterogeneity, subgroup (sensitivity) analyses were conducted for COVID-19 vaccine acceptance by parity, gravidity, employment status, income level of the country, continent and Europe versus other continents. The countries were grouped into three income categories: 'low income', 'middle income' or 'high income', using the World Bank's country classifications.[27] Furthermore, a correlation analysis was performed to determine the association between COVID-19 vaccine acceptance and knowledge of COVID-19.

PATIENT AND PUBLIC INVOLVEMENT

There was no patient or public involvement in this systematic review.

RESULTS

A total of 375 studies published from December 2020 to April 2022 were retrieved from four databases and through manual searches. After removing duplicate records and screening by title, abstract and full text, 17 studies were included based on the inclusion criteria[14–17 19 28–39] (online supplemental table 5, online supplemental figure 1). Finally, 25 147 participants from these 17 studies were included in the quantitative analysis. Out of the 17 studies, 11 studies were of good quality, 6 were of fair quality and two were of poor quality (online supplemental table 4). Online supplemental table 5 summarises the study features and characteristics of participants. Participants in this study were between the ages of 25 and 35, and it was observed that 62% of the study participants were employed.

The overall COVID-19 vaccine acceptance prevalence among pregnant women was 49% (95% CI: 42% to 56%, I^2=99.43% (online supplemental figure 2)). Vaccine acceptance prevalence ranged from 30% (Singapore

and Switzerland) to 77% (China). An acceptance prevalence of greater than 60% was reported by three studies conducted in China, South Africa and Ethiopia.

In terms of country income level, eight studies were from high-income countries (n=8545), three studies were from middle-income countries (n=2064) and two were from low-income countries (n=742), as illustrated in online supplemental figure 3. Additionally, two studies collected multi-country data, with one study (n=5294) including 16 countries and the other study (n=6661) including five countries in the research.[19 29] There was a progressive decrease in the overall prevalence of COVID-19 acceptance by income level. It was 47% (95% CI 38% to 55%, I^2=98.42%) for high-income countries, 48% (95% CI 19% to 77%, I^2=99.29%) for middle-income countries and 61% (95% CI 40% to 81%, I^2=97.58%) for low-income countries.

COVID-19 vaccine acceptance prevalence also varied substantially between continents, as presented in online supplemental figures 4 and 5. The highest vaccine acceptance was found in Africa (61%; 95% CI 40% to 81%, I^2=71.88%), followed by Asia (49%; 95% CI 33% to 65%, I^2=99.69%), the Americas (46%; 95% CI 35% to 56%, I^2=97.65%) and Europe/Oceania (45%; 95% CI 35 to 56%, I^2=97.65%).

Furthermore, as the vaccine roll-out first began in the UK, an analysis was conducted comparing Europe with other continents. The overall COVID-19 vaccine acceptance prevalence across five studies from Europe (n=9367) was 49% (95% CI 38% to 59%, I^2=97.45%) and for other continents, the prevalence was similar (49%; 95% CI 39% to 59%, I^2=99.33 (online supplemental figure 6).

Online supplemental table 6 presents the results of the subgroup analyses by parity, gravidity, comorbidities, employment status, education level, income level of the country and continent. Pregnant women who had given birth before had a lower COVID-19 vaccine acceptance (41%; 95% CI 28% to 55%, I^2=99.84%) compared with women who had never given birth (59%; 95% CI 43% to 74%, I^2=99.63%). It was found that pregnant women who had been pregnant earlier had a higher acceptance (62%; 95% CI 44% to 80%, I^2=99.08%) of the COVID-19 vaccine compared with women who were pregnant for the first time (51%; 95% CI 24% to 79%, I^2=99.16%). It was also noted that pregnant women who reported some health comorbidities had a higher prevalence of vaccine acceptance (35%; 95% CI 16% to 54%, I^2=99.77%) compared with pregnant women who were not experiencing health comorbidities (23%; 95% CI 1% to 44%, I^2=97.31%). COVID-19 vaccine acceptance prevalence was found to be higher among employed women (62%; 95% CI 51% to 74%, I^2=99.56%) compared with unemployed women (41%; 95% CI 28% to 55%, I^2=99.67%). Pregnant women who had completed at least twelve years of education (50%; 95% CI 41% to 61%, I^2=99.40%) were shown to have a higher prevalence of COVID-19 vaccine acceptance compared with women who had not completed twelve years of education (38%; 95% CI 19% to 58%, I^2=98.71%).

Online supplemental figure 7 illustrates a subgroup analysis by study quality. The overall COVID-19 vaccine acceptance prevalence was found to be higher in papers categorised as of 'fair' quality (51%; 95% CI 30% to 73%, I^2=99.73%) compared with papers categorised as of 'good' (49%; 95% CI 42% to 57%, I^2=99.18%) or 'poor' quality (41%; 95% CI 19% to 64%, I^2=95.08%). High heterogeneity was observed overall, as well as in all subgroups (sensitivity) analyses, and the presence of publication bias was observed (online supplemental figure 8).

A correlation analysis was conducted between COVID-19 vaccine acceptance and knowledge of COVID-19 among pregnant women, and an insignificant positive weak correlation was observed (r=0.164; 95% CI −0.946 to 0.972; p=0.8359).

DISCUSSION

This systematic review and meta-analysis were conducted to examine the prevalence of COVID-19 vaccine acceptance and its associated factors among pregnant women. Data were compiled from 25 147 participants from four continents across the globe. The overall COVID-19 vaccine acceptance prevalence among pregnant women was 49%, with the lowest in the Americas, with an acceptance prevalence of 45%. Furthermore, vaccine acceptance was found to be lower in some subgroups, such as among participants with fewer than twelve years of education, unemployed women and women who had previously given birth.

Given the severity of COVID-19, it is difficult to eliminate the transmission of this novel coronavirus; hence, it is recommended to increase the immunity rates among pregnant women so that the effects of COVID-19 can become manageable. However, this current study demonstrated that half of the population of pregnant women was hesitant to accept a COVID-19 vaccine. Pregnant women have generally been subjected to misinformation that has increased their apprehensions towards COVID-19 vaccination. It was observed that there were several indicators that resulted in COVID-19 vaccine hesitancy among pregnant women. A similar trend was observed in the uptake of previous pandemic influenza vaccines. A literature review conducted among risk groups and the general population in 2017 reported that the most frequently reported barriers to pandemic influenza vaccine uptake for pregnant women were lack of confidence, high levels of vaccine safety concerns, low perceived effectiveness of the vaccine and misconceptions about the disease or vaccine.[18] However, data related to pregnant women are limited (35 out of 470 studies reported barriers to vaccine acceptance among pregnant women). Most of the studies in this review were cross-sectional in nature. This review included studies that were in English or German and reported multivariable analyses of determinants. Since

these studies were cross-sectional in nature, attrition rates were not applicable, and risks of bias were not reported.

In this review, large variability in COVID-19 vaccine acceptance was found. However, certain patterns can be deduced based on a descriptive analysis of the reported prevalence of vaccine acceptance on different continents. In Europe, the overall COVID-19 vaccine acceptance level among pregnant women was 45%, which was lower than in Africa (61%) and Asia (52%). A scoping literature review reported that individuals residing in countries that are more affluent, question the efficacy and safety of the vaccines.[40] This may be a direct result of the disparities in access, cost and awareness of vaccine information between low-income and high-income countries.[40] Our findings are also in line with another study, which reported that European regions have a negative sentiment towards COVID-19 vaccine safety.[41]

Further analysis showed that COVID-19 acceptance was low among participants with fewer than twelve years of education and among unemployed women. According to a study on global attitudes towards immunisations, unemployed women were more likely to have negative feelings about vaccine safety and effectiveness.[41]

Subgroup analysis showed that the number of times a woman has been pregnant (gravidity) and has carried the pregnancies to a viable gestational stage (parity) is an indicator towards a low prevalence of COVID-19 vaccine acceptance among pregnant women. Multiparous women were less likely to accept the COVID-19 vaccine. Since the COVID-19 vaccine guidelines are recent, multiparous women may show more apprehension. Pregnant women with previous child birthing experience tend to be more confident based on experience; hence, they show lower acceptance towards the COVID-19 vaccines. A study conducted in France on the acceptance of the seasonal influenza vaccine identified that nulliparous women are more preventive during their pregnancy and, hence, have a higher influenza vaccine acceptance rate than multiparous women.[41]

Regarding the reported COVID-19 vaccine acceptance levels in this study, high heterogeneity was observed (≥98%). Various subgroup analyses were performed to identify the sources of heterogeneity but without success. However, factors such as sociodemographic, cultural and questionnaire content differences, as well as different measuring and scoring systems, may be associated with this heterogeneity.

A correlation analysis conducted in this study showed a weak relationship between knowledge of COVID-19 and COVID-19 vaccine acceptance. A study conducted in China reported lower COVID-19 vaccine acceptance in relation to higher knowledge of COVID-19. There is a possibility that pregnant women are exposed to negative information that causes higher vaccine hesitancy levels among this population group.[17]

There are various strengths and limitations to this systematic review and meta-analysis. First, most of the included studies were online surveys that covered large cities in the respective countries due to the difficulties in conducting research during the pandemic. As a result, vulnerable populations, such as the impoverished and urban slum residents, as well as persons living in remote rural areas without internet access, may have been missed. Second, high overall heterogeneity was observed. Despite conducting subgroup analysis, the sources of heterogeneity remained unidentified. Third, since data on pregnant women are scarce, this systematic review and meta-analysis could be used as a foundation for further studies. With very little information available about the effects of COVID-19 and COVID-19 vaccination on pregnant women, any form of information would lay a foundation for future research. Finally, while the findings of this study cannot be generalised, they throw light on the level of vaccine acceptance among pregnant women and emphasise the need for future studies. Despite the limitations, this is the first systematic review and meta-analysis of COVID-19 vaccine acceptance among pregnant women.

CONCLUSION

In this systematic review and meta-analysis, it was shown that overall COVID-19 vaccine acceptance was low among pregnant women. This research finding has implications for the development of effective interventions that could increase COVID-19 vaccination uptake among pregnant women. Furthermore, low COVID-19 vaccine acceptance was observed in high-income countries, multiparous women, unemployed women and women with fewer than twelve years of education. High heterogeneity was observed overall, as well as in all subgroups (sensitivity) analyses, and there was a presence of publication bias. A wide understanding of the indicators associated with vaccine acceptance among pregnant women is also a crucial public health consideration.

Contributors BB, OB and AS laid the foundation of the study and together with BNS and AS developed the protocol. The data were extracted by OB and AS which was verified by BNS. AA and OB synthesised the data. OB drafted the initial report with input from BB and AS. All authors after critical revision approved the final version of the report. The guarantor (OB) accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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ORCID iD

Oashe Bhattacharya http://orcid.org/0000-0002-8785-4943

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