Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Health Sciences Review 4 (2022) 100044

Contents lists available at ScienceDirect

Health Sciences Review

journal homepage: www.elsevier.com/locate/hsr

COVID-19: Consequences on pregnant women and neonates

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ARTICLE INFO

Keywords:
COVID-19
Neonates
Vertical transmission
Pregnant women

ABSTRACT

Introduction: Human species is confronting with a gigantic global COVID-19 pandemic. Initially, it was observed in Wuhan, China, and the COVID-19 cases spread across the globe with lightning speed and resulted in the 21st century pandemic. If scientific reports are taken care of, it is noteworthy that this virus possesses more specific characteristics due to its structure. The distinctive structure has a higher binding affinity with angiotensin-converting enzyme 2 (ACE2) protein, and this is used as an access point to gain access to hosts.

Methods: A complete literature search was conducted using PubMed, Google Scholar, SciFinder, and deep-diving Google Search using keywords such as "Pregnancy, COVID-19, Newborn, Fetus, Coronavirus 2019, Neonate, Pregnant women, and vertical transmission".

Result and discussion: The SARS-CoV-2 virus is unlike its former analogs: SARS-CoV, and MERS-CoV in 2002 and 2012, respectively, or anything mankind has faced earlier concerning viciousness, global spread, and gravity of a causative agent. The current review has delved into articles published in various journals worldwide including the latest studies on the impact of COVID-19 on pregnant women and neonates and has discussed complications and challenges, psychological health, immunological response, vertical transmission, concurrent disorders, vaccine debate, management recommendations, recent news of the approval of COVID-19 vaccine for 6 months and older babies, and future perspectives.

1. Introduction

COVID-19 emerged as a health emergency in the 21st century across the globe. In late 2019, pneumonia of an anonymous source in Wuhan of Hubei province, China was documented [1]. The transmission rate of SARS-CoV-2 is like SARS-CoV (3%) at 2–3%, and the estimated case-fatality ratio is much lower than that of SARS-CoV (9.6%) at 2% [2]. The disease name was updated to coronavirus disease 2019 (COVID-19) by WHO, and on February 11, 2020 [3], the International Committee on Taxonomy of Virus renamed the virus to SARS-CoV-2, which stands for severe acute respiratory syndrome coronavirus.

Different countries have responded to the epidemic in different ways [4]. Air travel routes were blocked by learning from the former SARS-CoV, MERS-CoV zoonotic coronavirus, as SARS-CoV-2 was spanning from one country to another through air travel and had spread worldwide [5], as shown in Fig. S1. Fig. 1 summarizes the various symptoms and human organs affected by coronaviruses. The bitter fact is that we are still unaware of many untouched aspects of this virus. Also, similarities between the COVID-19 outbreak and SARS during 2002–2003 are striking [6]. The origin of SARS was then unearthed from animal markets, and then bats were identified as actual animal reservoirs after palm civets were identified [7].

SARS-CoV-2 enters host cells to interact with angiotensin-converting enzyme 2 (ACE2) receptors [8]. The ACE2 receptors are also present in the skin, colon, brain, liver, kidney, and surface of the lung's alveolar epithelial cells. Thus, all these portions can be easily infected by SARS-CoV-2. However, upper respiratory tract tissue does not allow surface expression of ACE2 receptors on epithelial cells [9]. The computerized tomography (CT) scans of lower lungs show higher opacity, as this region has more ACE2 receptors. SARS-CoV-2 is obtained from mouth swabs, bronchoalveolar lavage fluid, and stool [10]. More viral loads have been seen in the nose than in the throat, and similar viral loads were seen in asymptomatic and symptomatic COVID-19 +ve cases [11]. Analyzing biologic aspects of SARS-CoV-2 eased scientific investigators to create detection diagnoses. Since this epidemic is new, less scientific material is available on the consequences on pregnant women and neonates. The interaction and binding mechanism of SARS-CoV-2 with host cells are shown in Figs. S2 and S3, respectively. It is the true hope

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https://doi.org/10.1016/j.hsr.2022.100044
Received 2 May 2022; Received in revised form 16 July 2022; Accepted 18 July 2022

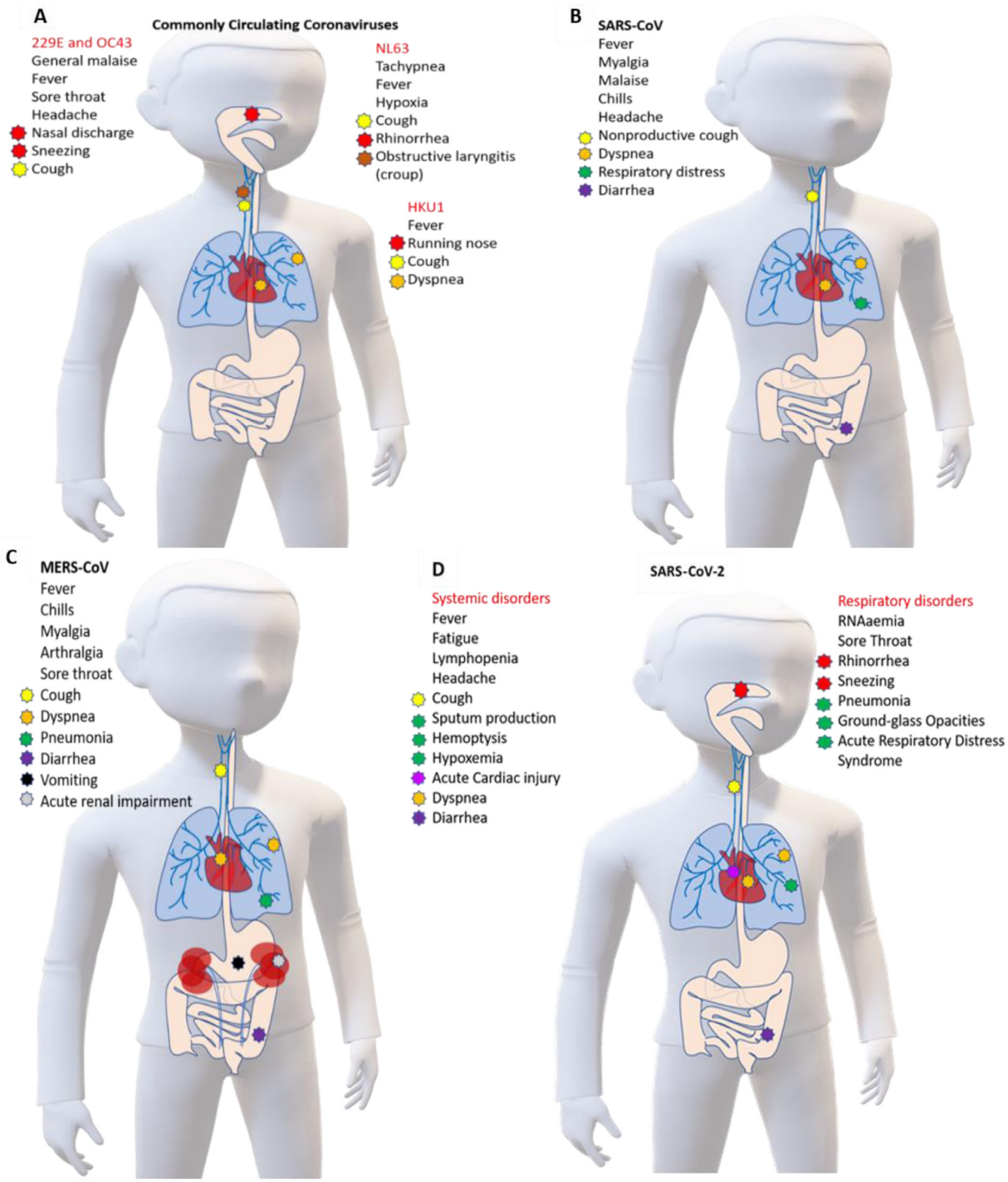

Fig. 1. Symptoms of various coronaviruses [(A) common circulating coronaviruses, (B) SARS-CoV, (C) MERS-CoV and (D) SARS-CoV-2] and organs affected in the human body.

and intent of the authors that this new analysis on what has become a "public health emergency of international concern" helps inform workers preparing for health and public health and any layman who is perhaps already experiencing COVID-19 in their area [12].

2. Methods

Although there are many reports on coronavirus , there is still a shortage of information about COVID-19 in pregnant ladies and neonates. Thus, COVID-19 and its effects on pregnant women and newborns were investigated using existing literature, and Fig. 2 illustrates the flowchart diagram to include studies. Using keywords such as " Pregnancy, COVID-19, newborn, Fetus, Coronavirus 2019, Neonate, Pregnant women, vertical transmission, vaccine and 6 months and older babies," searches were made using PubMed, Google Scholar, SciFinder, and Google Search to find relevant articles. Previously published papers were analyzed and integrated into this research.

3. Consequences of COVID-19 on pregnant women and neonates

COVID-19 affects a large group of women of fertility age, which is a cause of distress [13]. Although several reports are available on COVID-

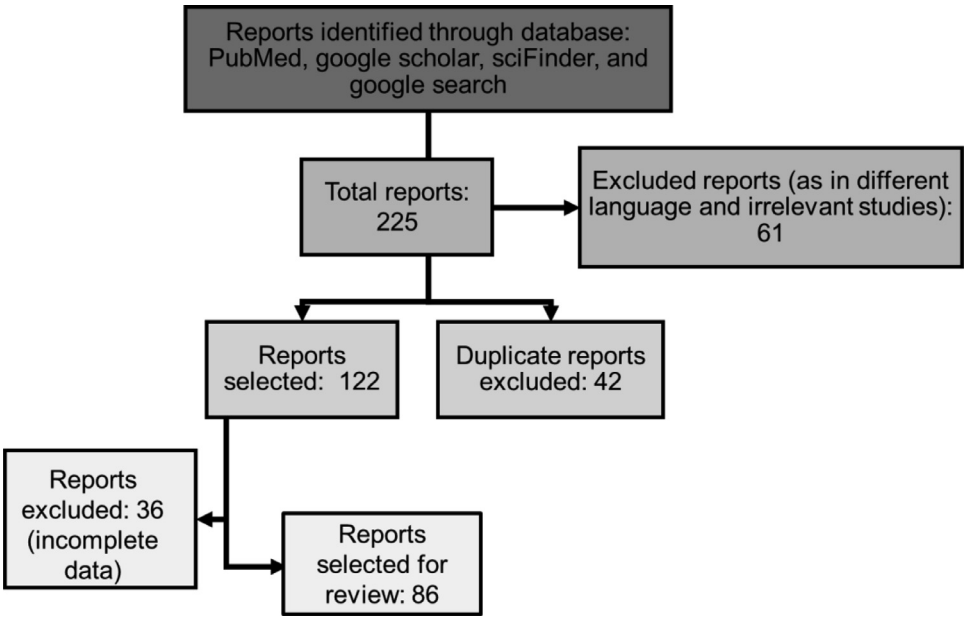

Fig. 2. Flowchart diagram for inclusion of studies.

19, its impact on pregnant women is understudied. Thus, it is crucial to gain more information about cases of COVID-19 +ve pregnant women. Fig. S4 represents an expectant mother and the SARS-CoV-2 virus model.

3.1. Complications and challenges

Cao et al. reported all patients after delivery had lung abnormalities as observed by the pulmonary CT images [14]. A study reported some symptomatic outcomes such as the mode of delivery, low birth weight, preterm delivery, C-section, unfavorable pregnancy outcomes, and vertical transmission [15]. An investigation found that most patients were suffering from common symptoms after six months of illness, such as fatigue or muscle weakness, sleep difficulties, and anxiety symptoms. Those severely ill patients had a high risk of pulmonary diffusion abnormality [16]. A study reported vitamin D deficiency in pregnant ladies infected with SARS-COV-2. Vitamin D supplements and adequate vitamin D levels may help minimize COVID-19′s severe influence during gestation [17].

During hospitalization, COVID-19 +ve patients had less leucocyte, alanine aminotransferase, C-reactive protein, and neutrophils in compassion to -ve cases. However, after delivery, leucocyte, C-reactive protein, eosinophils, and neutrophils counts were increased in ladies with +ve COVID-19. Maternal health problems increased preterm births in COVID-19 +ve patients [18].

In contrast to non-pregnant women, pregnant women are at a higher risk of COVID-19 for severe complications [19]. Altogether, placing the fetus at upsurge risk, pregnant women are more likely to be put on mechanical ventilators and admitted to the intensive care unit (ICU) than non-pregnant women. Therefore, it is vital to manufacture therapeutics without affecting the fetus, which may be a caring technique for pregnant women [20].

Pregnant women are more prone to extreme complications and mortality due to viral infections. Maternal and fetal well-being can be hampered by SARS-CoV-2 infection as it can change immune response. Preterm delivery was usually observed among +ve COVID-19 pregnant ladies. However, a lack of information persists in proving its vertical transmission and feeding [21].

3.2. Psychological health

A study showed that COVID-19 was a prominent reason for anxiousness and depression, which created the -ve emotional effect on pregnant women. Thus, nursing personnel must be aware of the need to care for physical and mental health with skill. [22]. In a study, 576 women were included, with an Impact of Event Scale of 31.4 ± 13.7. The study showed that women during their 2nd trimester of pregnancy have a more severe impact. The study reported moderate to profound stressful implications [23].

A report concluded that pregnant women suffered from psychiatric symptoms and had less sleep time. The exact relationship between sleeping and anxiety factors was seen in expectant mothers in the pandemic. The anxiety and depression outcomes amid the pandemic were 13.4% and 35.4%, respectively amongst pregnant women, and most outcomes were mild. The variations showed that bad sleep condition was highly connected with depression and anxiety [24].

During the COVID-19 infection, the two types of COVID-19 stress were: unpreparedness for birth and overstress about the prenatal COVID-19 infection. ≈30% of individuals indicated significant preparatory stress. Similar proportions reported newborn infection stress. Along with these, income loss, abuse history, and chronic illness were also reported [25].

3.3. Immunological response

Dhaundiyal et al. reported recompensation of preeclampsia through controlling angiotensin-(1-7) (Ang-(1-7)), and ACE2 is exceedingly articulated in pregnant women [26]. They have discussed the link between fetal ACE2 of SARS-CoV-2 and focused on its path of transmission risk in pregnancy. Also, the placenta shows the highest expression of renal ACE2 mRNA, which is also upregulated for pregnant women through the kidney and uterus. Although, in contrast to the uterus and placenta, the ACE2 activity is higher in the kidney [27]. In fetal tissues, for example, the lung, liver, and heart, the higher expression of ACE2 occur, but not in the kidney, which can upsurge the danger of transmission of COVID-19 from expectant mothers to neonates. This may also affect different organ systems with high expression of ACE2 and enable the disease transmission to develop in the fetus [28]. Preeclampsia is a complication of pregnancy identified by proteinuria and increased blood pressure. It is one of the prime reasons for fetal and maternal mortality and morbidity [29]. It was reported that the amount of mineralocorticoids, Ang II, and angiotensinogen are augmented in pregnancy, corresponding to preeclampsia [30].

The patients with +ve COVID-19 were hospitalized in ICU. The patient was lymphogenic during all measurements. The total B, T, and NK cells were low across the treatment [31]. An investigation found that 6.2% of pregnant women were influenced by Immunoglobulin M (IgM) and Immunoglobulin G (IgG) SARS-CoV-2-specific antibodies. 64% of women were +ve during pregnancy out of the 72 seropositive ladies who were exposed to nasopharyngeal polymerase chain reaction testing [32].

Thus, ladies during pregnancy have increased liability of acquiring viral infections. The impact of COVID-19 on expecting mothers and immune responses still requires further and targeted study [33].

3.4. Vertical transmission

A research group reported no vertical transmission in mothers and their neonates and advised that preventive steps must be taken following childbirth [34]. In contrast, a COVID-19 +ve baby was delivered by expectant mothers infected with SARS-CoV-2. It confirmed the silent unknown vertical virus transmission to the fetus from the mother observed by this study in the neonatal pharyngeal swabs, diagnosed +ve with COVID-19 [35]. Although in a few recent studies, virus in the mother's milk and placenta has been documented; still, whether this virus during pregnancy can be transmitted vertically or not remains under investigation [36].

During pregnancy, the increased expression of ACE2 handles the entry of SARS-CoV-2, which can cause favorable circumstances for SARS-CoV-2 contamination. The virus could affect fetal development through access via the placenta, which is proposed because of the virus in fetal membranes and placental villi. The SARS-CoV-2 vertical transmission is not yet completely ruled out, and data appears to be limited [37]. COVID-19 infection corresponds to an upsurge in India's intrauterine fetal demise rate and maternal mortality. Compared to other countries, India's vertical transmission rate is 2.99% [38]. A study conducted on 9 COVID-19 +ve pregnant women concluded no proof of infection spread from mother to fetus [39].

Through gestation, the transmittance of viral infections within the uterus from mother to neonatal is a very severe obstacle [40]. It can be caused by maternal infection by congenitally transmitted toxoplasma, rubella, cytomegalovirus, and herpes agents [41]. The transmittance of viral infection from mother to fetus takes place via blood. In these cases, transmittance occurs as follows: the mother's virus-infected blood invades the placenta and thus makes its way to the fetus's circulatory system. However, this transmittance mode is not shown by SARS and MERS [42].

3.5. Neonates

In a study, the newborns have examined -ve for COVID-19, although some were observed with perinatal complications. Also, in the instance, where the placenta was examined for COVID-19, and -ve results were found [40]. Other studies documented that newborns were infected with COVID-19 due to coming in contact with infected person [43].

The contrary effects on neonates, for example, premature labor, fetal distress, thrombocytopenia allied with the abnormal function of the liver, respiratory distress, and death, have been reported by prenatal SARS-CoV-2 exposure. Infants' -ve swab test reports challenged the spread of the virus from mother to fetus. Further, one infant born preterm died because of disseminated intravascular coagulation, refractory shock, and multi-organ failure [44]. Preterm birth, intrauterine growth restriction, neonatal death, and intrauterine death can be caused by COVID-19 during pregnancy [45]. In the serum samples, two newborns exhibited a high level of IgM antibodies out of six newborns with asymptomatic SARS-CoV-2 [46]. The obstetric ultrasound report observed the multivariate and dysplastic right kidney in the fetus. But these flaws were not proven due to COVID-19. The report displays that pregnancy can upsurge vulnerability to respiratory pathogens and corresponds to an immunosuppressive state [47]. Anemia decreased fetal movement, SARS-CoV-2 infected newborns, and dyspnea was experienced by pregnant women infected with SARS-CoV-2 in the 3rd trimester [48].

The viral contaminations in pregnancy could cause adverse consequences on maternal health, fetal development, and pregnancy results. Here, fetal and maternal immune defense mechanisms arose after establishing chronic infection. The inflammation triggered through viral infections, its potential downstream pathological effects in pregnancy, i.e., fetal demise and tissue damage, and the role of maternal immune activation is highlighted [49].

Another investigation reported no maternal deaths, no intrauterine viral transmission, and newborns were found -ve for COVID-19 [50]. Fan et al. found no malformations in SARS-CoV-2-infected mothers and neonates were also safe [51].

3.6. With concurrent disorders

Sickle cell disease (SCD) is a life-threatening and complex congenital blood ailment and the utmost common hereditary illness worldwide. A study strongly correlated pulmonary complications and SCD during pregnancy [52]. Pregnancy in SCD patients has been linked to augmenting fetal and maternal problems [53]. The SARS-CoV-2 infection may correspond to multiple organ failure and an acute respiratory distress syndrome (ARDS) [54]. In expectant mothers with SCD, severe pulmonary complications were common [53]. Ostling et al. studied a case report of 2 pregnant cases. The major difference between both patients was the severity of symptoms, and, based on these symptoms, both women were classified as ARDS caused by SARS-CoV-2 according to the Berlin definition [55].

Abdoli et al. reported that vulnerability to helminth infections also increases during pregnancy. Also, synergistic immunoregulatory effects of pregnancy and helminth infections may enhance hereditary infection susceptibility. An upsurge in severity and vulnerability of inherited transmission besides SARS-CoV-2 infection is possible with helminth infections in pregnant women, although inadequate data are accessible about SARS-CoV-2 inherited transmission [56]. Thus, co-infection with helminths and SARS-CoV-2 can lead to additional consequences than expected [57]. According to a study, helminth co-infection showed an extenuating effect on the severity of COVID-19 [58]. To explain the relation between SARS-CoV-2 and helminth co-infection, further research in clinical studies and animal models is required [59].

In contrast to non-infected women, infected women had elevated rates of the hypertensive disorder preeclampsia, preterm delivery, and preterm premature rupture of membranes [60]. Though, recent research is prone to biases concerning case series or case reports. To precisely examine the data, exploring additional aspects and attempts are required. Therefore, when advancing the research efforts and reading the copious yet inadequate body of evidence, this assessment hopes to offer proposals to assist clinicians in mitigating and highlighting some of these complications and making reasonable conclusions.

3.7. Vaccine debate

Skirrow et al. surveyed women's views and 81.2% said they would 'absolutely' get the COVID-19 vaccination if not expecting or pregnant. Acceptance of the COVID-19 vaccine was suggestively lesser for infants (69.9%, $p < 0.005$) and throughout pregnancy (62.1%, $p < 0.005$). In contrast to ladies from White ethnic groups ($p < 0.005$), the COVID-19 vaccine was rejected by twice times by ethnic minority women for infants, and for themselves when not expecting. Also, women under 25 years from some geographic regions and lower-income households were more likely to refuse the COVID-19 vaccine for infants and when not expecting. For rejecting the COVID-19 vaccines, the lack of trust in health system and vaccines were also the reasons given by women [61].

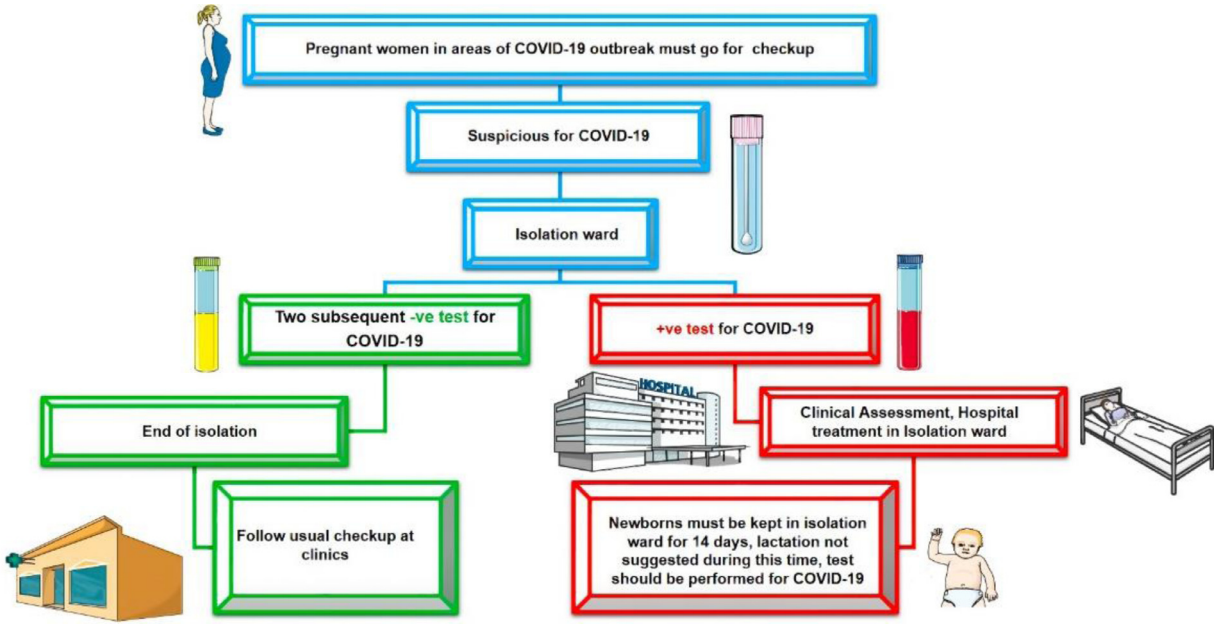

Fig. 3. Flowchart of consultation process for pregnant women with suspected COVID-19 infection.

More scientific studies about the cure of SARS, MERS, and COVID-19 are needed for new treatments and vaccines for pregnant women and better interpretation of the danger and advantages of vaccines [39]. Because of ethical and inadequate documentation, ladies during pregnancy are debarred from COVID-19 vaccine assay, despite being at equivalent risk of acquiring the concerning infection [62].

Today, up-to-date guidance is obtainable for managing COVID-19 during gestation [63]. Pregnant women must be considered in the vaccine development process, scientific examination, and later in promising vaccine trails except if the risk is more significant than the prospective advantage [64]. Other than these, case series and cohort studies illustrating other maternal consequences are summarized in Table S1.

4. Management recommendation for pregnant women

SARS-CoV-2 infection must be differentiated from other infectious and non-infectious disorders, and when concurrent with other infections must be carefully monitored and treated [65]. As noted before, COVID-19 has no specified therapy, and supportive care is the main treatment. With time passing, humans will have more detailed knowledge of COVID-19, whilst regular diagnoses and observation of COVID-19 in pregnant women must be contemplated. Also, standard design, medical check-ups, and execution of SARS-CoV-2 vaccines for pregnant women are suggested. The authors aspired humans can interchange the valuable experience with each other to help humankind against this alarming pandemic. During gestation, women are in greater danger of acquiring contracting infections. Thus, Table S2 and Fig. 3 illustrate the summary of management recommendations and consultation procedures for pregnant women with an uncertainty of SARS-CoV-2, respectively.

One report exhibited that among pregnant ladies +ve with COVID-19, 47% had premature delivery; Table S3 shows the observations in the study. Thus, this led to a strain on neonate health care services [66]. Personal protection must be used to reduce the risk ofacquiring COVID-19 [67], some tips are illustrated in Fig. S5. Timely screening and check-ups of pregnant women must be considered [68]. COVID-19 effects on pregnant women and their developing fetuses and newborns have not been thoroughly studied. Thus, it is crucial to keep patient samples of pharynx swabs, blood, tissue of the placenta, and amniotic fluid to get further knowledge on COVID-19 [69].

5. Approval of COVID-19 vaccine for 6 months and older babies

On June 18, 2022, a year and a half after the 1st US case, COVID-19 vaccines from Pfizer-BioNTech or Moderna are now available for children aged 6 months to <5 years. It will add roughly 20 million youngsters. But polling reveals most parents are wary. Even if vaccination uptake is poor, experts say most restrictions on young children should be eased. It is proposed that daycares and schools should improve ventilation and filtration [70,71]. Also, children aged 6 months to 4 years will get a lower vaccination dosage than youngsters of age ≥ 5. As newborns' and younger children's legs have more muscle than their arms, thus most will receive injections on their legs. Exceptions will be made for older children whose parents want the injection in the arm. The immunizations are timely, according to MUSC children's health. Since early April 2021, pediatric and adult cases have risen statewide [71].

COVID-19 vaccines undergo the most thorough safety monitoring. Because children are more susceptible demographically, it has been meticulously researched for far longer, and in various ways than any adult study. Injection-site pain, crankiness for one or two days, and occasionally a low-grade fever are common side effects of the vaccination. But, vaccines kept people safe and out of hospitals. 140 children from 6 months to 4 years old had been hospitalized with COVID-19 since the outbreak began, this data itself is a convincing justification for vaccinating young children. Experts claim vaccines protect more than just the recipient, since these youngsters live with adults, grandparents, and immunocompromised persons. The appropriate choice beyond the kids' vaccination might also benefit the upcoming school year. This should lower COVID-19 rates in preschool and elementary school [72].

On the contrary, an article by Dr. Marty Makary suggests the following:

- When examining effectiveness versus mild or serious COVID-19, the sample sizes of the trials were insufficient for statistical significance.
- The FDA lowered its standards for how effective a vaccine must be to be approved (lowered to below 50% efficacy).
- Most kids possess natural immunity.
- The research was done on small sample size, ignoring side effects like myocarditis causing electrocardiogram (ECG or EKG) abnormalities in youngsters. Establishing safety takes time.

- COVID-19 has a shallow risk of significant consequences in healthy youngsters.
- Lack of proper clarity and insufficient data on the impact of the vaccine on kids led to less trust of parents in case of vaccination of their kids. A CDC study showed that 18% of parents only approve of vaccinating their children of <5 years of age [73].

6. Latest studies

The below information includes the latest studies published on COVID-19 influence and pregnant women and their offspring or fetuses. Wilkinson et al. observed that pregnancy complexity overlap with COVID-19 risk parameters and examined SARS-CoV-2 consequences during gestation in England. To designate COVID-19 risk parameters in January 2020 for each pregnancy, modeled COVID-19 transmission statistics were used and fitted into a birthweight regression model. 43,802 pregnancies and 8,348 birthweight models were used to analyze COVID-19. Throughout the epidemic, stillbirth and infant mortality rates did not rise. This study showed no evidence of pandemic-related perinatal mortality. These findings suggest attempts to reduce COVID-19 instances in gestation, although extra fetal growth monitoring after COVID-19 may not be required [74].

Dileep et al. studied the link between COVID-19 infection's gravity throughout pregnancy and its consequences on the infant, as COVID-19 affects both mother and newborn. Classification of patients was done from mild-to-moderate contingent upon the infection. The bulk population, i.e., 74%, was multigravida. Women with serious illnesses gave birth to neonates with COVID-19 and were admitted to the Neonatal intensive care unit (NICU). The COVID-19 gravity or seriousness and multigravida led to premature labor, reduced birth weight, newborn infection, and NICU hospitalization. Thus, policies must be updated to lower the danger of unfavorable effects on newborns and pregnant mothers with +ve COVID-19 [75].

Jorgensen et al. reviewed remdesivir consequences throughout gestation and nursing. Pregnant women have a higher risk of COVID-19-related problems than non-pregnant women, highlighting the need for preventative and treatment initiatives. Despite innovative and adaptive trial designs in the COVID-19 outbreak, strategies exclude pregnant and nursing women from scientific research. Remdesivir, a wide-ranging antiviral, was the first medicine approved for COVID-19 therapy because it sped up hospitalized patients' recoveries. Pregnant and lactating women were disbarred from all COVID-19 remdesivir clinical studies, however post-marketing databases, compassionate use programs, and studies are gathering data [76].

Patel et al. used propensity score matching (PSM) to analyze COVID-19 and complications in pregnant women. Researchers conducted a retrospective case-controlled investigation on COVID-19 and pregnancy. Researchers enrolled 18–45-year-old females infected with SARS-CoV-2. In this peer group research, 2,374 individuals were found -ve, and 100 were found +ve for COVID-19. For the +ve COVID-19, unfavorable pregnancy outcomes were higher [77].

Kasraeian et al. studied COVID-19 in pregnant women and neonatal pneumonia. The study reviewed 9 publications comprising of 87 pregnant COVID-19 patients. 65% of patients were intimately related to an infected individual, 78% had lenient to mediocre symptoms, and 99.9% were cured. No indication of vertical transmission in late pregnancy was observed [78].

Vimercati studied COVID-19 in gestation, obstetrical risk parameters, and newborn consequences. 112 unvaccinated expectant mothers with +ve COVID-19 participated in a single-cohort trial. 35.25% of ladies had concurrent diseases, and 66.66% were obese, albeit only 4.1% were hospitalized with significant COVID-19 infection. COVID-19 was diagnosed in the 3rd trimester in multiparous mothers. And moderate to significant COVID-19 symptoms impacted delivery mode [79].

Liu et al. evaluated the COVID-19 pandemic's influence on newborns. This research examined lockdown tactics at a children's hospital. Diagnostics included two time intervals, i.e., pre-COVID-19 (12,082) and COVID-19 impacted (4,558) admissions totaled 16,640 babies. Per-week neonatal admissions were reduced by nonpharmaceutical interventions (NPIs). Thus, it was deduced that in the COVID-19 pandemic and related NPIs, infant admissions in tertiary care hospitals decreased [80].

He et al. evaluated the planning and contemplation for developing an isolation maternity unit in a tertiary hospital in the COVID-19 outbreak. It was teleconsultation research comprising pregnant women and their family members, and discussed the manner of delivery, newborns' after-birth disposition, and safety of nursing. The researchers reviewed the key aspect considered when developing an isolated maternity care unit and presented the ways for prepartum and postpartum care [81]. de Medeiros et al. investigated coronavirus effects on pregnancy and neonates. This research examined the maternal and fetal morbidity and death rate. The study comprised 10,047 expectant mothers with COVID-19, out of which 71.6% were in their 3rd trimester. Pregnant patients' placenta, breast milk, navel string, and amniotic fluid did not indicate COVID-19 [82].

Shook examined COVID-19 influence on fetal brain development. SARS-CoV-2 infection in pregnant women led to fetal, placental, maternal immune system activation and neurodevelopmental morbidity. An early intrauterine infection might affect fetal brain development through the microglial progenitor pool by affecting yolk sac-derived precursor cells [83].

Concerning concurrent diseases, Tessier et al. analyzed the COVID-19 influence on Bordetella pertussis and England's immunization program. Investigators analyzed pertussis patterns by age cohort and on monthly basis. Pertussis incidences throughout England's eased lockdown from July 2020 to June 2021 were analyzed. This pertussis prevalence ratio was compared to previous statistics (July 2014–June 2019). From April 2020, pertussis cases in all age categories decreased significantly, marking the least incidence in ten years. No concurrent SARS-CoV-2 cases were detected. Prenatal pertussis prevalence was 2.7% lesser during 2020–2021 [84].

Also, Venkata et al. studied hypoxic-ischemic encephalopathy (HIE) and associated illnesses before and during the COVID-19 epidemic. Multiple newborn fatalities were the prominent outcome. Frequency and seriousness of HIE in inpatient neonates, overall mortality, brain damage, etc., were subservient outcomes. This research included 1,591 neonates with HIE. Odds ratio (OR) and confidence intervals (CI) were determined. Primary outcomes did not change significantly (15% vs. 16%; OR 1.08; 95% CI 0.78–1.48). HIE severity, related morbidity, and death did not change throughout the lockdown phase and before the pandemic [85].

Contemplating the maternal C-reactive protein (CRP) use in medical examination, Geng et al. studied the influence of term nulliparas with premature rupture of membranes (PROM) delays at home in the newborn. This study created two models for diagnoses: the univariate CRP model and composite CRP cut-off value (CRP with PROM waiting time at residence). The study inferred that the acute COVID-19 national shutdown might continue to affect PROM infants' health during the COVID-19 easing period [86].

Considering the vaccine debate, Kons et al. examined the exclusion of reproductive-age women from COVID-19 vaccination and medical investigations. The US database defined the inclusion and exclusion criteria for all COVID-19 vaccines. Most COVID-19 vaccination and medical studies excluded pregnant and nursing women. 97.8% and 81.1% of the vaccination trials excluded pregnant and nursing women, respectively, while 62.2% needed contraception. Despite documented safety descriptions, COVID-19 vaccine and therapy medical research restricted women who are pregnant, nursing, and non-user of contraceptives, thus reflecting patterns or trends seen in the historic patterns of vaccine trials [87].

Also, Nunes et al. studied vaccination's effects on pregnancy. SARS-CoV-2 causes unfavorable outcomes and preterm labor in pregnant women. The researchers highlighted the mRNA COVID-19 vaccine,

frequently given to pregnant women, as evidence of its safety and efficacy. The mRNA vaccination showed no harmful effects. Inactivated viral and protein-based vaccines need more exploration [88].

Goldshtein et al. observed BNT162b2 COVID-19 vaccination effects on pregnancy and newborns. This study includes all singleton live births in a large Israeli health care organization through September 2021. Out of 24,288 eligible neonates, 16,697 in the 1st and 2nd trimesters were vaccinated in utero. Thus, it was concluded that newborns of ladies who received BNT162b2 mRNA immunization during pregnancy are not different—however, observational design limits this study's conclusion [89].

Further, Prasad et al. assessed COVID-19 vaccination's efficacy and perinatal effects. 23 studies involving 117,552 pregnant ladies vaccinated with mRNA COVID-19 provided the evidence. The RT-PCR assay showed that mRNA vaccination effectiveness was 89.5% for SARS-CoV-2. Also, mRNA vaccination does not lead to early labor, placental abruption, lung embolism, maternal death, etc. Thus, the study concluded that COVID-19 mRNA vaccination sounds safe and reduces stillbirth [90].

Thus, these data emphasizes on the current studies and their pieces of evidences. Also, this information highlights the major knowledge gaps to aid clinical decision-making concerned with pregnant ladies, their neonates or fetuses, lactation, concurrent disease, associated COVID-19 risk parameters, and effects of the vaccine on the expectant mothers and their newborns/infants/toddlers i.e all the stages of early childhood.

7. Future perspectives

To sum up, all reviews and the literature mentioned above reported how the novel SARS-CoV-2 virus affects pregnant women, neonates, and related consequences from the infectious stage to the post-COVID-19 period. Although, in terms of specific outcomes and associated preventive measures to be taken are still unclear. However, the critical cases of COVID-19 have been detailed and discussed in the present review. This virus can be asymptomatic or show mild to intense symptoms in pregnant women. Data suggests that COVID-19 may affect the placenta. Intriguingly transplacental virus transmission and unfavorable pregnancy outcomes are also not explored much. Also, the influence of SARS-CoV-2 on the placenta requires additional research [91]. Many strategies and preventive measures have been utilized to diagnose COVID-19 but still their is scope of improvement, Treatment of pregnant women (irrespective of age) who are diagnosed with the COVID-19 in the early stage is required, thus to restrict its severity of complications during pregnancy and to avoid its transmission in their offspring and other pregnant women whom they may have encountered in clinics or hospitals during a routine checkup. Many randomized trials have been employed for the development of universal treatment against COVID-19. The development of a new drug and vaccine is needed to keep in mind the vulnerable effect and continuous mutation of the novel COVID-19. The newly developed vaccine trials must be practiced on animal models to evaluate the several aspects of human diseases and determe the factors of vaccine safety and efficiency. This review has assembled worldwide studies on outcomes of COVID-19 infection in pregnant women and neonates, thus making it easier to understand the complications and risk factors of contracting COVID-19 by the vulnerable and susceptible population i.e. pregnant women and their newborns/ infants/ toddlers.

8. Conclusion

The studies reported were established on a sizable number of pregnant COVID-19 cases. But still, there is a need to include more cases of pregnant patients +ve for COVID-19 to set up a piece of strong evidence, and therefore, has a broad scope to be explored. Also, the effect of the SARS-CoV-2 virus on the placenta needs more study. Insufficient information, corresponding studies, deficiency in check-up span, inborn biased nature of current literature, dissimilar incorporation standards, and restrictions of systematic eviews further hampers the potential for precise date extrapolation. As COVID-19 patients grow internationally, focus on improving the current situation, instant awareness, and further detailed research regarding the COVID-19 virus nature is an urgent requirement. The accumulated knowledge will form a base to support and hasten the urgent research necessary to understand and respond to pregnant women and neonated diagnosed with COVID-19. Also, the preparation required for restricting transmission of COVID-19 from pregnant mother to their newborn or fetus is required. As COVID-19 has become a worldwide catastrophe, the world must brace for its return. This review accumulates the latest studies of COVID-19 impacts on pregnant women and newborns, vaccine debate and management recommendations, updates regarding COVID-19 vaccination approval for 6 months and older babies; prospects, etc. but still there is a window for exploring more about the same. Finally, we salute the global frontline health workforce working day and night to fight against the COVID-19 pandemic.

Funding

N/A.

Ethical approval

N/A.

Participation consent

N/A.

Publication consent

N/A.

Availability of data and material

N/A.

Availability of code

N/A.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Kritika S. Sharma: Methodology, Data curation, Writing – original draft. **Rekha Sharma:** Data curation, Writing – original draft. **Sapna Nehra:** Writing – original draft. **Naresh A. Rajpurohit:** Writing – original draft. **Kaushalya Bhakar:** Formal analysis, Writing – original draft. **Dinesh Kumar:** Writing – review & editing.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hsr.2022.100044.

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