Corona in Infants: New Drugs and Vaccinations for Mothers

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ABSTRACT

Corona viruses are a group of enveloped viruses that cause respiratory, intestinal, liver, and neurological diseases of varying severity in a wide range of animal species, including humans. The virus has caused a great deal of concern around the world. As viral pneumonia is an important cause of complications and mortality in pregnant women, one of the concerns related to the dangerous outbreaks of viruses is the health of mothers and infants.
The findings show that children are vulnerable to the infection. Preventing the spread of the COVID-19 virus is the first step in controlling the epidemic in mothers and children.
 There are many questions about the effect of the virus and ways to prevent it from affecting mothers, but the important thing is to provide a reliable treatment, such as vaccination. Vaccination of mothers can be considered as a way to protect their health against corona virus.
Keywords: Corona, infants, new drugs, vaccinations, mothers

INTRODUCTION

Coronaviruses (CoVs) are a group of various enveloped viruses that cause various diseases in humans and animals[1]. These viruses belong to the subfamily Orthocoronavirinae in the family of Coronaviridae of the order Nidovirales[2]. In December 2019, a new Coronavirus was found in China, first named 2019-nCOV and then SARS-CoV-2, and its resulting disease as COVID-19[3]. Human Coronaviruses are broad-spectrum RNA viruses that cause one-third of the colds in adults[4]. Viral pneumonia is one of the most important causes of complications and mortality in pregnant women[5]. Although the early stages of this epidemic disease were widely reported among the adults, further studies have indicated that young children and infants are also vulnerable to the infection[6,7]. Therefore, in the present study, it is tried to examine the published articles on the neonatal and maternal incidence of new Coronavirus, in other to investigate the virus effect and ways to prevent maternal and neonatal infection.

MATERIALS AND METHODS

The present literature study was conducted in May 2020 with the aim of examining the aspects of neonatal Corona virus and reviewing new drugs focusing on maternal vaccination. Search engines and scientific databases of Google Scholar, Science Direct, PubMed, Medline and Cochrane were used to make this assessment and to obtain the desired articles on the findings of neonatal Coronavirus infection and treatment. To gather information in this area, in terms of content, keywords were searched in the desired databases, such as Coronavirus, outbreak in the world, outbreak in infants and mothers, clinical symptoms, vaccination, etc. Out of 192 articles, 57 were considered in terms of subject coverage, content structure, appropriate purpose, and citation possibility.
Corona virus: Coronaviruses are a group of viruses that cause respiratory, intestinal, liver, and neurological diseases of varying severity in a wide range of animal species, including humans[8]. Coronaviruses have caused three epidemics: Severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and COVID-19 (Coronavirus Disease 2019)[9]. The new Coronavirus (COVID-19) was first discovered in Wuhan, the center of Hubei province in China[5] . These Coronaviruses are zoonotic and can be transmitted from one animal to another, from animal to human, and from human to human[10]. Corona viruses have a a helical capsule, and their approximate genome size is 26-32 kb[11]. The virus's genome encodes at least four major structural proteins including the spike-shaped protein (S), and membrane (M), envelope (E), Nucleocapsid proteins (N), and also the other proteins required for the virus's replication and entry into the cell[12]. The incubation period of this disease is about 7 to 14 days[13]. The mortality rate from COVID-19 (3%) has been much lower than the mortality rate for SARS (10%) or MERS (40%)[14].
Clinical Symptoms: The clinical symptoms of COVID-19 are classified into four levels based on the severity of the symptoms: Mild, moderate, severe, and critical. Mild patients have only mild symptoms and no radiographic features. Moderate patients with fever, respiratory symptoms, and radiographic features. Severe patients have one of the following criteria: (a) shortness of breath (SOB) and respiratory rate (RR) more than 30 times per minute, (b) oxygen saturation less than 93% in ambient air, and (c) PaO2 / FiO2 less than 300 mm Hg. Critical patients also have three criteria: a) respiratory failure, b) infectious shock, and (c) multiple organ failure (15). The symptoms of this disease are completely shown in Table 1.
Although COVID-19 relatively affects the respiratory and cardiovascular systems, the patients with severe symptoms are more likely to have neurological symptoms (such as headaches, dizziness, decreased sense of smell and taste, and nerve pain) and the complications such as encephalopathy, acute brain diseases, awareness disorder,

and skeletal muscle damage are also seen[16]. In China nine admitted infants were reported with COVID-19 diagnosis. The minimum age of these infants was 1 month and the maximum was 11 months. Of the nine infants, four had fever, two had mild respiratory symptoms, one had no symptoms, and no information was available on the symptoms of the two. The duration of hospitalization and diagnosis was one to three days. All the nine infants had at least one infected family member, and the infant infection occurred after infection of the family members. These nine infants did not require intensive care or mechanical ventilation and no serious complications[6].

Table 1: *Clinical, laboratory and radiographic symptoms of new Coronavirus (COVID-19)(15)*

Clinical symptoms	1. Fever, dry cough, muscle aches, fatigue, SOB, and anorexia. Fever and cough are the main symptoms; diarrhea is not common. 2. Insufficiency of several organs, including kidney damage, liver damage, and testicular tissue damage 3. Mild patients: low fever, mild fatigue, and no pneumonia 4. Severe patients: SOB or hypoxemia one week after the onset 5. Critical patients: Acute Respiratory Distress Syndromes (ARDS), facial shock, etc. SOB, abdominal pain, and anorexia are also common. 6. 80.9% having mild/common, 13.8% having severe and 4.7% having critical pneumonia.
Laboratory symptoms	1. Decreased total lymphocyte, long-term PT, increased LDH, AST, ALT, blood urea and creatinine 2. Most patients had C-reactive protein (CRP) and high levels of red globules deposition and normal procalcitonin. 3. Severe cases: D-dimer increases and cutaneous lymphocytes gradually decrease. 4. Patients with critical: High inflammatory factors 5. In fatal cases: the number of neutrophils, D-dimer, blood urea and creatinine is very high.
adiographic symptoms	1. Bilateral distribution of stained shadows and background glass turbidity was a prominent feature of CT scanning for NCIP. 2. Radiological abnormalities occur in a significant number of patients in the initial presentation. Lung extraction is rare.

The Worldwide Outbreak: So far, three pathogenic human Coronaviruses have been diagnosed, including MERS-CoV, SARS-CoV, and the new Coronavirus, COVID-19. SARS-CoV was first reported in 2002 in China. The death rate from the virus is about 10%, while MERS-CoV was first reported in 2012 in Saudi Arabia, and the death rate is 34.4%. COVID-19, first reported in December 2019 in Wuhan, China, has a higher transmission rate than the two Coronavirus types (SARS-CoV and MERS-CoV)[14,17] but with a mortality rate of 3%, it has the lowest mortality rate in comparison with the other Coronaviruses[14]. From mid-December 2019 to early June 2020, the virus crossed the global borders of 215 countries and regions, infecting more than six million people and killing about 400,000[15,18]. The United States has the highest incidence of mortality[18].

Neonatal and Maternal Outbreak: Although the evidences of COVID-19 epidemics in the early stages of the disease illustrate that adults over the age of 15 were involved, further studies showed that young children and infants were also vulnerable to the infection and could be infected[6,7,19]. Symptoms such as fever and respiratory distress have been reported in infants[20]. While children with COVID-19 rarely have severe complications, the infection may be more severe in infants[21]. Despite the development of the COVID-19 epidemic, little is known about its infection in infants and children and their clinical picture. The most important question is whether COVID-19 can be transferred vertically from the pregnant mother to the fetus and causes a significant clinical infection?[22]. In general, pneumonia or viral pneumonia is an important cause of death in pregnant women and has adverse side effects such as premature rupture of membranes and preterm delivery, intrauterine fetal death, intrauterine growth restriction and neonatal death[5,23]. Adverse side effects (such as abortion and death) have been reported from Coronaviruses in infants. It is unknown at this time whether the COVID-19 virus can be transmitted through breast milk, but it is clear that an infected mother can transmit the virus to her baby through respiratory droplets while breastfeeding[5]. Limited information on COVID-19 disease is available during pregnancy. However, the information about diseases associated with other highly pathogenic Coronaviruses (such as SARS-CoV and MERS-CoV) can be helpful in determining the effects of Coronavirus 2019 during pregnancy[24]. According to the data from these Coronaviruses (SARS-CoV and MERS-CoV), pregnant women are at higher risk for severe disease or death than the other members of society[5,23]. Physiological and immunological changes, such as increased heart rate, stroke volume, decreased oxygen consumption, and lung capacity, as well as the development of immune adaptation, as natural events during pregnancy, can have systemic effects and increase the risk of complications from respiratory infections[3]. There has been no evidence of uterine transmission in SARS or MERS Coronaviruses[24]. The report, presented by Chen et al., found no evidence of positive testing among the infants born to the mothers (during the 3rd trimester) with positive testing result. Therefore, there is no evidence of intrauterine infection due to vertical transmission in the women with COVID-19 pneumonia in late pregnancy[22]. As COVID-19 may increase the risk of pregnancy complications, careful and close monitoring of the mother and fetus should be performed in a management medical center. These management measures may include early isolation, methods of infection control, oxygen therapy, experimental antibiotics, laboratory tests for virus and infection, monitoring of fetal and uterine contractions, initial mechanical ventilation for progressive respiratory failure, personal delivery planning, and a team-based approach with multi-purpose consultations[24].

Risk Factors: Several studies have reported risk factors for death in the patients with COVID-19[25]. age over 65 greatly increases the risk of COVID-19 mortality. According to their study, there was no significant relationship between gender and mortality. They also reported a positive relationship between diabetes, hypertension, COPD, COV

and COVID-19 mortality[25]. Wu and colleagues also found that age, high blood pressure and diabetes were among the factors influencing the increase in mortality from the virus[25]. Factors such as history of smoking, maximum body temperature during hospitalization, respiratory failure, albumin, and CRP can also lead to the development of COVID-19 pneumonia[26].

Other studies have shown that age, heart failure, diabetes, chronic lung disease, high blood pressure, cancer, brain disease, and kidney disease have all been important factors in COVID-19. The age of over 80 years was 21% and infants were less than 2%[27,28].

The Disease Prevention and Treatment: Control of virus-infected patients is recommended as a step to control and prevent the widespread transmission among individuals[29]. People should be follow their local health guidelines, and by cutting off the transmission chain, prevent further spread of the virus[30]. Medical masks can help prevent direct exposure to respiratory droplets from the infected patients[29]. Washing their hands regularly with soap and water for at least 20 seconds or rubbing hands is another preventative measure. They should also stay home if they feel unwell or sick, except when they need medical care outside the home. Social distance, it means at least one-meter distance between a person and others, should be maintained and close contact with people who are ill should be avoided[30,31].

Due to the volume of the virus in closed and indoor places, it is important not to be in crowded and covered places to reduce the incidence of the virus[32,33]. Increasing the performance of the immune system can be another preventative and safety factor. Increasing the immune system of mothers can be enhanced with the help of physical activity, antioxidant consumption, and stress reduction, and can protect mothers against the virus[34,35].

Studies of pregnant women have also shown promising results, and it has been shown that pregnancy does not increase the risk of Coronavirus infection. However, the findings indicated that all the reported pregnant patients were under 30 years of age and may not have severe symptoms due to their young age[36], but 44% and 36% of the pregnant women had an initial onset of fever, which clinically showed a less rate in the symptoms and severity than in non-pregnant people[37,38].

Vaccination and its Hypotheses: Rapid diagnosis, vaccination, and treatment are important factors in managing the spread of the new Coronavirus[14]. Given the potential threat of the epidemic to public health, scientists and physicians are competing to understand the new virus and the pathophysiology of the disease, to discover possible treatments and effective vaccines. The disease can pose major challenges to global health systems, and if left unchecked, it will have far-reaching consequences for the global economy[39]. To date, no antiviral factor or drug for SARS-CoV-2 has been developed[39], but many vaccines have been successfully tested in the laboratory. Japan, Australia, and Canada have introduced the vaccines with reasonable immunizations and are awaiting the approval for health procedures.

Vaccines prevent and protect against the infection and incidence of the disease when exposed to specific pathogens, especially in vulnerable populations. Regarding the current outbreak of the new coronavirus, vaccines help control and reduce the spread of the disease by creating herbal immunity in addition to protecting healthy people from the infection. However, there are social, clinical, and economic barriers to vaccination programs such as the public's enthusiasm for the vaccination with a new vaccine, the side effects and severe complications of the vaccination, potential differences or low efficacy of the vaccine the in populations different than the clinically tested population, and the vaccine access for a specific population[14].

The developing vaccines include virus- based vaccines, DNA vaccines, peptide-based vaccines, virus-like-particles-based (VLPs) vaccines, inactive whole-virus (IWV) vaccine, and vaccines with alive but weaken virus[14]. Some vaccines are also made based on the S protein of these viruses. The virus's genome encodes several structural proteins, including glycosylated S protein, which acts as a major factor in the host's immune response. These viral proteins, which are responsible for the virus entry into the host cells and its reproduction, are structurally similar to the proteins associated with them in SARS-CoV. Therefore, research on SARS and MERS Coronaviruses can be useful for the development of therapeutic and preventive drugs for COVID-19[39]. S protein, which plays the most important role in the fusion of the virus and its entry, serves as a target for the production of antibodies, the inhibitors of the virus and vaccines[17]. The entry of SARS-CoV and SARS-CoV-2 viruses into the host cell occurs through binding to a receptor protein called Angiotensin-Converting Enzyme 2 (ACE2) located on the membrane surface of the host cells[39]. The S protein mediates the entry of the virus into the host cells by binding to the host receptor through the receptor binding domain (RBD) under the subunit S1 and then aligning the virus and host membranes through the subunit S2[8]. RBD protein binds strongly to human and bat ACE2 receptors. The RBD binding orientation in SARS-CoV-2 to the ACE2 receptor is significantly higher than the RBD in SARS-CoV and therefore can block the RBD binding in SARS-CoV-2 and RBD in SARS-CoV to ACE2 expression cells, followed by the host cells infection. Specific SARS-CoV RBD antibodies can interact with SARS-CoV-2 RBD protein, and SARS-CoV RBD antisera can counteract SARS-CoV-2 mutually. This suggests the potential for the development of SARS-CoV RBD vaccines to prevent SARS-CoV-2 and SARS-CoV infections[17].

RBD is also targeted in many drug design studies. A peptide sequence with a sequence similar to the RBD of S protein hinders the interaction of S1‑RBD: ACE-2 and prevents Coronavirus from entering the host cells. Some of these drugs include OC43 HR2P (a regions S2 HR-derived peptide), Chloroquine (an antimalarial drug), SSAA09E2 (inhibitor of S binding to ACE-2), and SSAA09E3 (inhibiting the fusion of the host cells and virus[39]. Remdesivir (GS-5734), the most promising antiviral drug against RNA viruses, is also used to fight the virus[40]. The recommended dose of Remdesivir for children and infants weighing between 3.5 to 4 kg is 5 mg / kg IV (injection over 30 to 120 minutes) on the first day, followed by 2.5 mg / kg IV (over 30 to 120 minutes) once a day for 9 days (days 2 to 10) as an injection[40]..

Immune System, Pregnancy and Infants: Studies have indicated that infant mortality rates for Coronavirus are low. Examination of the children with Corona has indicated that these children have very high levels of specific lymphocytes in their blood levels compared to adults. CRP protein has also been lower in children. CRP protein plays an important role in the inflammatory response of the immune system. During pneumonia in adults, the inflammatory response and inflammatory proteins in the blood increase, and this inflammation makes the healing process difficult. But in young children and infants, the immune response acts more quickly and destroys invasive microbes[41,42,42]. Despite this, the hypothesis can be stated that in most cases, infants who have died of Corona have a weakened immune system.

Studies on the immune system in pregnancy have shown that the women infection with infectious diseases during pregnancy predisposes them to dangerous childbirth. The immune system continues to function during pregnancy, but the factors such as diet, sedentary lifestyle; gestational diabetes, etc. affect the immune system. After hosting the virus, the immune response in the blood of the pregnant women increases, and the immune system of the fetus and the placenta continues to function. However, the findings suggest that any infection in the pregnant women could be dangerous to the fetus and should be considered[44-49].

CONCLUSION

The findings illustrate that infants, like other age groups, are at risk for Coronavirus, but the symptoms are less common in infants. There have been reports of neonatal deaths, indicating that they pose many risks if they become infected. Babies do not have a language to talk and express their problems when it comes to the disease, so no symptoms such as sore throat and body aches have been reported, but they certainly feel the symptoms.

The findings showed that the fetus did not have the virus in mothers carrying the disease, and there was no evidence of intrauterine infection due to vertical transmission in mothers. However, due to the complications of pregnancy, it is important for the mother and fetus to closely monitor the management of treatment.

Scientists and doctors are working around the clock to discover possible treatments and effective vaccines for the disease. Vaccination helps to control and reduce the transmission of the disease by creating herbal immunity in addition to protecting healthy people from the infection. Therefore, maternal vaccination can be effective as a treatment option.

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