REVIEW ARTICLE

Pandemic of COVID-19 and Pregnancy

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ABSTRACT

Background and Objective: Infectious disease outbreak caused by novel Coronavirus is a global public health concern. In this pandemic, pregnant women are high risk population. Knowledge and data on the effect of this COVID-19 disease on pregnant females and their newborns is limited. Number of cases is increasing day by day. Aim of the current study was to provide evidence-based knowledge related to effects of Coronavirus on pregnancy to improve the understanding of the COVID-19 disease.

Methods: This is a systematic review, carried out in the Department of Obstetrics & Gynecology at Shalamar Medical and Dental College, Lahore. The available published research data from January 1st 2020 to May 13th 2020, on the effects of Coronavirus in pregnancy was collected. On the basis of Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines the articles in English were selected from electronic databases PubMed and Goggle scholar.

Results: The information gathered is organized in five main themes namely; Clinical manifestations of COVID-19 during pregnancy, risk of vertical transmission, issues related to breast feeding, care during antenatal period and labor and strategies for prevention. The main concern is to focus on best clinical practices for care of pregnant females.

Conclusion: Clinical manifestations of Coronavirus infection in pregnant females are not different from general population. There is on strong evidence of risk of vertical transmission. Best antenatal care and care during labor is the right of all pregnant females whether suspected or infected and it must be according to the standardized guidelines. Breast feeding is encouraged either with full protection of transmission of droplet infection or my expressing milk manually. Vaginal delivery is safe and preventive strategies for the disease available for general population must be adapted by the pregnant women also to avoid getting the infection.

KEYWORDS: COVID-19, Pandemic, Pregnancy, PRISMA, FIGO.

How to Cite This:

Sohail S, Dar LR. Pandemic of COVID-19 and pregnancy. Biomedica. 2020; 36 (COVID19-S2): 206-12.

INTRODUCTION

Coronavirus disease-2019 (COVID-19) which began as viral epidemic in Wuhan city of China in December 2019 has now inundated the entire planet.[1] Initially it was reported as an outbreak of pneumonia of unknown etiology in Wuhan but on January 9th 2020, Chinese Centers for Disease Control and Prevention (CDC) reported a novel Coronavirus as a causative agent.[2] This viral disease is highly contagious. The outbreak which was started in December 2019 in China spread rapidly and World Health Organization (WHO) declared it as pandemic on March 11,2020 and by March 25, 2020 in just three months 4,16,916 cases were reported worldwide involving 150 countries both developed and undeveloped.[3,4] Disease is still progressing and by May 13, 2020 a total of 213 countries and territories were involved.[5] Almost

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every person of planet earth is affected by this pandemic directly and indirectly. Elderly population and people with underlying comorbidities are more susceptible. The causative agent 'severe acute respiratory syndrome Coronavirus-2' (SARS-CoV-2) is an encapsulated single stranded RNA virus which spreads through droplets from the cough or sneeze of infected person. The spectrum of symptoms of the disease ranges from mild flu like symptoms to severe respiratory illness needing intensive care units care and ventilator support. Incubation period is 5 to 7 days on average, however can be up to 14 days. Most of the people suffer from mild to moderate form of the disease which is settled in one to two weeks.[6] Number of COVID-19 cases are increasing rapidly as currently no vaccine or standardized treatment is available and the health professionals are still in learning phase because the course and effects of the disease is new and emerging. Globally the aim is protecting the most vulnerable population from severe illness and reducing transmission in general population. Physiologic changes in immune system make pregnant women more susceptible to it. United Kingdom has also declared pregnant women as a vulnerable population .[7]

Research on the effects of COVID-19 infection in pregnancy is still in infancy and limited data is available about the pregnant women with COVID-19. This systematic review was carried out of the published research to understand the gaps in the knowledge of effect of COVID-19 during pregnancy with the aim that this research will provide the evidence to improve our understanding of the disease during pregnancy for more effective care of the pregnant women affected by COVID-19.

METHODS

A systematic review of published research on the COVID-19 during pregnancy was conducted from January 1st to May 13th 2020 in the Department of Gynecology & Obstetrics, at Shalamar Medical and Dental College, Lahore. Preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines were used. Articles were selected from electronic databases PubMed and Goggle Scholar. A selection criterion was to collect the research published in English language on the effects of novel Coronavirus infection in pregnancy. Duplicate items were excluded. Further screening was performed by exclusion of articles in language other than English and not having relevant information. The information gathered was analyzed and organized in different themes. Eight reference articles related to inclusion criteria were finally selected.

RESULTS

The screening of the clinical data available as far as COVID-19 with pregnancy is concerned is given in the Table-1 as follows:

Table-1: *Summary of the Clinical Data on Pregnancy with COVID-19.*

Author Name	*Country*	*Title*	*Study Type*	*Key Findings*
Chen et al[8]	China	Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records.	Retrospective review	Main symptoms being fever and cough. No evidence for vertical transmission in late pregnancy.
Zhu et al[9]	China	Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia.	Retrospective study	No evidence for vertical transmission in pregnancy. Perinatal 2019-nCoV infection may have adverse effects on newborns, causing problems such as fetal distress, premature labor, respiratory distress, thrombocytopenia accompanied by abnormal liver function, and even death.
Yu et al[10]	China	Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective single-centre, descriptive study.	Retrospective descriptive study	The maternal, fetal, and neonatal outcomes of patients who were infected in late pregnancy appeared very good. The clinical characteristics of these patients with COVID-19 during pregnancy were similar to those of non-pregnant adults with COVID-19.
Rasmussen et al[11]	USA	Coronavirus disease 2019(COVID-19) and pregnancy: what obstetricians need to know.	Review article	Standard interventions to manage any severe respiratory infection are the foundation of care for

Author Name	*Country*	*Title*	*Study Type*	*Key Findings*
				any pregnant woman with COVID-19 and should be implemented aggressively in a team-based care model.
Schwartz and Graham[12]	USA	Potential maternal and infant outcomes from Coronavirus 2019-nCoV (SARS-CoV-2) infecting pregnant women: lessons from SARS, MERS, and other human Coronavirus infections.	Review article	There is limited knowledge regarding Coronavirus infections that occur during pregnancy. Previous experiences with SARS and MERS suggest pregnant women should be considered at high risk for developing severe infection during this current outbreak of 2019-nCoV.
Wu etal[13]	China	Coronavirus disease 2019 among pregnant Chinese women: Case series data on the safety of vaginal birth and breastfeeding.	Cohort study	Vaginal secretions are negative for virus suggesting vaginal delivery is a safe option.
Bauer et al[14]	USA	Obstetric anesthesia during Coronavirus disease 2019 pandemic.	Narrative review article	Best strategies is to ensure safe care for parturient and to prevent health workers exposure required. General anesthesia should be avoided women who are untested or known to be COVID 19 positive. Early neuraxial analgesia is recommended in labor. Spinal anesthesia is the choice for caesarean.
Stumpfe et al[15]	Germany	SARS-CoV-2 infection in pregnancy – a review of the current literature and possible impact on maternal and neonatal outcome.	Review article	Clinical course of COVID-19 disease may be complicated by pregnancy. No vertical transmission of COVID-19. Breast feeding can be started once disease is cured.

Clinical Manifestations of COVID-19 during Pregnancy

The studies show that the clinical manifestations of COVID-19 infection during pregnancy are not different from the non-pregnant population. Common symptoms are fever, myalgia, cough, diarrhea, loss of sense of taste, shortness of breath. A study conducted in Zhongnan hospital in Wuhan, China on nine cases of COVID-19 infection in pregnancy 78% cases manifest fever as a main symptom.[8]Fever range from 36.5ºC to 38.8ºC. Fever is usually not associated with chills. These studies show other common symptoms are cough and myalgia. A study at Tongji Hospital Wuhan also reported fever in 86% of pregnant females with COVID-19 infection. Pregnancy increases the susceptibility of respiratory infections due to changes in the immune system. Studies described above showed the severity of pneumonia is not different from the non-pregnant population.[10]Chen et al[16] also reported that from December 8, 2019, to March 20, 2020, they identified 118 pregnant women with COVID-19 in Wuhan and the present data do not suggest an increased risk of severe disease among pregnant women, as has been observed with influenza.

Risk of Vertical Transmission

A study on 31 infected mothers indicated no vertical transmission patients admitted to hospitals outside Wuhan December 8th 2019 to February 25th 2020, found no serologic evidence suggestive of vertical transmission of SARS-CoV-2.[17] A retrospective review of records of patients in Wuhan from January 20th to January 31st 2020 also showed no risk of vertical transmission.[8] Chen's results also indicated that COVID-19 infection in the third trimester were less likely to be associated with neonatal complications and adverse outcomes.[16] A study by Zheng et al[18] also suggests that there may be no cells that are potentially susceptible to COVID-19 in the maternal–fetal interface, hence there is no risk of vertical transmission. Zhu H et al.[9] in clinical analysis of 10 neonates born to mothers with COVID-19 found no risk of vertical transmission. In most of these studies samples were taken from amniotic fluid, umbilical cord and placenta and newborn were assessed and monitored by neonatologists for developing the signs and symptoms of disease. Infection is suspected due to vertical transmission in one or two cases but there is no strong evidence for it and literature supports no vertical risk of infection in neonates.

Breast Feeding

The available literature suggests that there is no evidence of secretion of the virus in infected mother's breast milk. Study in China on specimens

of breast milk of eight females show that no virus is detected in samples. However there is risk of transmission of the disease from the infected mothers due to droplet infection during breast feeding.[15] UNICEF recommend that mothers can breast feed their babies by taking precautions like wearing masks and shields.[19] However in most centers newborns are kept separated from the infected mothers for two weeks as a precautionary measure to avoid infection. Mother can express the breast milk for baby.[13]

Need of Care during Antenatal Care and Labour

Pregnancy is a stressful experience in pandemic of Corona. Pregnant females are anxious about the effect of Corona on their fetus. International Federation of Gynecologists and Obstetrics (FIGO) recommend the pregnant females must be monitored for health and wellbeing by Obstetricians.[7] FIGO has issued comprehensive guidelines for pregnant females' algorithm 1, 2 and 3 described below for care of the pregnant females in this pandemic of Coronavirus infection. It is important to emphasize that pregnant females must remain in contact with their health care providers and if they develop symptoms of fever, cough, shortness of breath and have history of travel or contact with the COVID-19 disease patient they must inform their health facility. In case of mild symptoms of fever, or cough they stay at home and self-isolate for at least seven days, during which they avoid contact with others. They must remain in contact with their maternity service provider telephonically and if symptoms deteriorate admission is required. Obstetrical Scan for assessment of fetal wellbeing is required two weeks after the recovery. All pregnant women with fever and signs and symptoms of cough, shortness of breath, diarrhea and history of any possible exposure must be screened and evaluated. For routine care and antenatal checkup prior telephonic appointment must be taken as hospitals are trying to minimize the contact and spread of infection so routine antenatal visits are reduced. Antenatal care is essential for wellbeing of mother and fetus but the maternity team member must assess the pregnant lady telephonically. Six face to face appointments are recommended.[20] C-section is reserved for obstetric indications. COVID-19 infection is not an indication for C-section.[21] Study of showed that there is no evidence of detection of virus in the vaginal secretions of the infected mother, so vaginal delivery is safe for the baby.[13]

In order to handle the situation of COVID-19 in the department of Gynecology and Obstetrics, there is an urgent need for the guidelines and protocols by authentic boards and governing bodies which can be helpful in providing some suitable solutions to various queries as well as to manage the unlimited burden of gynecology and obstetrics. For this purpose, Poon et al[20] has been successful in providing algorithms for presentation to triage for pregnant women and for intrapartum and postpartum care as shown in the Fig.1.

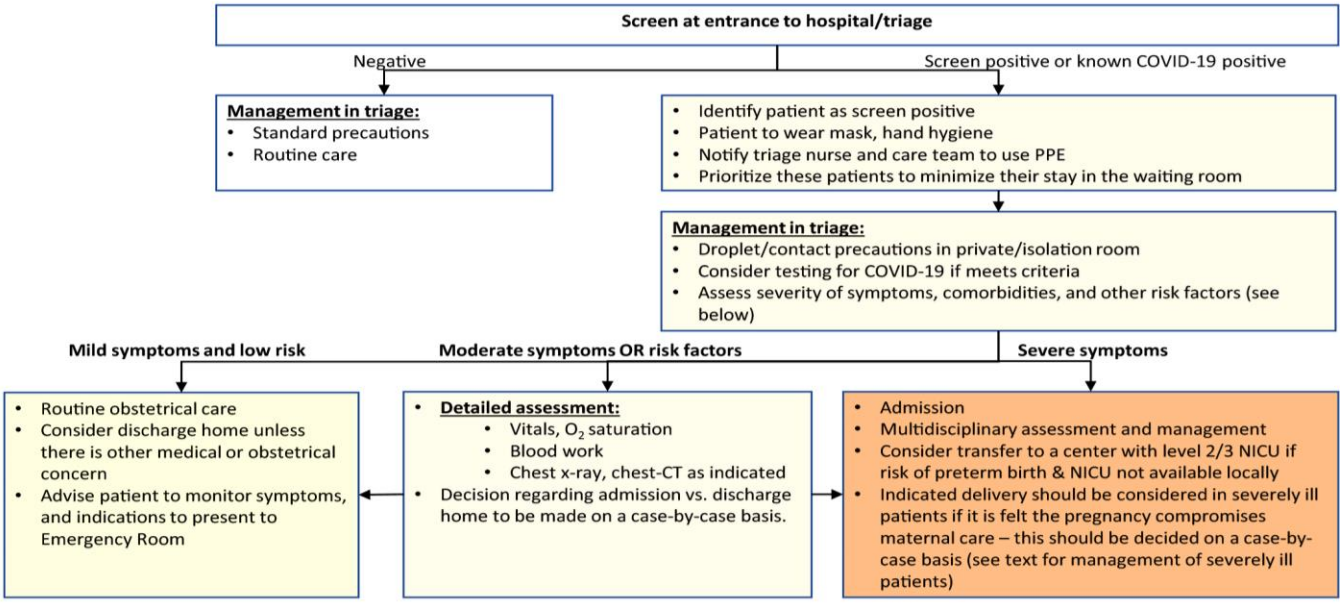
Obstetric Analgesia and Anesthesia

For pain relief during labour, epidural analgesia is recommended it has a benefit of avoiding exacerbation of respiratory system due to pains in infected pregnant patients. Nitrous oxide and high flow oxygen are suspended as they are aerosols. If caesarean section is indicated it must be performed under spinal anesthesia in patients with COVID-19. General anesthesia should be avoided due to high risk of exposure to the health care providers during intubation. Care must be taken to avoid transmission of infection by measures like patient must wear mask all the time in theatre, providers must wear impermeable gowns/surgical masks and eye protection to avoid exposure. As studies in China suggest COVID-19 infection is usually associated with fall in platelet count so platelets count needed to be checked prior to anesthesia. Regional anesthesia is considered safe to perform if count is more than 70,000×06/L. N-95 respirator mask is recommended unless patient is known to be negative.[14,22]

Strategies for Prevention

As pregnant women are susceptible to infections due to physiological changes the health care providers must educate the pregnant females about strategies for preventing infection.[11] Literature suggest pregnant women should follow the same recommendations as non-pregnant persons for avoiding exposure to the virus these include hand hygiene, regular hand washing, care during

coughing and sneezing, avoiding contact with someone who is having symptoms of Coronavirus like fever and dry cough, avoiding unnecessary use of public transport as much as possible, if possible work from home, avoid large and small gatherings in public spaces, and restaurants as infections spread easily in closed spaces where people gather, to keep in touch with friends and family by using technology such as phone, internet, and social media try to use telephone or online services to contact your general physician or other essential services.[20,23]



Suggested modified antenatal care schedule for low-risk pregnancies (to decrease exposure, decrease workload in case of understaffing of medical teams)

Severity	Symptoms & signs	Risk factors
Mild	• Asymptomatic • Mild fever, mild cough, running nose	• No comorbidities or obstetrical concerns • Good compliance and easy access to care
Moderate	• High fever • Mild dyspnea • Severe cough	• **Comorbidities** — hypertension, diabetes, renal disease, cardiovascular disease, lung disease, HIV, immunosuppressive medications • **Obstetrical concerns** — preeclampsia, fetal growth restriction, preterm labor • **Social concerns** — poor compliance, limited accessibility to care
Severe	• Shortness of breath, dyspnea • Hypotensive • Cough >1 teaspoon of blood • Suspected superimposed bacterial infection • System failure – renal, liver • Dehydration • Confusion, decreased responsiveness	

Fig.1: Algorithm for Intrapartum and Postpartum Care. (doi:10.1002/ijgo.13156)

CONCLUSION

Pregnant women require special attention and are considered as a susceptible population during global problem of COVID-19 pandemic. Obstetricians and maternity health care providers must keep their knowledge up to date according to emerging WHO guidelines regarding care of pregnant women and their own self-protection. All confirmed and suspected cases of COVID -19 have a right for quality care during antenatal, intra-partial and post-natal period. On the basis of available data the characteristics and symptoms of COVID-19 infection during pregnancy are similar as in other general population. There is no sound evidence of

vertical transmission. Mode of delivery should be considered according to the status of fetus and mother. Breast feeding can be started by manual expression taking full precautions for avoiding droplet infection spread to the neonate. General anesthesia must be avoided due to increased risk of spread during intubation. Preventing strategies like hand washing, social distancing and avoidance of contact and overcrowded places must be adopted.

LIMITATIONS OF STUDY

The literature search for COVID-19 could be retrieved from developed countries of the world only as data from the developing countries was not yet published at the time of submission of manuscript. Only two case reports were published from developing countries which mainly addressed the co-morbidities facing by the pregnant females leading to adverse event during pregnancy. A separate review for this aspect may be published in due course of time.

ACKNOWLEDGMENT

Authors extend their gratitude to Higher Education Commission (HEC) and library for the facility of E-library and online search of appropriate content at the Department of Gynecology & Obstetrics, Shalamar Medical and Dental College, Lahore.

CONFLICT OF INTEREST

None to declare.

FINANCIAL DISCLOSURE

None to disclose.

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Author's Contribution

SS: Acquisition of the published data, drafting of manuscript.

LRD: Conception and design of study, critical analysis with intellectual output, final approval of the manuscript.