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Review Article

PREGNANCY OUTCOMES OF COVID-19 POSITIVE PATIENTS; A SYSTEMATIC REVIEW OF LITERATURE

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Abstract:

Objective: Coronavirus disease 2019 became a pandemic and had many adverse effect on whole world this review is to estimate the pregnancy outcomes of Covid-19 positive patients and its effect on neonates.

Study Design: In this study, digital databases including PubMed, EMBASE and Google scholar were searched from January 2020 to August 2020. All relevant studies on Pregnancy and COVID-19 were reviewed and systematic reviews, meta-analysis, case studies were excluded. Prospective, Observational, Retrospective Cohorts and a Case series is included in this review.

Results: A total of 647 covid-19 positive pregnant women in their 2nd and 3rd trimester and 439 neonates were analysed from 9 selected studies. Maternal and neonatal mortality rate is 0. No major deformity is seen in neonates However, factors like low birth weight, pre-term delivery, neonatal pneumonia and increased C-section rate is observed.

Conclusion: Effects of covid-19 varies in all studies because of study design, duration, place, race and study population. Only 3% neonates were tested positive for Covid-19. Rate of C-section is highest in Chinese population (97%). No neonatal asphyxia, Fetal demise or acidosis seen.

Key Words: Covid-19, Severe Acute Respiratory Syndrome Coronavirus 2 Infection, lymphopenia, vertical transmission, preterm delivery, Neonatal pneumonia, Cesarean section, Middle Eastern Respiratory Syndrome.

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INTRODUCTION:

Novel corona virus breaks in December 2019 in Wuhan China and rapidly spread through the country by the end of January China was completely isolated, Covid-19 became the biggest public health threat¹⁻². COVID-19 currently affects over 210 countries and territories worldwide³ On 11 March 2020 World Health Organization declared Covid-19 a Pandemic⁴. Corona virus disease is a pneumonia like disease that causes Severe respiratory syndrome and organ failure leading to death.⁵ Majority of Covid-19 patients shows mild to moderate symptoms, around 15% patient form severe pneumonia and just 5% Acute respiratory syndrome⁶. Elderly patients with underlying conditions as Hypertension, Heart conditions and diabetes are at high risk of disease development and mortality⁷⁻⁸. Pregnant women are more likely to be effected by Respiratory pathogens. Therefore, pregnant women infected with SARS-CoV-2 are considered high risk⁹. Evaluation of maternal and neonatal outcomes is an important aspect of current pandemic. Numerous studies have been published on the negative effects of Covid-19 on pregnant women and infection status of neonates.⁶⁻⁹

Important epidemiological characteristics, transmission mechanism of Covid-19, Clinical and lab findings, diagnosis, treatment and prevention is obtained from all over the globe in short period of time.¹⁰⁻¹¹ Knowledge about Management of disease in pregnant women is limited, but is associated with pre-term birth, fetal tachycardia, fetal distress, fetal pneumonia Lymphocytopenia and elevated C-reactive protein (CRP) levels were seen in women.¹²⁻¹³ A recent review revealed that there is high risk of maternal mortality and neonatal death association with covid infections. Although transmission of virus is not detected.¹⁴

METHODOLOGY:

A detailed search on PubMed, EMBASE and Google scholar was made for studies reporting on impacts of Corona virus on pregnant female prior to September 2020. Combination of words as 'SARS-CoV-2', 'Corona Virus', 'Pregnancies', 'Maternal and Neonatal outcomes' to screen relevant articles. Full articles and abstracts were reviewed all systematic reviews, meta-analysis, duplicate articles, case studies and abstracts were excluded. Only Retrospective, Prospective, Observational Cohorts and A case series were included in study in order to evaluate the outcomes of a large population.

INCLUSION AND EXCLUSION CRITERIA:

Only pregnant females tested positive for Covid-19 by quantitative real-time polymerase chain reaction (RT-PCR), reported data on pregnancy outcomes, C-section incidence, preterm birth, low birth weight and neonatal pneumonia and researches written in English Language. Unpublished reports not confirmed Covid-19 population without pregnancy outcomes and researches in languages other than English were excluded.

RESULTS:

Dehan Liu et al conducted a study in China they CT examination results and Clinical Data of 15 Covid-19 positive patients admitted from 20 January 2020 to 10 February 2020. Eleven of fifteen patients delivered during study period 10 C-sections and 1 vaginal delivery. No cases of neonatal asphyxia, neonatal death, stillbirth, or abortion were reported. All neonates were tested negative for Covid-19.¹⁵ Another retrospective study conducted in China by Zhang Lu et al involved 16 positive pregnant women by the end of study period 10 women delivered all 10 deliveries were C-section. No maternal or neonatal death, No Covid-19 positive neonate reported.¹⁶

Valerie M et al conducted a prospective cohort study between February 23 and March 28, 2020 in 12 maternity hospitals of Italy. 77 patients included in this study, 14 had severe disease, 84% were symptomatic at the time of admission. 11 out of 77 patients had emergency delivery for respiratory compromise (16%), and 6 of 77 admitted to the ICU (8%). no deaths occurred. Preterm delivery occurred in 12% patients and 9 neonates were admitted to NICU. Out of 77 patients 36 underwent vaginal delivery and 31 had cesarean. No neonatal or maternal death reported. However, 3 neonates delivered vaginally and 1 neonate delivered with C-section tested positive for SARS-CoV-2 swab specimen testing¹⁷

S. Khan et al conducted a case series study of 17 covid-19 positive patients in China from January 2020 to march 2020. All 17 patients were tested positive using RT-PCR or CT scan imaging. All 17 women underwent C-section, 3 preterm deliveries, no neonatal or maternal deaths or other fetal complications seen. 2 neonates were tested positive for Covid-19 and neonatal pneumonia is seen in 5 neonates.¹⁸ Viktoriya London et al conducted a Retrospective Cohort study in Texas on 68 Covid-19 positive pregnant patients. By the end of study 55 neonates were delivered 33 symptomatic 22 asymptomatic, out of 33 symptomatic neonates mode of delivery for 16 was cesarean a total 12 preterm neonates delivered 9 at <37 weeks and 3 <34 weeks. In 22 asymptomatic 6 were delivered

through C-section. No maternal or neonatal deaths were observed during study. No mother-to-child transmission is seen. Zero positive neonates.¹⁹

E Ferrazzi et al conducted a study in Northern Italy involving the SARS-CoV-2-infected women who delivered between 1 to 20 March 2020. Study Data is obtained from 12 hospitals in Northern Italy. Study included 42 positive pregnant patients and 42 delivered neonates. 24 out of 42 neonates delivered vaginally and 18 neonates delivered through elective C-section. Spontaneous preterm delivery occurred in 5 patients except for low birth weight, pre term delivery nothing abnormal is seen no fetal distress, maternal or neonatal death reported. However, one neonate delivered vaginally tested positive for Covid-19.²⁰ Augusto Pereira reviewed clinical data of 60 pregnant women with COVID-19 who were managed at Puerta de Hierro University Hospital, Madrid, Spain from 14 March to 14 April 2020 it includes lab data, radiological finding, Demographic data, treatment and

outcomes. By the end of study period 23 out of 60 patients admitted for delivery mode of delivery was Cesarean in 5 and vaginal delivery in 18. 2 neonates were preterm and 2 fetus had Respiratory distress syndrome. No maternal or neonatal death reported. All neonates tested negative for SARS-CoV-2²¹

An observation Cohort study is conducted by Emily H. Adhikari from March 2020-August 2020 which included 3374 pregnant women who were tested for Covid-19 but only 252 patients tested positive. SARS-CoV-2 positivity was more common in Hispanic women 230 [91%]. 188 neonates were tested for SARS-CoV-2 only 6 were tested positive. Mode of delivery is Cesarean in 65 and spontaneous vaginal delivery in 174. Abnormal fetal heart rate is reported in 7 neonates, preeclampsia with severe feature in 26, preterm births <34 weeks in 9, <36 weeks in 18, between 37-38 weeks in 75 neonates. No maternal or neonatal death reported²²

TABLE 1: STUDY CHARACTERISTICS

Study Design	Author	Place And Year	Positive Population	Deliveries by the end of study	Pregnancy outcomes	Covid-19 positive neonates
Retrospective cohort study	Viktoriya London	New York 2020	68 pregnant women	55	33 symptomatic 9 preterm <37 weeks 3 preterm <34 weeks 16 Caesarean 22 asymptomatic 6 cesarean No Deaths or Still Births Except 1 at 17 weeks	0
A Preliminary Analysis	Dehan Liu	Wuhan 2020	15 pregnant women	11	10 cesarean 1 vaginal delivery No neonatal death or neonatal asphyxia	0
A retrospective comparison	Zhang Lu	Hubei China	16 pregnant women	10	10 Cesarean Section No fetal distress Neonatal asphyxia or Fetal demise	0
observational cohort study	Emily H. Adhikar	Dallas, texas 2020	252 pregnant women	248 188 tested	Cesarean delivery 65 abnormal fetal heart rate 7 vaginal delivery 174	6 out of 188 3%

Retrospective Cohort study	Alexandre J. Vivanti	Paris, France 2020	100	36	Pre-term deliveries <37 weeks in 39% 16 cesarean 17 normal 1 neonate low birth weight No Neonatal acidosis	1
retrospective analysis	E Ferrazzi	Northern, Italy	42	42	24 vaginal deliveries 18 elective cesareans Spontaneous pre-term deliveries in 5 elective cesarean 6	1
prospective multicenter cohort study	Valeria M. Savasi	Italy 2020	77	57	12 preterm deliveries 36 vaginal deliveries 31 cesarean No fetal death	4
Retrospective study	Augusto Pereira	Madrid, Spain 2020	60	23	Vaginal delivery 18 Cesarean 5 Pre-term 2 No Fetal demise 2 fetus Respiratory distress syndrome	0
a case series study	S. Khan	Hubei, China	17 women	17	17 cesarean deliveries 3 pre term No fetal or neonatal deaths	2 positive Neonatal pneumonia in 5
TOTAL			647	439		14

DISCUSSION:

This systematic review of 9 studies conducted between January 2020 – August 2020 include the pregnancy outcomes of 647 SARS-CoV-2 positive pregnant women admitted to different hospitals around the world and 439 neonates were born at the end of study period out of these 439 neonates only 12 neonates tested positive for SARS-CoV-2 (3%) there was no maternal or neonatal death observed in all studies. The results of this systematic review shows that the rate of mother to child transmission of SARS-CoV-2 is very low (3%). Rate of preterm birth or adverse pregnancy outcomes are high if infection was acquired early in 25–35 weeks of gestation. Hence women should follow intensive practice to avoid contracting infection in early stages of pregnancy if pregnant women contracts virus it should be detected early to minimize the risks associated with adverse effects of pregnancy. Respiratory distress is a symptom which can cause complications during pregnancy these women have higher chances of preterm birth. In Iqbal Sn et al and Silverstein JS et al studies two cases were diagnosed at 35 weeks of gestation one had no adverse effect on

pregnancy and other had preterm delivery.^{23,24} In 3 studies where 4 cases were diagnosed before 35 weeks of gestation are observed with preterm birth and low birth weight²⁴⁻²⁵⁻²⁶ Positive patients of our study had prevalent symptoms of cough, fever and shortness of breath.²⁷ Positive women who delivered did not have a significantly higher frequency of a of preterm birth, preeclampsia with severe features, or cesarean delivery for abnormal fetal heart rate. There were no significant differences in other adverse pregnancy outcomes.

Rate of C-section in China, Europe and US in our study is 97%,44% and 28.7% respectively. Maternal outcomes involved postpartum fever 49.5%, Dyspnea 33.3% and cough 61 %. Preterm birth rate is 14%. No spontaneous abortions, maternal or neonatal death reported. No severe abnormalities or complications seen in neonates on 3% neonates tested positive and neonatal pneumonia is observed in 1.1% neonates.

All these studies can be a proof that vertical transmission is rare. Multiple studies were conducted

on placenta, amniotic fluid and neonate samples immediately after birth and SARS-CoV-2 was not detected.²⁸⁻²⁹⁻³⁰ Most of neonates were tested negative despite of mode of delivery.

CONCLUSION:

Rate of infection transmission is relatively low. No severe pregnancy outcomes were reported however high C-section rates were observed in Chinese population. No termination of pregnancy is observed but SARS-CoV-2 positive women required oxygen support. However, infection in early stages of pregnancy can be lethal therefore regular screening for coronavirus infection is necessary early detection in asymptomatic patients can be proved as a safe practice to avoid infection in early stages of pregnancy and unfavorable pregnancy outcomes.

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