

The Effects of Covid 19 on Premature Delivery: Clinical Findings, Control and Diagnosis Methods

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Abstract

Background & aim: Corona viruses are an infectious respiratory pathogen among humans and animals that are transmitted through respiratory particles and body secretions. At the end of 2019, a new case of corona virus was detected in Wuhan, China [1]. The disease spread rapidly, leading to an epidemic across China and then around the world. In February 2020, the World Health Organization declared the disease Covid-19, which stands for 2019 coronavirus disease, previously called 2019-nCoV. Studies have shown that women who are infected with Covid-19 during pregnancy are at a higher risk of premature delivery. This study was conducted with the aim of the impact of covid-19 on premature birth and diagnostic and therapeutic methods.

Methods: This descriptive review study was conducted with the aim of investigating the effects of covid-19 on preterm birth, clinical findings, control and diagnosis methods. This narrative study was conducted in Pub Med, Magiran and Google Scholar databases during 2017-2024 by studying more than 100 articles using the keywords of preterm birth, covid-19, low birth weight, high-risk pregnancy, Pandemic, Sars Covid-19.

Results: The covid-19 epidemic has different consequences on pregnancy and childbirth, which are explained in detail below in the components of the effects of covid on premature birth, its preventive and treatment methods, the consequences on preterm babies, and diagnostic methods.

Conclusion: The collected results show that covid-19 is associated with premature birth, the complications of this disease, including fever and hypoxia caused by the virus, cause premature rupture of the water sac and abnormal changes in the heart rate of the fetus. It is recommended to quarantine pregnant mothers to control adverse pregnancy outcomes. Quarantine during this period caused social and behavioral changes, including reducing the mental burden caused by the anxiety of contracting the virus and endangering the health of the fetus, which was effective in prolonging pregnancy.

Keywords: preterm birth; covid-19; low birth weight; high-risk pregnancy; Pandemic; Sars Covid-19

Introduction

Premature birth in humans is defined as the birth of a baby before the 37th week of pregnancy. The cause of premature birth is unknown in most cases. However, factors such as diabetes, cigarette and hookah consumption, high blood pressure (pre-eclampsia), multiple births, pregnancy with assisted reproduction methods and Frequent and harsh curettages play a significant role. Premature babies are at greater risk of mental and physical developmental disabilities [1, 2]. It is very important to identify women with premature contractions that lead to delivery at a gestational age of less than 37 weeks. At the same time, it is one of the most common reasons for hospitalization of pregnant women with Covid-19. Accurate identification of women with labor contractions that have the characteristics (bleeding, deformation and dilation of the cervix and the

duration of contractions between 30 and 60 seconds every 5 to 20 minutes) of Braxton Hicks contractions can lead to the appropriate use of interventions and save time and becomes vital for the health of the newborn. It improves neonatal outcomes, these measures include: treatment with corticosteroids before birth, prevention of group B streptococcal infection, The use of magnesium sulfate from the 27th to the 32nd week of pregnancy to protect the nervous system of the fetus, and transfer to the center with the appropriate level. Infant care [3-5].

There are sub-categories of preterm birth, based on gestational age: [6, 7]

- extremely preterm (less than 28 weeks)
- very preterm (28 to less than 32 weeks)
- moderate to late preterm (32 to 37 weeks).

The global PTB rate increased from 9.8% to 10.6% between 2000 and 2014, with an expected 13.4

million cases (1 in 10 newborns) in 2020. In 2020, India accounted for 3.02 million PTBs, or almost 23% of all PTBs globally, the most significant number of preterm births worldwide, and the fourth highest PTB rate after Bangladesh, Malawi, and Pakistan [3, 8, 9].

The relationship between COVID-19 and premature birth

Maternal mortality is one of the important indicators of the quality of health services in advanced and developed countries. One of the common problems in midwifery is premature birth. The study of premature birth is important because it is the main cause of death and adverse consequences, including respiratory and cerebral in infants, and despite many efforts to control it, its prevalence is increasing in low- and middle-income countries [10, 11]. While it was found that the main cause of premature birth is idiopathic in half of the cases, other factors can also be mentioned, including the fertility of assisted reproductive technology, polyhydramnios, multiple births, and most importantly, the history of premature birth. Since the start of the Covid-19

pandemic, several studies have identified an association between preterm delivery and adverse perinatal outcomes such as stillbirth and preterm delivery [5, 12, 13]. One of the most important underlying mechanisms for premature birth is the activation of inflammatory factors [14]. Inflammatory factors such as (IL6-IL8) may cause softening of the cervix and contraction of the uterus through the increase of prostaglandins. Corona virus infection is a systemic inflammatory disease. which causes an increase in CRP, which is an inflammatory factor, and when the infection increases, it is released from the liver cells and enters the mother's blood serum. Therefore, it can lead to premature birth. For example, among women with pneumonia, empirical evidence suggests an increased rate of preterm delivery [15]. The results showed that during the epidemic years of 2020 and 2021, premature births increased significantly compared to the periods before the epidemic. The increase has not been uniformed across the country, and in some areas, the epidemic has accelerated the pattern of premature births. As observed in the northeastern, southeastern and southern regions [16-18].

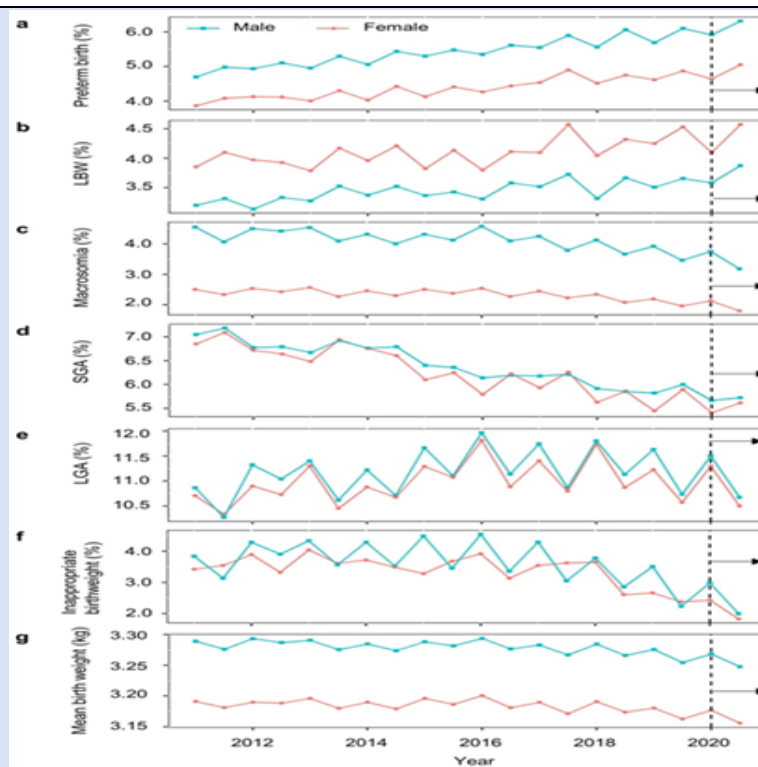


Figure: Trends in preterm birth during the pandemic in 2020

Materials and Methods

This descriptive review study was conducted with the aim of investigating the effects of covid-19 on preterm birth, clinical findings, control and diagnosis

methods. This narrative study was conducted in Pub Med, Magiran and Google Scholar databases during 2017-2024 by studying more than 100 articles using the keywords of preterm birth, covid-19, low birth

weight, high-risk pregnancy, Pandemic, Sars Covid-19.

Results

The covid-19 epidemic has different consequences on pregnancy and childbirth, which are explained in detail below in the components of the effects of covid on premature birth, its preventive and treatment methods, the consequences on preterm babies, and diagnostic methods [19].

Factors affecting premature birth

The pathophysiology of premature birth includes at least four main causes:

Spontaneous preterm delivery (multiples - bleeding - placental infarction - cervical insufficiency - maternal infections - fetal abnormalities - uterine fundus disorders) [15, 20] :

The spontaneous preterm labor mechanism includes:

- Desidwa's old age
- Loss of maternal-fetal tolerance
- Cervical disorders
- Stress (Psychological stress caused by racial discrimination, diabetes, infection, depression)
- Unknown

Inflammation and infection

In three ways, infection causes premature birth and rupture of the amnion sac

- Placenta transfer
- Backward flow into the peritoneal cavity through the fallopian tubes
- Ascending path of infection

Clinical findings

The following signs and symptoms may begin a few hours before the onset of pain, which are the diagnostic criteria for labor [21, 22]

- Menstruation-like pains
- Mild and irregular contractions
- Back pain
- Feeling pressure in the vagina or pelvis
- Vaginal mucous discharge that may be clear, pink, or slightly bloody (i.e., mucous plaque, bloody display)
- Spotting, mild bleeding
- Decreased fetal movements [23].

Changes in the cervix in the physical examination performed before or in conjunction with the actual birth include dilation (dilatation) and softening (affection). The speed at which the cervix changes, which occur over days to weeks, differentiates the

actual delivery from the actual delivery, because the change in the cervix occurs within a few minutes to a few hours. A short or dilated cervix may be the first clinical manifestation of imminent preterm birth [24]

. 3-Diagnostic Evaluation Components: In most women, diagnostic evaluation is done in the maternity unit or the maternity triage unit [25].

History and Initial Examinations

History and initial examinations: The initial evaluation of women suspected of premature labor includes the following:

Examining past obstetric and medical history, including the risk factors of premature birth (history of premature birth, colic, diabetes, interval between pregnancies, etc.)

Although many cases appear to be idiopathic, the physician and midwife should consider possible causes of premature contractions based on the history and physical examination.

Premature delivery may be caused by a medical disorder (such as appendicitis, intestinal obstruction, pyelonephritis), which occurs most often in the third trimester of pregnancy due to anatomical changes in pregnancy that require special intervention. It may have similar symptoms. Preterm delivery, such as abdominal pain, back pain or diarrhea appear [26-28]. Performing ultrasound in the third trimester of pregnancy to check amniotic fluid level, fetal health, placenta condition and check gestational age is the best evaluation method.

Evaluation of signs and symptoms of preterm labor is done by the following examinations:

Speculum examination

Examination is performed using a wet speculum without the use of gels and lubricants (lubricants may interfere with tests performed on vaginal specimens). The objectives of this experiment are as follows [28, 29].

- To estimate cervical dilation, which supports the diagnosis of preterm labor if the cervical dilation is ≥ 3 cm.
- Evaluation of the condition of the fetal membrane (intact or torn) with standard methods, often premature rupture of membranes (PPROM) occurs before preterm birth or during preterm labor.
- Fetal fibronectin (fFN) is a protein that helps hold the amniotic sac to the uterine wall during pregnancy. Fetal fibronectin acts like a glue that helps the amniotic sac adhere to the uterine wall.

If this connection is broken, the fetal fibronectin can leak into the vagina and eventually cause premature birth [18].

Transvaginal Ultrasound Examination [28, 30]

Cervical length measurement is useful for the diagnosis of preterm labor. Vaginal ultrasound for singleton pregnancy after 16 weeks, short cervix before 34 weeks of pregnancy (<25 mm) increases the risk of preterm labor, while long cervix (≥ 25 mm) has a high negative predictive value for preterm delivery [30, 31].

Laboratory Evaluation

If the risk factors of premature birth are suspected, the following measures are recommended:

1. Cultures of group B rectovaginal streptococcus should be done because it can affect preterm labor, the results of which depend on the use of antibiotic prophylaxis.
2. Urine culture: Since asymptomatic bacteriuria and upper and lower urinary tract infection stimulate the smooth muscles of the uterus and increase the risk of premature birth.
3. Tests should be requested to diagnose sexually transmitted infections (e.g., chlamydia, gonorrhea, and syphilis) [30, 31].

Detection

We diagnose preterm birth based on the clinical criteria of regular painful uterine contractions with cervical changes (dilation and/or aphasia). Vaginal bleeding and/or rupture of the membrane in this condition increases diagnostic certainty [32, 33].

We use the following very important criteria for diagnosis:

- uterine contractions (≥ 4 every 20 minutes or ≥ 8 every 60 minutes) plus
- Cervical dilation ≥ 3 cm or
- Cervical length <20 mm in transvaginal ultrasound or 20 to 30 mm cervical length in transvaginal ultrasound and positive fetal fibronectin

Complications of premature birth for the baby

Premature delivery in infants the earlier the baby is born, the more likely it is to develop medical problems. A premature baby may show these symptoms after birth [24]:

- low weight
- Inability to maintain a constant body temperature
- Less than normal activity
- Movement and coordination problems

- Nutritional problems
- Abnormal skin
- Decreased sucking reflex
- Cerebral hemorrhage
- Pulmonary hemorrhage
- Low blood sugar
- Neonatal sepsis

Therapeutic and preventive treatment of premature birth

Effects of glucocorticoids on the fetus of pregnant mothers with COVID-19:

One of the necessary treatments for preterm fetuses in pregnant mothers with COVID-19 is the use of glucocorticoid because there is a high probability of premature delivery in these mothers and this drug is necessary for the maturation of the fetal lung in pregnancies less than 34 weeks, but excessive use of this drug has been associated with adverse effects such as (undesirable neurological outcomes, small head circumference, fetal growth restriction and increased risk of neonatal hypoglycemia) [34]. Prednisolone 40 mg orally or intravenous hydrocortisone 80 mg twice daily can be replaced in these patients [35]. As an ideal agent, a total of 32 mg/day of oral or intravenous methylprednisolone is equivalent to a dose of dexamethasone [36].

Vitamin D and preterm birth

Vitamin D is formed in the skin under the influence of ultraviolet rays or obtained by consuming dairy products. Vitamin D plays an important role in the absorption of calcium and phosphate, secretion of progesterone and estriol, human chorionic gonadotropin (hCG) during pregnancy. Which leads to the increase of anti-inflammatory cytokines and T lymphocytes. The most important functional mechanisms of vitamin D₃ are at the level of maternal-genital contact [38, 39]. During pregnancy, around the 12th week, the concentration of 1,25(OH)₂D more than doubles, which confirms the important role of vitamin D in supporting pregnancy and controlling fetal growth processes [38, 40]. Deficiency of this vitamin can lead to pre-eclampsia, low birth weight and premature delivery. Therefore, it is recommended to consume 1000 mg of vitamin D₃ daily during pregnancy [41, 42].

Cerclage

Cerclage is a method to keep the cervix closed in women with a weak cervix and a history of repeated abortions in the second trimester during pregnancy to prevent premature birth.

Cerclage conditions

- Singleton pregnancy
- Gestational age less than 24 weeks
- The length of the cervix is less than 25 mm
- A history of spontaneous preterm delivery

Aspirin

Acetylsalicylic acid is a cyclooxygenase inhibitor with anti-inflammatory and anti-platelet properties that is used to prevent and delay preeclampsia and premature birth [23, 43, 44].

Beta-adrenergic agonist receptor

The mechanism of these drugs prevents the activation of myometrial contractile proteins by reducing intracellular calcium. The complication of this drug is pulmonary edema.

Terbutaline is another beta-adrenergic agonist drug that is widely used in the United States to prevent premature birth.

Oxytocin receptor antagonists

Etosiban acts as an oxytocin receptor antagonist and has been developed exclusively for the management of preterm labor [45-48].

Mechanism of action

- Atosiban acts as a competitive antagonist of oxytocin receptors in the uterus.
- Oxytocin is a hormone that plays a key role in stimulating uterine contractions during labor.
- By blocking oxytocin receptors, atosiban inhibits the effects of oxytocin and leads to reduction of uterine contractions and relaxation of uterine muscles.
- This mechanism helps prevent or delay preterm labor and maintain pregnancy.

Prohibited usage

- Atosiban is contraindicated in people with known sensitivity or allergy to atosiban or any of its components.
- Should not be used in cases where vaginal bleeding is not related to preterm labor or when immediate delivery is necessary for maternal or fetal reasons.
- Conditions, such as placental abruption, high blood pressure due to pregnancy, or intrauterine fetal death, are contraindications for the use of Atosiban.

Calcium channel blockers

Nifedipine is a calcium channel blocker. This drug inhibits uterine contractions by reducing calcium

concentration. Low blood pressure and tachycardia are side effects of using this medicine.

Another prostaglandin inhibitor such as indomethacin is administered orally or rectally. Its dose is 50-100 mg every 8 hours [23, 45, 46].

Discussion

Pregnant women are more susceptible to respiratory pathogens due to anatomical and physiological changes in the system that occur during pregnancy, and these diseases such as covid-19, influenza, etc. be.3-6 This study aimed to investigate the relationship and impact of covid on premature birth [49]. Oltean et al.'s review shows that the rate of cesarean section, pre-eclampsia, decollement, low birth weight, premature delivery in women with covid-19 with high CRP compared to healthy pregnant women [50]. Therefore, an increase in CRP level is a risk factor for preterm delivery. Therefore, increased CRP level is a risk factor for preterm delivery. Women with severe respiratory symptoms are more prone to adverse outcomes such as preterm delivery [51-53]. Elevated levels of inflammatory markers are a risk factor associated with other immunological processes thought to contribute to preterm labor syndrome [54, 55]. According to Silva et al., the state of inflammatory factors can cause conditions such as preeclampsia, low birth weight or premature birth [56]. Fever and hypoxia caused by the virus cause an increase in inflammatory factors, premature rupture of the amniotic membrane and fetal tachycardia. According to clinical research, gestational age decreases with increasing levels of inflammatory markers and causes an increase in adverse outcomes. Therefore, it may be the driving factor of premature birth in pregnancies during the covid-19 period. According to the Bellos meta-analysis, of the available case series, the number of preterm births and cesarean section is higher than expected in pregnant women with covid [57]. Several studies have shown that the incidence of preterm births and caesarean sections increased during the pandemic period due to reduced transmission rates.

Conclusion

The collected results show that covid-19 is associated with premature birth, the complications of this disease, including fever and hypoxia caused by the virus, cause premature rupture of the water sac and abnormal changes in the heart rate of the fetus. It is recommended to quarantine pregnant mothers to

control adverse pregnancy outcomes. Quarantine during this period caused social and behavioral changes, including reducing the mental burden caused by the anxiety of contracting the virus and endangering the health of the fetus, which was effective in prolonging pregnancy.

Declarations

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Conflicts of interest

Authors declared no conflicts of interest

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