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Maternal and perinatal outcomes of pandemic Covid-19 in pregnancy in Basrah

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Abstract

Objective:

To evaluate the maternal, fetal and neonatal complications in pregnant women with Covid-19 infection.

Setting and design:

A prospective descriptive study was carried out in Basrah Teaching Hospital, Iraq during the period 15/3/2020 till 1/11/2020. There were 135 infected pregnant women with Covid-19.

The maternal information's were obtained included Age, parity, residence, travel history, gestational age at time of diagnosis. The pregnancy measures of interest were evaluated according to the severity of the disease, medical disease, history of antepartum hemorrhage, mode of delivery, type of delivery, post-natal complication and admission to intensive care unit and maternal death.

The neonatal outcomes of interest were fetal weight, neonatal Apgar score, admission to neonatal intensive care unit and neonatal death.

Results:

The mild type of the disease was common (41.48%) in comparison to severe conditions (17.77%).

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Admission to ICU was 10 cases, out of them 7 deaths taken place due to respiratory failure. The maternal risk factors that may worse the prognosis of the disease were maternal hypertension (5.1%) and diabetes (2.9%) . The completed cure was 95% for the diseased women, with just 5% death. While 2 pregnant women survive from risky condition postnatal. The mode of delivery was vaginally (4.4%) and abdominally (6.6%).

Out of 23 (17.03%) neonates admitted to the intensive care unit, 5 (3.7%) perinatal deaths were observed.

Conclusion :

There are low rates of maternal and neonatal mortality as well as ICU admissions associated with COVID-19.

Key words: Covid-19, Maternal outcome, Pandemic, Pregnancy.

Introduction

Previous epidemiological evidence strongly suggests that pregnant women have a higher risk of serious illness and death during pandemics for viral infections (1) such as influenza, ebola and SARS (2-4). These have been proved to be closely related to physiological changes in the respiratory, circulatory, secretory, and immune systems during pregnancy.

Anatomically, the effects of progesterone and relaxants in the first trimester of pregnancy can lead to relaxation of ligaments in the ribs and the diaphragm will move up as the uterus grows (5). In addition, elevated progesterone can be transmitted through estrogen-dependent progesterone receptors in the hypothalamus, thus stimulating the respiratory center and increasing tidal volume by 50% compared with non-pregnancy (6). Pregnant women are more likely to get the disease than ordinary people and are infected by droplets, aerosols, and other means.

Interestingly, the impact of Covid-19 infection on pregnant women appears to be less severe. Chen *et al*. (7) reported the clinical characteristics of 9 pregnant women infected with Covid-19 in the third trimester, which comprised mainly fever, cough, myalgia, malaise, sore throat, diarrhea and shortness of breath. Data from laboratory tests showed that the majority of patients had lymphopenia and increased C-reactive protein. Chest CT scans showed multiple patchy ground-glass shadows in the lungs. Pregnancy complications that appeared after the onset of Covid-19 infection included fetal distress and premature rupture of the membranes in 2 of 9 patients. None of the patients developed severe Covid-19 pneumonia or died.

The mother's response to infection tends to promote the fetus inflammatory response, which is defined as the fetal inflammatory response syndrome, characterized by high levels of inflammatory cytokines in placenta, such as IL-1, IL-6, IL-8, and TNF-α but a lack of culturable microorganisms. These

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cytokines have an effect on the central nervous system and circulatory system and tend to cause fetal abnormal morphology in animal models, including ventricular expansion and bleeding (8,9).

The major concern is whether the virus can be transmitted from mother to baby or not. In the study by Chen *et al*. (7) no death, neonatal death or neonatal asphyxia were observed among studied 9 pregnant women with Covid-19 in the third trimester. Although 4 neonates were born prematurely, none of these deliveries was related directly to Covid-19 infection. All newborns had an Apgar score ≥ 9 at 5 min. Amniotic fluid, cord blood and neonatal throat-swab samples collected from 6 patients tested negative for Covid-19, suggesting there was no evidence of intrauterine infection caused by vertical transmission in women who developed Covid-19 pneumonia in late pregnancy (7,10). Furthermore, it appears that there is no risk of vertical transmission via breastfeeding. The same study confirmed that the virus was not detected in the colostrum of Covid-19-infected patients.

It is, therefore, probable that Covid-19 infection during pregnancy cannot lead to transplacental vertical transmission. We acknowledge that available clinical data on Covid-19 infection in pregnancy are limited at present, and most cases on which data are available presented in the third trimester of pregnancy. There is, therefore, a need to continue collecting data on clinical cases of COVID-19 infection in pregnancy, and to improve our understanding of the course of the disease throughout pregnancy (10).

Covid-19 infection is highly contagious and thus must be taken into consideration when planning intrapartum care. It is unclear whether, for the safety of both baby and healthcare professionals, a pregnant woman with Covid-19 infection should be allowed to deliver vaginally, which can be a rather long process. There have not yet been any studies examining whether Covid-19 infection can be transmitted during delivery. Future research could explore whether vaginal delivery increases the risk of transmission from mother to child during delivery by testing vaginal secretions. Since Covid-19 itself is transmitted mainly through respiratory droplets and by close contact, if a newborn is in close contact with an infected mother, contact infection is likely to occur. It has been reported that the youngest patient with Covid-19 infection was diagnosed 36 h after birth (11). Particular attention, therefore, should be paid to the protection of neonates born to women with Covid-19 infection. The aim of the study is report the maternal, fetal and neonatal complications in pregnant women infected with Covid-19.

Patients and methods

A prospective study was carried out at Basrah Teaching Hospital during the period from 15/3/2020 till 1/11/2020. There were 135 women (Age range 15-45 years) who were infected with Covid-19 were reported in Maternity

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Departments during the study period. The study was proved ethically by the Ethical Committee of the College of Medicine, Basrah, Iraq.

Two data sources were used to obtain the information of cases, the first source recorded all the pregnant cases who were admitted to Basrah Teaching Hospital in the infectious ward and intensive care unit ward prospectively.

The second source is retrospective data collected from the pregnant women with previous history of Covid-19 during pregnancy with recovery who visited ANC clinics. The obtained information includes age, parity, residence, travel history, gestational age at time of diagnosis.

The pregnancy measures of interest were:

- Symptoms on presentation
- Maternal investigations for COVID-19
- Period between initial symptoms presentation and delivery of the baby (TTD)
- Preterm delivery (PTD)
- Mode of delivery
- Fetal distress, as defined by the authors
- Intensive care unit (ICU) admission
- Need for respiratory support
- Maternal mortality rate

The neonatal outcomes of interest were:

- APGAR scores at 1 and 5 minutes
- Birth weight
- Neonatal symptoms at birth which were defined by the authors as the presence of either fever, lethargy, nausea, respiratory symptoms or intolerance to feeding
- Neonatal intensive care unit (NICU) admission
- Neonatal investigations for COVID-19
- Evidence of vertical transmission

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Classification of disease severity:

In the United States, the National Institutes of Health have categorized disease severity in non- pregnant persons as [56]:

1- Asymptomatic or pre-symptomatic infection – Positive test for SARS-CoV-2 but no symptoms.
2- Mild illness – Any signs and symptoms (eg, fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea, or abnormal chest imaging.
3- Moderate illness – Evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SaO_2) >93 percent on room air at sea level.
4- Severe illness – Respiratory frequency >30 breaths per minute, SaO_2 ≤93 percent on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300, or lung infiltrates >50 percent.
5- Critical illness – Respiratory failure, septic shock, and/or multiple organ dysfunction.
6- Disease severity has also been categorized as (Wu classification) [57]:
7- Mild – No or mild symptoms (fever, fatigue, cough, and/or less common features of COVID-19).
8- Severe – Tachypnea (respiratory rate >30 breaths per minute), hypoxia (oxygen saturation ≤93 percent on room air or PaO_2/FiO_2 <300 mmHg), or >50 percent lung involvement on imaging).
9- Critical (e.g, with respiratory failure, shock, or multi-organ dysfunction).

History of labor: includes mode of delivery, gestational age at time of delivery, maternal antpartum, intrapartum and postpartum complications and maternal mortality beside neonatal outcome which includes Apgar score, fetal weight and history of admission to neonatal care unit.

Statistical analysis was by statistical package for social sciences (SSPS-version).

Results:

The study covered the pattern and outcome of epidemic of Covid-19 during pregnancy in Basrah, 135 pregnant ladies were included in the study who were infected with Covid-19 virus.

The ages of the majority of cases were 25-35 years representing 62.96% out of whole studied women beside the higher percent of infected women with parity between 1-4 (57%) (Table 1).

The higher number of women who infected by Covid-19 are at 3rd trimester (62.9%) and those from rural area (60.7%) with no difference in the educational level between the diseased women (Table 1).

Table 1: Demographic features of the positive Covid-19 pregnant women.

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Variable		N(135)	%
Age	**15 - 25** **>25 - 35** **>35 – 45**	**30** **85** **20**	**22.22** **62.96** **14.81**
Pariy	**Prim.** **1-4** **>5**	**47** **77** **11**	**34.81** **57.03** **8.14**
Gestational age At time of diagnosis	**1st trimester** **2nd trimester** **3rd trimester**	**15** **35** **85**	**11.11** **25.92** **62.96**
Residence	**Rural** **Urban**	**82** **53**	**60.74** **39.25**
Educational status	**Primary school** **Secondary school** **High level**	**51** **34** **50**	**37.77** **25.18** **37.03**

Infected women with mild type were common (41.48%) in comparison to severe conditions which were (17.77%) of the disease. Admission to ICU was 10 cases, out of them 7 deaths were reported due to Covid-19 complications (Table 2).

Table 2: The presentation of the disease according to the severity.

Type of presentation	PCR	Lung scan	Number of cases	%
Asymptomatic	**+Ve**	**- Ve**	**16**	**11.85**
Mild	**+ve**	**-ve**	**56**	**41.48**
Moderate	**+ve**	**+ve**	**38**	**28.14**
Severe	**+ve**	**+ve**	**24**	**17.77**
Admission to ICU			**10**	**7.4**

The Table (3) presents the maternal risk factors that may worse the prognosis of the disease. There is low percent of maternal hypertension (5.1%) and low percent of diabetes (2.9%).

Table 3: maternal complications.

Complication	N (135)	%
Hypertension: **Gestational** **Chronic**	**7** **5** **2**	**5.1** **3.7** **1.48**
Diabetes: **Gestational** **Non gestational**	**4** **3** **1**	**2.9** **2.2** **0.7**

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APH		
Abortion: **1ST TRIMESTER** **2ND TRIMESTER**	 **3** **10**	 **2.2** **7.4**

Table (4) shows the prognosis of completed cure was 95% of the diseased women, with death just 5%, while 2 pregnant women survive from risky condition postnatal. Complete cure was obtained in home management at a rate of 49.25%.

Table 4: Place of conducted treatment of the infected women.

PLACE	N(%)	PROGNOSIS	N(%)
HOME	**68(49.27)**	**Complete cure**	**68(49.25)**
ISOLATION WARD	**57(42.2)**	**Complete cure**	**56 (41.2)**
ICU	**10(7.4)**	**Death**	**7 (5.18)**

Table (5) shows that (74.8%) of the infected pregnant women get their infection at term. Regarding the mode of delivery about (4.4%) were delivered vaginally and (6.6%) were delivered abdominally. Out of 135 pregnant ladies 7 cases died after delivery due to respiratory failure. Out of 23 (17.03%) neonates admitted to the intensive care unit, 5 (3.7%) perinatal deaths were observed (Table 5).

Table 5: Labor outcome.

Variable	N(135)	%
Gestational age at time of delivery **Preterm:** **Term:**	 **9** **101**	 **6.6** **74.8**
Mode of delivery: **Vaginal delivery** **Caesarian section**	**15** **6** **9**	**11.11** **4.4** **6.6**
PPH	**7**	**5.18**
Fetal wt. (mean + SD)	**3.14+ 2.3**	
Apgar score after 5 minute	**7**	**5.18**
Admission to neonatal ICU	**23**	**17.03**
Prenatal death	**5**	**3.7**
Maternal death	**7**	**5.18**

Disscusion :

It was reported that pregnancy and childbirth generally do not increase the risk for acquiring SARS-CoV-2 infection, but may worsen the clinical course of Covid-19 compared with non-pregnant women of the same age. However,

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most (>90 percent) infected mothers recover without undergoing delivery (12). The present study has indicated that 41.48% of women in Basrah suffered from mild condition with good prognosis.

The clinical course of severe or critical Covid-19 in hospitalized pregnant women may be shorter than in hospitalized non-pregnant patients (4). It is known that some patients with severe Covid-19 have laboratory evidence of an exuberant inflammatory response (similar to cytokine release syndrome), which has been associated with critical and fatal illness that was been reported by the investigators in China (13) and USA (14). The investigators note that the types of studies have shifted with the spread of the pandemic, not only by country, but also from the initial small case series and case reports, to large observational studies, with the most recent providing comparative data.

The most common symptoms in pregnant women with Covid-19 were fever (40%) and cough (39%); and the most common laboratory abnormalities were lymphopenia (35%) and elevated C-reactive protein level (49%). Pregnant women with Covid-19 were less likely than non-pregnant women, however, to manifest symptoms of fever (15).

Differences in diagnostic reliability of RT-PCR versus CT were identified. In our sample (n = 135), nearly 46.14% were diagnosed by imaging studies. CTs superior sensitivity has already been documented in the general population (98% vs 71%; n = 51; $p<0.001$) (16). Although RT-PCR remains the gold standard for diagnosing Covid-19, clinicians should be aware of the potential for false negatives in pregnant women.

It was observed in this study that 11.85 % of the positive PCR patients are asymptomatic while the highest percent (41.48) of positive cases are in mild condition. Huang *et al*. (16) (first reported a cohort of 41 pregnant patients with laboratory-confirmed Covid-19 pneumonia. They described the epidemiological, clinical, laboratory and radiological characteristics, as well as treatment and clinical outcome of the patients. The diagnosis of Covid-19 pneumonia is based on clinical manifestation, laboratory results, findings on computed tomography (CT) of the chest and a positive Covid-19 test result based on quantitative reverse transcription polymerase chain reaction (qRT-PCR) analysis of specimens acquired from the respiratory tract.

In the worst-hit areas in China (Hubei Province), suspected cases with typical chest CT findings may be diagnosed clinically with Covid-19 pneumonia, as the qRT-PCR test has a false-negative rate of at least 30%.Thus, in addition to using nucleic acid tests as the gold standard for diagnosis of Covid-19 pneumonia, a combination of laboratory results, chest CT findings and a comprehensive evaluation of the patient's medical history, epidemiological exposure and symptoms are of great importance.(16)

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In the present study 10 cases were died due to respiratory failure, 5 cases out of them had hypertension.

With respect to maternal ICU admissions and mortality rates during Covid-19, the available data appears reassuring. In contrast, SARS and MERS respectively had 15–18% and 25–27% mortality rates; 30% and 60% ICU admission rates, and a requirement for mechanical ventilation in 35% and 41% of women (17,18).

In comparison to non-pregnant women with Covid-19, pregnant women with the disease had higher odds of admission to the intensive care unit (1.62, 95% PI 1.33-1.96) and need for invasive ventilation (1.88, 1.36-2.60). A pre-existing maternal comorbidity further increased odds of requiring intensive care (4.21, 1.06-16.72) and for invasive ventilation (4.48, 1.40-14.37) (19).

Pregnant women with Covid-19 had an overall preterm birth rate of 17% (13-21), and 6% (3-9) rate of spontaneous preterm births. The odds of any preterm birth were higher with Covid-19 than without (3.0, 1.15-7.85). There were no statistically significant differences in other maternal outcomes between those with or without Covid-19; or in neonatal outcomes, other than neonatal unit admissions (20).

The preterm labour rates in our study appear lower than the baseline in China of 8.7% (21). Previously it has been reported that 42.7% of PTB in China were iatrogenic in nature but given the lack of indications for delivery, we are unable to discern the level that this is contributory. It begs consideration, that similar PTB rates occur with MERS (13–25.0%), SARS (0–27%) and parturients with severe viral pneumonia as well, thereby implicating viremia in the process (21). It was observed from the present study that 74.8% of the cases were delivered at term with incidence of vaginal delivery was (4.4%) and low perinatal death(3.7%) with comprising to previous study(21)

Our opinions are in line with the recommendations of the Centers for Disease Control and Prevention (22). Covid-19 infection should not be the sole indication for delivery; rather, the patient should be duly assessed, and management, timing and mode of delivery should be individualized, dependent mainly on the clinical status of the patient, gestational age and fetal condition

All 9 of these pregnant women underwent Cesarean delivery as they were symptomatic with Covid-19 pneumonia in the third trimester of pregnancy. The time interval from the clinical manifestation of Covid-19 infection to Cesarean delivery was short (range, 1–7 days). It is therefore uncertain whether there is a risk of vertical transmission if the clinical manifestation-to-delivery interval is more than 7 days. Although previous studies have

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reported no evidence of congenital infection with SARS-CoV(23). Currently, there are no data on fetal and perinatal complications, such as miscarriage, congenital anomalies, fetal growth restriction and spontaneous preterm birth, when Covid-19 infection is acquired during the first or early second trimester of pregnancy (24).

In conclusion, are low rates of maternal and neonatal mortality as well as ICU admissions associated with COVID-19. Also there is no evidence of vertical mother-to-baby transmission of COVID-19.

Limitations

The quality of evidence generated is low due to the small sample size, missing data, potential for reporting bias and the quality of included studies. Additionally, as this study incorporates data from hospitalised patients alone, it is unclear if similar findings are extrapolatable to the general pregnant population. As the pandemic evolves, an update will be required with improved data sources to address these aspects

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