

Clinical Features and Outcomes of COVID-19 Infection among Pregnant Jordanian Women

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Abstract

Background: Studies of pregnant women who had COVID-19 are limited. Although earlier reports had shown that COVID-19 during pregnancy is associated with increased risk of spontaneous miscarriage, intrauterine growth restriction, and preterm delivery, more evidence is needed as most published studies involved small numbers. This study reviewed the clinical features and outcomes of COVID-19 positive pregnant women in Jordan.

Methods: A retrospective review was undertaken of the medical records of 112 COVID-19 positive pregnant women in Jordan between March–October 2020. The data collected included maternal age, comorbidities, gestational age, presenting symptoms, laboratory results, maternal and neonatal outcomes.

Results: The mean (\pm SD) for age and gestational age were 30 (\pm 5.4) years and 32(\pm 8.9) weeks, respectively. Additionally, 88 women (79%) were in the third trimester, and 79 women (70.5%) were multiparous. Data analysis showed that 62 women (55.4%) were symptomatic, and the most common symptoms were cough and dyspnea in 66% and 47%, respectively. The most common obstetric complications were preterm delivery (19%) and anemia (18%). 68% were delivered by cesarean section and 4.5% died.

Conclusion: Most pregnant women in this study were symptomatic with cough being the most common symptom, and the majority were diagnosed in the third trimester, suggesting that advanced gestational age may be a risk factor for catching the infection and being symptomatic. Therefore, pregnant women and healthcare practitioners should consider the impact of gestational age on the disease's behavior, and the rate of preterm labor and maternal death.

Keywords: COVID-19, pregnancy, delivery, Jordan, gestational age.

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Introduction

COVID-19 is the causative agent of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Knowledge of COVID-19 is rapidly evolving and international

management guidelines are constantly being updated. Additionally, COVID-19 has spread globally at an accelerated rate with a rapid increase in cases and mortality since its first identification in 2019 [1].

Viral pneumonia is one of the leading causes of death among pregnant women who were diagnosed with COVID-19 [2], and this probably is related to pulmonary physiological changes which happen during pregnancy and may lead to increased susceptibility to pulmonary infections that worsen outcomes

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[3]. The clinical presentation, radiological and laboratory characteristics of COVID-19 pneumonia in pregnant women are similar to non-pregnant women [4–5].

Because of the recent history of COVID-19, there are a limited number of published reports addressing the clinical courses, outcomes, and potential fetal risks. Additionally, there is no evidence of intrauterine vertical transmission [4].

Earlier reports have shown that SARS-CoV-2 during pregnancy is associated with increased risk of spontaneous miscarriage, intrauterine growth restriction, and preterm delivery [6]. While the literature about the effects of COVID-19 on pregnancy is rapidly evolving, published reports have indicated few maternal and neonatal complications [7]. In addition, more evidence is needed as most published studies involved small numbers and had only a short follow up period.

The main aim of this study is to the report the clinical course and outcomes of COVID-19 among pregnant Jordanian women.

Material and methods

This was a retrospective study of 112 pregnant Jordanian women who had COVID-19 between March and October 2020 in one of the three hospitals where the study took place. At the beginning of the pandemic, all pregnant women who tested positive for SARS-CoV-2 were admitted to hospital for isolation and management, even if they were asymptomatic, and later were discharged home after negative SARS-CoV-2 test results.

Inclusion criteria required the woman to be pregnant and tested positive for SARS-CoV-2. Medical records were retrieved, and data were collected and analyzed. The data collected

included age, parity, gestational age on admission to hospital, and comorbidities such as diabetes mellitus, hypertension and thyroid diseases. Additionally, the clinical presentation, laboratory investigations, disease course, pregnancy outcome and complications were recorded.

Statistical analysis was performed using IBM SPSS Statistics® Ver. 22. Numerical variables are shown as means and standard deviation (SD), and categorical variables as frequencies and percentages. For better comparison, variables were regrouped, such as the presence or absence of comorbidities, women being asymptomatic or symptomatic, and disease severity, where women were further subgrouped into mild disease (had normal vital signs and required no specific treatment or only symptomatic treatment), moderate disease (required admission to hospital for specific COVID-19 treatment) and severe disease (required admission to intensive care). A Chi-Square test was used to study correlations where appropriate. Statistical significance was defined as p -value < 0.05 . Ethical approval was granted by the Institutional Research Board of Jordan University of Science and Technology and King Abdullah University Hospital.

Results

A total of 112 pregnant Jordanian women were included in the study. The mean (\pm SD) of maternal age was 30 (± 5.4) years. The mean (\pm SD) of gestational age (GA) at the time of diagnosis was 32 (± 8.9) weeks. Additionally, 88 women (79%) were in the third trimester at the time of diagnosis. Regarding parity, 79 women (70.5%) were multiparous, and 33 (29.5%) were primigravidae. Table 1 summarizes the characteristics of the study population.

Table 1: Maternal characteristics of COVID-19 positive patients

Patients (n=112)	
Maternal age groups (years)	Number (%)
20–29	60 (53)
30–39	44 (39)
• 40–46	8 (7)
Pregnancy trimester at the time of diagnosis	Number (%)
• 1 st trimester	6 (5)
• 2 nd trimester	18 (16)
• 3 rd trimester	88 (79)
Comorbidities	26 (23)
• Diabetes	12 (10)
• Hypertension	5 (4)
• Thyroid disease	5 (4)
• Multiple sclerosis	2 (1.7)
• Cardiac disease	1 (0.9)
• Migraine	1 (0.9)
Pregnancy course	
• Discharges home with ongoing pregnancy	28 (25)
• Delivery	80 (71)
▪ Cesarean section	54/80 (67.5)
▪ Vaginal delivery	26/80 (32.5)
• Miscarriage	4 (3.6)
Maternal outcome	
• Recovered	107 (95.5)
• Death	5 (4.5)

The results showed that 26 women (23%) had comorbidities such as diabetes (10%) and hypertension (4%). Other comorbidities are shown in Table 1. Data analysis showed that

62 women (55.4%) were symptomatic and the most common symptoms were cough (66%) and dyspnea (47%). Table 2 summarizes the presenting symptoms.

Table 2: Presenting symptoms of the 62 symptomatic pregnant women (55.4%)

Presenting symptoms (n=62)	
Symptoms	Number (%)
Cough	41 (66)
Shortness of breath	29 (47)
Not feeling well (malaise)	22 (35)
Fever	18 (29)
Sore throat	15 (24)
Loss of smell	14 (23)
Loss of taste	12 (19)
Headache	10 (16)
Abdominal pain	8 (13)
Diarrhea	7 (11)
Vomiting	7 (11)
Runny nose	5 (8)
Loss of appetite	3 (5)
Chest pain	3 (5)

Of the women who had comorbidities, the results showed that 14 (54%) were symptomatic, and 12 (46%) were asymptomatic. The Chi-square test showed no statistically significant association between the presence of comorbidity and if women were symptomatic or not ($p = 0.56$).

Data analysis showed that among symptomatic women ($n = 62$, 55%), the

numbers and percentages of women who had mild, moderate and severe disease were four (71%), 11 (18%) and seven (11%), respectively.

Additionally, among women who had blood investigations, the results showed that lymphocytopenia, thrombocytopenia and high lactate dehydrogenase were found in 41%, 17%, and 75% of women, respectively. (Table 3).

Table 3: Laboratory results of COVID-19 positive pregnant women

Laboratory Investigations			
Category	Platelets ($n=110$) ^a	Lymphocyte ($n=95$) ^b	LDH ($n=24$) ^c
Mean (SD)	232 (± 70.4)x 10^9 /liter	1.64 (± 0.51)x 10^9 /liter	454 (± 189.4)x U/liter
Minimum	112x 10^9 /liter	0.40x 10^9 /liter	156x U/liter
Maximum	486x 10^9 /liter	6 x 10^9 /liter	855x U/liter
Women with normal count N(%)	81 (80)	45 (47)	6 (25)
Women with Low count N (%)	17 (17)	38 (41)	0 (0)
Women with High count N (%)	3 (3)	2 (2)	18 (75)

^a Platelet count less than 150×10^9 / liter is defined as thrombocytopenia

^b Lymphocyte count less than 1.5×10^9 /liter is defined as lymphocytopenia

^c LDH count of more than 400 U/liter is defined as high LDH count

Regarding the association between abnormal laboratory results and women being symptomatic or not, data analysis showed that of the 38 women who had lymphocytopenia, 30 (79%) were symptomatic, and the association was not significant ($p = 0.1$). Furthermore, of the 17

women who had thrombocytopenia, 11 (65%) were symptomatic, and the association was not significant ($p=0.4$). Of the 18 women who had high LDH results, all were symptomatic and the association was statistically significant ($p = 0.04$) (Table 4).

Table 4: Maternal and fetal complications of COVID-19 positive pregnant women

Maternal complications (maternal) ($n=112$)		Fetal complications ($n=112$)	
	N (%)		N (%)
Placental abruption	2 (1.7 %)	Intrauterine growth restriction	2 (1.7%)
Preterm labor	21 (19 %)	Intrauterine fetal death — IUFD	2 (1.7%)
PROM	4 (3.5%)	Miscarriage	4 (3.5%)
Anemia	20 (18%)	Neonatal death	2 (1.7%)

Antenatal complications were observed in 48.5% of women, with maternal complications being reported in 51 women (45%) while fetal complications occurred in four (3.5%). Table 4 summarizes maternal and fetal complications.

Eighty women (71.4%) delivered during the study period. The mean GA (\pm SD) at the time of delivery was 38 (\pm 2.1) weeks. Additionally, the majority of women (54, 68%) had a cesarean section, while 26 (32%) had a vaginal delivery. Four women (3.6%) had a miscarriage and 28 women (25%) were discharged home with ongoing pregnancy.

The majority of cesarean sections (CS) were performed due to obstetric indications (43, 80%), and to improve respiratory status in 5 (9%) women. Furthermore, 6 (11%) women underwent CS upon their request.

Data analysis showed that 107 women (95.5%) were discharged home in good condition and five women (4.5%) died. Data analysis of the women who died showed that the mean age (SD), mean number of pregnancies (SD), mean number of deliveries (SD), and mean gestational age (SD) were 36.3 (8.1) years, 2.2 (1.9) pregnancies, 1.0 (1.4) delivery, and 30.7 (3.1) weeks, respectively. None of the women had comorbidities, and all were pregnant in the third trimester and presented with shortness of breath and died because of severe respiratory disease. Additionally, all were delivered by emergency CS to help improve their respiratory status.

Regarding neonatal outcome, the mean (\pm SD) of birthweight was 3,000 (+480) grams, and nine newborn babies were admitted to a neonatal intensive care unit (NICU). Additionally, two newborns died, one of complications of Edward's syndrome and the other because of severe prematurity; only one newborn baby tested positive for SARS-CoV-2.

Discussion

This was the first study addressing the clinical features and outcomes of COVID-19 infection among pregnant Jordanian women. Over two thirds of our study population were multiparous, and while similar findings were shown in another study, a lower rate of 45% was reported by other studies [8–9]. This may reflect differences in the study populations in different reports. The results of this study showed that comorbidities were reported by 23% of women. This is in keeping with other published reports [8–10]. Additionally, the percentage of diabetes mellitus in our study was 10%. This finding is supported by other published reports which showed a rate between 4% and 20% [8, 12]. Regarding hypertension, the other major comorbidity in our study population, this was reported by 4% of women who tested positive. Other reports report a rate between 7% [13] and 23% [8, 10, 12]. The wide range in the rate of hypertension may be explained by the differences in the study populations.

Our rate of asymptomatic COVID-19 positive women was 45%. While the rate is similar to one published report [8], lower rates are reported by other published studies and the rate ranges between 13–33% [5, 10]. Such differences in the rates of asymptomatic women may reflect differences in the study populations, and if the study was single or multicenter. We acknowledge that our study was based on a small number of women as the pandemic was at its beginning at the time of the study and the number of infected patients was low.

Regarding symptomatic women, the most common symptoms in this study were cough in 66%, followed by shortness of breath in 47%, while fever occurred in only 29%. Other studies show different rates of presenting

symptoms, with one report showing the rate of cough to be 62% [8]. Other reports showed that fever was the most common symptom [10, 12]. This probably reflects different disease behavior among different study populations. Furthermore, regarding disease severity among symptomatic women, our results showed that over two thirds had mild disease, which is similar to other reports where the percentage ranges between 62–93% [5, 8, 10]. Additionally, the rates of severe disease and death were 11% and 4.5%, respectively. This is in keeping with other reports [11].

Our results showed that most COVID-19 positive symptomatic women were in the third trimester. Similar results were shown in reports from the United Kingdom and Spain [14, 15]. This can be attributed to immunological changes that occur during pregnancy and may lead to increase susceptibility to infections. This should encourage healthcare practitioners to educate pregnant women in particular women in the latter half of pregnancy about the possibility of having symptoms if they catch the infection in the third trimester, which may encourage pregnant women to take extra precautions during the third trimester.

Some hematological changes were observed among COVID-19 positive women, which included lymphocytopenia, thrombocytopenia, and high lactic dehydrogenase (LDH). Laboratory investigations were requested depending on disease severity, and therefore the majority of asymptomatic women did not have advanced laboratory investigations; in addition, all women who had the LDH test were symptomatic. Our results showed that the rate of lymphocytopenia was 41%, which is in keeping with the rate of other reports ranging

from 20–80% [5, 8, 16]. All patients with high LDH levels were symptomatic and this was statistically significant, which might imply that high levels of LDH may be used as a predictor of disease severity. Furthermore, the rate of thrombocytopenia was 17%, and the published rate ranges between 9–38% [8, 10].

The rate of antenatal complications in our study was 48.5%. The published rates range between 21–56% [5, 10, 12]. Preterm labor was the most common complication (19%). Published studies show different rates of preterm labor of between 8–41% [8, 17]. Additionally, miscarriages complicated 3.5% of the women in our study, but other studies have reported higher rates up to 65% [8, 17]. A possible explanation of the differences in the rate of preterm labor and miscarriages may include the different study population, and the different population may have had other risks factors for preterm delivery and miscarriage.

The rate of cesarean section in our study was 68%, and a higher rate is reported in studies from China (up to 100%) where COVID-19 infection was an indication for cesarean section [8, 10–12]. Additionally, Cesarean section was performed for obstetric indications in most cases, while in 11% of women it was performed upon maternal request.

Adverse neonatal outcomes were reported in 3.7%, and a similarly low rate is shown in another study; however, other studies report a higher rate of 9% [8–10]. There was one SARS-CoV-2 positive neonate. This probably reflects that COVID-19's effect on the fetus is limited.

Maternal death was reported in 4.5%, whereas the range of published maternal mortality is between 1–78% [8, 10, 18]. This wide range may reflect differences between

study population and the different rate of severe disease.

We acknowledge the limitations of our study as being that the sample is small, details of the antenatal care booking and investigational results were not available, and nor were details of the antenatal obstetric scans. Furthermore, we were unable to report on the pregnancy outcome of women discharged from hospital after recovery with ongoing pregnancies.

Conclusion

Most pregnant women in this study were

symptomatic and cough was the most common symptom; the majority were diagnosed in the third trimester. This suggests that advanced gestational age may be a risk factor for catching the infection and for women to be symptomatic. Therefore, pregnant women and healthcare practitioners should consider the impact of gestational age on the disease behavior, and maternal mortality. However, the adverse neonatal outcomes were low with little or no risk of vertical transmission.

Disclosure

The authors declare no conflict of interest

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المظاهر السريرية ونتائج الإصابة بفيروس كورونا - 19 لدى النساء الحوامل الأردنيات

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الملخص

الهدف: الدراسات بين النساء الحوامل المصابات بـ(COVID-19) محدودة، وأظهرت تقارير سابقة أن (COVID-19) في أثناء الحمل يرتبط بزيادة مخاطر الإجهاض التلقائي وتراجع النمو داخل الرحم والولادة المبكرة، وهناك حاجة إلى مزيد من الأدلة؛ لأن معظم الدراسات المنشورة تضمنت أعداداً صغيرة، وهدفت هذه الدراسة إلى مراجعة السمات والنتائج السريرية للحوامل المصابات بـ(COVID-19) في الأردن.

الأساليب: مراجعة بأثر رجعي للسجلات الطبية لـ (112) امرأة حامل ومصابة بفيروس (كورونا-19) في الأردن خلال الفترة من مارس إلى أكتوبر (2020)، تضمنت البيانات التي تم جمعها: عمر الأم، والأمراض المصاحبة، وعمر الحمل، وعرض الأعراض، والنتائج المخبرية، ونتائج الأم والوليد.

النتائج: كان المتوسط (\pm SD) للعمر، وعمر الحمل 30 (± 5.4) سنة، و32 (± 8.9) أسبوعاً، على التوالي، بالإضافة إلى ذلك، كانت 88 امرأة (79%) في الثلث الثالث من الحمل، و79 امرأة (70.5%) كن متعددات الأحمال، أظهر تحليل البيانات أن 62 امرأة (55.4%) لديهن أعراض، وكانت الأعراض الأكثر شيوعاً هي السعال وضيق التنفس في (66%) و (47%) على التوالي، وكانت مضاعفات الولادة الأكثر شيوعاً هي الولادة المبكرة (19%)، وفقر الدم (18%)، إضافة إلى أن (68%) ولدوا بعملية قيصرية، وتوفي (4.5%) من النساء الحوامل.

الخلاصة: كانت معظم النساء الحوامل المصابات بفيروس (كورونا-19) في هذه الدراسة تعانين من أعراض، وكان السعال أكثر الأعراض شيوعاً، وتم تشخيص غالبية الإصابات في الثلث الثالث من الحمل، وهذا يشير إلى أن عمر الحمل المتقدم قد يكون عامل خطورة للإصابة بالعدوى وظهور الأعراض، لذلك يجب على النساء الحوامل ومقدمي الرعاية الصحية النظر في تأثير عمر الحمل على سلوك المرض، ومعدل الولادة المبكرة، ووفيات الأمهات.

الكلمات الدالة: (COVID-19)، حمل، ولادة، الأردن.