# Covid-19 Infection of Pregnant Women in Morocco: Experience of a Tertiary Hospital

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*Abstract:  **Introduction** : Coronavirus disease 2019, caused by severe acute respiratory syndrome coronavirus 2, is spreading globally at an accelerated rate .This is a serious public health emergency, especially fatal in vulnerable populations and communities where medical service providers do not have sufficient capacity to manage infections. **Materials and methods**: We conducted a descriptive and analytical observational study. Among the 90 pregnant women tested COVID positive, from 16Mars to 30 November 2020, 44 hospitalized were included in the study. We described and compared maternal characteristics including comorbidities, symptoms, gestational age at diagnosis, length of hospitalization, pregnancy and fetal outcomes between the two groups according to the severity of disease. **Results**: Compared with nonsevere cases (77.2%), women with serious disease (22.8%) were elder with associated comorbidities. It seems that they express more caught, dyspnea and myalgia, fever is statistically higher but not significant. High leukocyte count, lymphopenia and elevated C reactive protein were more frequent in pregnant group with severe infection. Among the women who gave birth, 11.7%(2/17)had a vaginal delivery, 76.6%(13/17) had cesarean for obstetrical indication, and only 11.7%(2/17) had cesarean for worsening of pneumonia .Rates of preterm birth in all delivered women 17.6% (3/17),.oxygen-requiring, and critical COVID-19 were. We described 4 maternal death and 3 fetal dismisses of patients with critical COVID-19. All neonates have been tested negative. **Conclusion**: COVID-19 infection in pregnant women may be a serious disease, early diagnosis and timely obstetric management are essential to improve maternal and neonatal outcomes.*

**Keywords—** COVID-19 pandemic, pregnancy outcomes, fetal outcomes, SARS-CoV-2

## 1. INTRODUCTION

Coronavirus is an enveloped, positive-stranded ribonucleic acid (RNA) virus of the family of Coronaviridae and belonging to the Nidovirales order [1], generally responsible for severe pulmonary and extrapulmonary disease or even death.

The Covid-19 pandemic has exploded since cases were first reported in China on December 31, 2019 [2]. By January 30, 2020, coronavirus disease has been declared a public health emergency of international concern [3]. It is responsible for almost 69 million cases and more than a million deaths worldwide [4]. It hit Morocco in early March 2020; lockdown was imposed on March 16.the most common symptoms of COVID-19 pneumonia are fever, malaise, anosmia, ageusia, nausea, diarrhea, dry cough, shortness of breath and respiratory distress [5]

Different Studies on COVID-19 have shown that older age and comorbidity are major risk factors for adverse outcomes and mortality [6].

It is crucial to understand the pathophysiology and molecular mechanisms of COVID-19 to understand the COVID-19 phenotype during pregnancy. Based on current pathogenetic knowledge SARS-CoV-2 infects pulmonary cells via the SARS-Covid receptor angiotensin-converting enzyme 2 (ACE2) .Then transmembrane serine protease 2 (TMPRSS2) is used for S protein priming which is followed by viral replication and release of the virus, causing pyroptosis .A cascade of inflammatory reaction will take place leading to excessive inflammation and damage the integrity of the lung , resulting an infection with other (host) microbes .The inflammation caused by SARS-CoV-2 may likewise result in a "cytokine storm" that can prompt  multisystem organ failure .

Among the peculiarities of COVID 19 infection in pregnant women, pregnancy can have an impact on the response to infections, and specifically to viruses due to the modulations of the maternal immune system to tolerate the implantation of a semi allogeneic or allogeneic fetus. Also, the anatomical changes have an impact on lung function due to the reduction in chest volume leading to a decrease in functional residual capacity, end-expiratory volumes, and residual volumes.

In addition, the hypercoagulable state in pregnancy COVID-19 may have additive or synergistic risk factors for thrombosis [7]. As for the vertical transmission of SARS-CoV-2 , not much scientific proof has been provided [7].

The purpose of this study was to describe the clinical manifestation of pregnant women with COVID 19 infection risk factors, short-term pregnancy, and perinatal outcomes.

## 2. METHODS

Our hospital is designated as a referent hospital for patients with COVID-19 in the Eastern Region of Morocco. Out of the total 11488 COVID positive patients diagnosed in 9 months, 90 patients were pregnant, among those women and only 44 were admitted. The reason for hospital admission was obstetrics reason, COVID 19 severity illness or transferred from another region with no disposable of COVID 19, unity for pregnant women. Approval of the ethical committee was taken.

We conducted a descriptive and analytical observational study. Prospective clinical information was collected at the time of presentation to the maternity unit over a period of 9months (March-November 2020). All pregnant women included had confirmed COVID-19 using RT-PCR for SARS-CoV-2 nucleic acid from nasopharyngeal samples.

The medical comity of the hospital was considered patients recovered from COVID-19 if, 10 days after treatment or 14 days after symptoms began, they were asymptomatic for more than 72 h. Otherwise, COVID-19 cases were considered active.

At first, we characterized patients into two categories according to disease severity. The first one was named non-severe illness including patients with asymptomatic, mild and moderate illness. The second category was named severe illness including patients with severe and critical illness we used the classification defined by The National Institutes of Health in the United States(table1) [5].

We described and compared maternal characteristics including age, comorbidities, symptoms, gestational age at diagnosis, length of hospitalization, pregnancy and fetal outcomes between the two groups.

Table 1: COVID-19 disease severity
(From :
https://www.covid19treatmentguidelines.nih.gov/overview/clinical-presentation/ [5])

| Illness category | Characteristics |
|---|---|
| Asymptomatic | • Positive test for SARS-CoV-2 but no symptoms |
| Mild illness | • Any signs and symptoms (fever, cough, sore throat, malaise, headache, muscle pain)<br>• without shortness of breath, dyspnea, or abnormal chest imaging |
| Moderate illness | • Evidence of lower respiratory disease by clinical assessment or imaging<br>• Saturation of oxygen (SaO2) >93 percent on room air at sea level. |
| Severe illness | • Respiratory frequency >30 breaths per minute,<br>• SaO2 ≤93 percent on room air at sea level,<br>• PaO2/FiO2 <300 mmHg,<br>• lung infiltrates >50% |
| Critical illness | • Respiratory failure, septic shock, and/or multiple organ dysfunction |

## 3. RESULTS

### 3.1 DEMOGRAPHIC PROFIL AND PREEXISTING COMORBIDITIES

Table 2 shows demographic profile and associated comorbidities of pregnant women in severe and non-severe group.

By the end of November, 44 pregnant women had been admitted in our maternity. The mean age was 27.9(±4.8) years in nonsevere cases and 33.3(±.4) in severe cases. The rate of obesity was significantly higher in severe cases (60%) compared with non-sever cases (2.9%). As many as 3 (6.8%) had no severe cases and 5 (50%) severe cases had comorbidities. More number of women in our study were in the third trimester.

Table 2: Demographic Profile and associated comorbidities of the patients (n = 44) (All data are expressed as number (%)

| | No sever cases (n=34) | Sever cases (n=10) | Adjusted P-Value |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Maternal age | 27.941 ±4,84 26 | 33,300 ±4,08 38 | 0.001 |
| obesity | 1(2.9 %) | 6(60%) | 0.001 |
| Preexisting diabetes 1/2 | 0 | 3(30%) | 0.009 |
| Gestational diabetes | 2(5.9%) | 1(10%) | 0.5 |
| History of pre-eclampsia | 0% | 0% | |
| Gestational hypertension or pre-eclampsia | 0% | 1(10) | 0.5 |
| Tabaco use | 1(2.9%) | 0% | 0.7 |
| Presence of comorbidity * | 3 (8.8%) | 6(60%) | 0.002 |
| First trimester | 3(8.8%) | 1(10%) | |
| Second trimester | 4(11.8%) | 1(10%) | |
| Third trimester | 27(79.4%) | 8(80%) | |

\* At least one comorbidity, the same patient can present more than one

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## 3.2 CLINICAL CHARACTERISTICS AND LABORATORY FINDING

The clinical characteristics and laboratory findings of 44 pregnant women are demonstrated in Table 3 .

The most common presenting symptoms (many patients had more than one symptom) were fever, anosmia/ageusia, asthenia, and dyspnea. Comparing with the group of nonsevere cases, it was noted that the group of severe cases had significantly high leukocytes count, lymphopenia, and elevated C reactive protein.

Table 3 : The clinical characteristics and laboratory findings of 44 pregnant women according to the severity of illness (All data are expressed as number (%)

| | | No sever cases (n=34) | Sever cases (n=10) | Adjusted P-Value |
|---|---|---|---|---|
| Symptoms of COVID-19 | fever | 17 (50%) | 7(70%) | 0.2 |
| | Anosmia/ageusia | 23(67.64%) | 9(90%) | 0.1 |
| | cough | 14(41.17%) | 9(90%) | 0.007 |
| | dyspnea | 2(5.88%) | 10(100%) | 0.001 |
| | myalgia | 7(20.58%) | 7(70%) | 0.006 |
| | asthenia | 19(55.9%) | 9(90%) | 0.05 |
| Laboratory finding | High leukocytes count > 9.5 | 19(55.9%) | 10(100%) | 0.008 |
| | lymphopenia | 8(23.5%) | 10(100%) | 0.001 |
| | Elevated C reactive protein | 20 (58.8%) | 10(100%) | 0.01 |

## 3.3 MATERNAL AND PREGNANCY OUTCOMES

Table 4 shows maternal and pregnancy outcomes in both the groups. 60% of severe cases (13.6% among all admitted patients) were admitted to the intensive care unit with a length of hospitalization ranging from 4-20 days (median: 9.5days). 6 required noninvasive ventilation, 4 required mechanical ventilation and ECMO for 2 patients. As for nonsevere cases, they were admitted in non-intensive care units with a length of hospitalization ranging from 2-6 days(median:5.8days), only 3 patients required nasal oxygen therapy. Maternal death occurred in 4.4% of all reported CoV-related disease cases (4 of 90), 9.1% of admitted patients, and 40% of the severe group. It was significantly (p=0.002) higher, they were, all of them with a critical COVID-19.

Low-molecular weight heparin was administered in 17(38,63%) cases. Azithromycin was the most common (92,45%) and Hydroxychloroquine was the least common (6,8%) administered medication

17 (38.63%) of the 44 delivered and 2 (4.5%) had a miscarriage. Intra uterine fetal death was noted in 3 pregnant women, each having a comorbid situation with such diabetes or gestational hypertension. 90.9% had recovered.

Table 4 : Maternal and pregnancy outcomes according to the severity of illness

| | No severe cases (n=34) | Severe cases (n=10) | Total (n=44) |
|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| Maternal outcomes | Maternal death | 0% | 4(40%) | 4(9.1%) |
| | Total of delivered women | 13 | 4 | 17(38.63%) |
| | Miscarriage | 1(2,94%) | 1(10%) | 2(4.54%) |
| | Intra uterine fetal death | 1(2,94%) | 2(20%) | 3(6.8%) |
| | Maternal recover | 34 | 6 | 30 |
| Respiratory support | Nasal oxygen therapy* | 3(8.82%) | 10(100%) | |
| | Noninvasive ventilation | 0 | 5(50%) | |
| | Invasive mechanical ventilation | 0 | 3(30%) | |
| | ECMO | 0% | 2(20%) | |
| COVID 19 Therapy | Low molecular weight heparin | 7(20,58%) | 10(100%) | 17(38,63%) |
| | Azithromycin | 34(100%) | 8(80%) | 42(92,45%) |
| | Hydroxychloroquine | 3(8.82%) | 0 | 3(6,8%) |
| | Systemic corticosteroid | 1(2.94%) | 10(100%) | 11(25%) |
| | High-dose vitamin C | 34(100%) | 6 (60%) | 40(90,9%) |
| | Antibiotherapy for other pathogens | 0 | 4(40%) | 4(9,09%) |
| Length of stay | ICU (n,%,days) | 0 | 6(9.5days±6) | 6 (13.6%) (9.5days±6) |
| | NICU** | 34 (5.4days±1.89) | 7(8.1days±3.4) | 41 (93.2%) (5.87days±2.4) |
| Di | Asymptomatic | 2(5,88%) | - | |

| | | |
|---|---|---|
| Mild illness | 25(73,52%) | - |
| Moderate illness | 8(23,52%) | - |
| severe illness | - | 6(60%) |
| Critical illness | - | 4(40%) |

\* The patient who had nasal oxygen therapy could have another respiratory support
\*\* Patients admitted initially in ICU and transferred to NICU after stabilization are included in the count
Abbreviation: ECMO = extracorporeal membrane oxygenation, ICU: intensive care unit, NICU: non-intensive care unit

### 3.4 MODE OF DELIVERY AND NEONATAL OUTCOMES

Among those women, 11.7% (2/17) had a vaginal delivery, cesarean delivery was indicated for COVID-19 pneumonia in 11.7 % (2/17) for critical stage of the disease and in 76.6% (13/17) for obstetrical reasons.

The rates of preterm delivery before 37 weeks were 17.6% (3/17), which was related to the severity of illness in two cases and preterm pre-labor rupture of membrane in the other one complicated with fetal distress.

Among the 17 neonates, there was 1 case of severe neonatal asphyxia which was admitted in ICU. The mother of this neonate had preterm pre-labor rupture of the membrane complicated with fetal distress, and it was delivered at 34 weeks' gestation by cesarean delivery. The neonate was discharged home 10 days later.

All neonates have been tested for SARS-CoV-2 viral nucleic acid on pharyngeal swab samples and the results were negative.

Table 5, Mode of delivery and neonatal outcomes

| | | Non severe (n=13) | Severe (n=4) | Total (n=17) |
|---|---|---|---|---|
| Mode of delivery | Vaginal delivery | 1(7.7%) | 1(25% | 2(11.7%) |
| | Cesarean for obstetric reason | 12(92.3%) | 1(25% | 13(76.6%) |
| | Cesarean for covid 19 symptoms | 0 | 2(50% | 2(11.7%) |
| Term of | Preterm birth | 1 | 2 | 3(17.6%) |

| | | | | |
|---|---|---|---|---|
| | Birth after 37 w | 12 | 2 | 14(82.4%) |
| Neonatal outcomes | Birth weight | | | 3356 ±520 (2100 ;4300) |
| | SARS COV 2 positive | 0 | 0 | 0 |
| | Admission in ICU | 1 | 0 | 1(5.8%) |
| | Neonatal death | 0 | 0 | 0 |

Abbreviations: COVID-19, novel coronavirus disease 2019/ ICU: intensive care unit

## 4. DISCUSSION

To our knowledge, this is the first case-controlled study carried out nationally on pregnant women with COVID-19 infection pneumonia.

The present study involved 44 admitted patients, among 90 pregnant women tested COVID positive. We focused on investigating the demographic profiles, pregnancy, maternal, and fetal outcomes according to the severity of illness.

### 4.1 DEMOGRAPHIC PROFILE

Our study shows that women with sever disease are those with advanced age(p=0.001) with the highest rates of comorbidities .The most prevalent comorbidities were obesity (p=0.001) diabetes(p=0.009) ,hypertension(p=0.5) .This was identified in France ,China ,The United State and The United kingdom [8,10-12].

Yan et al. [13] and Kayem et al. [8] reported that most pregnant women acquired the infection in the second and third trimester of pregnancy, which much higher with our findings .

### 4.2 CLINICAL CHARACTERISTICS, LABORATORY FINDINGS

Most of patients of both groups expressed fever(p=0.2), anosmia /ageusia (p=0.1) but the difference between the two groups was not statistically significant, (p > 0.05) .Thought cough (p=0.007)dyspnea(p=0.001) ,myalgia (p=0.006)and asthenia(p=0.05), were more likely reported in severe group , suggesting that signs and symptoms of COVID-19 might differ according to the illness severity .

Kong et al. [14] reported that severe cases presented lower lymphocyte counts, higher neutrophil levels, and elevated biomarkers for infection .In our study, severe cases were more likely to present lymphopenia , high count of leukocytes and C reactive protein.

### 4.3 MATERNAL AND PREGNANCY OUTCOMES

Among 44 pregnant women with COVID-19 admitted, 22.7% were categorized as severe (severe 13.6% critical 9.1%). Similar findings were noted in in France [8] (severe 15 %, critical 6%), the United States [9] (severe 9%, critical 5%) and China (6.9%) [13].

The proportion of pregnant women with COVID-19 admitted in ICU was 10% in The United Kingdom [10] , 7.4% in The United States and 6.9% in China [13] .Comparing to the reported rates of ICU admission ours (13.6%) may be overestimated because the study included only hospitalized patients ,also during the pandemic maternal care has remained a high national and regional priority. Hospital length of stay was higher in severe groups wither in ICU or not. That's can be explained that pregnant women who experienced severe disease had a slower recovery time

Maternal death occurred in 0.7 % (3/427) in The United kingdom [10] 0.2% (1/617), (16/8207) respectively in France [8] and united state [15]. nevertheless, 3 maternal deaths were reported in a case series of 12 pregnant women with SARS-CoV in Hong Kong, China [16], and 7 maternal deaths among 9 pregnant women with severe COVID-19 disease in Iran [17].

Whereas in our case series maternal death occurred in 4.4% (4/90) with significant difference in rate of mortality and severity of disease (p=0.009). Hence, this discrepancy may be referred to their critical situation. It should be noted that 3 of our gravidae unlikely were 35 years of age or older, obese in the third trimester with preexisting diabetes in 2 of them and gestational hypertension in the other one. As for the fourth one, she was 29 years old, non-obese, in the third trimester with no comorbidities.

### 4.4 MODE OF DELIVERY AND NEONATAL OUTCOMES

The rate of preterm delivery before 37 weeks was 44% in China [13], 35% in France [8] and 27.6% in The United Kingdom [10]. Compared with the reported rates, the prematurity rate is lower which is more reassuring. In our study, 88.3% of women gave birth by caesarean section; most caesarean births were for obstetrical indications 76% and the other 11.7% for worsening pneumonia which is similar to the rate of severe disease that has been reported across China 85.9% (38.8% for COVID 19 pneumonia) [13]. However cesarean delivery rate was 60% in United Kingdom [10] and 48.1% in France [8]. This increased rate cannot be avoided since the indications were in the majority of obstetrical reasons.

There are few reports of miscarriages or fetal death related to COVID-19 during pregnancy[18]. Kayem et al. reported 7 (1.3%) cases of intrauterine fetal death and 5(2.8%) fetal loss in French women. Richtmann et al. [18] described five cases of fetal demise in Brazilian women .As for Hantoushzadeh et al. [19], he reported four fetal deaths in Iranian women with severe COVID-19, with three maternal deaths. In our case study, fetal death could be attributed to causes other than

COVID-19 hypertensive context, diabetes, hypoxemia according the critical condition. However, we cannot define the cause of death as the fetuses did not benefit from an autopsy, anatomopathological study of the placenta or pharyngeal swab samples

The major limitations in those reports are the small size of sample which makes it necessary to use a larger sample by collaborating with nearby centers. The second limitation was the exclusion of pregnant women who had not been hospitalized. The third situation, we do not have a precise idea on the number of infected pregnant women who have not been consulted in our maternity and who have confined themselves to their homes

Koltyar et al. [20] reported in a recent systematic review that of 936 neonates from mothers with coronavirus disease 2019, 27 neonates had a positive test. He suggests that vertical transmission is possible and seems to occur in a minority of cases without significant consequence to the newborns. Our findings are in agreement with what was observed with SARS-CoV in the whole world, all neonates tested were negative for SARS-CoV-2

In conclusion, COVID-19 infection in pregnant women may be a serious disease, related to severe acute respiratory distress syndrome, potentially fatal. Severe cases were elders with comorbidities and took a longer recovery course. Thus, early diagnosis and timely obstetric management are essential to improve maternal and neonatal outcomes.

The arrival of the COVID-19 vaccine has brought great hope and optimism to people and personal health, hoping it will end this pandemic.

## 5 ACKNOWLEDGMENT

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