

COVID-19 Coronavirus Infection and Trimesters: Is There a Link?

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Abstract

Objectives: Despite serious challenges, humanity has been able to adapt and take measures to limit the spread of COVID-19 and minimize its negative consequences. This pandemic has emphasized the importance of global collaboration, scientific and medical progress, and raised questions about the need to strengthen health systems and international crisis response mechanisms. Although humanity continues to face new challenges associated with COVID-19, including the emergence of new strains, the development and introduction of vaccines and effective therapeutic agents have raised hope for overcoming the pandemic and creating a more sustainable health system for the future. The aim of our study was to investigate the course of the disease according to trimesters.

Material and methods: We retrospectively analyzed the case histories of women with COVID-19 coronavirus infection treated in the mentioned hospitals between December 2020 and February 2022. The study considered the following parameters according to the trimester of pregnancy: number of previous pregnancies, age, disease severity and presence of comorbidities.

Results: Mild COVID-19 accounted for a smaller proportion of the sample (3.2-13%) due to treatment at home or in outpatient settings. More than half of those hospitalized (209 – 51.0%) were admitted in severe condition. Analysis of COVID-19 severity distribution by trimester showed statistically significant differences ($p < 0.05$). Associated diseases were detected in 306 patients, accounting for 74.6% of all cases. Statistically significant differences were found when evaluating comorbidities according to trimester. The main complaints included dry cough (394), weakness (388), sore throat (372), fever (367), malaise (365) and headache (287).

Conclusions: Infection is more frequently observed in pregnant women in the third trimester, which may be related to the increased frequency of diagnosis in this period. The presence of comorbidities is a factor that increases the severity of the condition.

Keywords: COVID-19, pregnancy, symptoms, trimesters, SARS-Cov-2

Introduction

The 21st century began with a thorough rethinking of the epidemic and pandemic potential of betacoronaviruses, which required a control system as multilayered as that for influenza. This system covers all stages – from the natural reservoir of the virus, which is bats (Chiroptera, Microchiroptera), to the organization of prophylactic and anti-epidemic measures. [1].

COVID-19 is characterized by a lower maternal mortality rate than SARS or Middle East respiratory syndrome. Asymptomatic women may develop respiratory symptoms after delivery. [2]. Therefore, it is important for physicians of all specialties to consider the possibility of asymptomatic forms of the

disease, as they most often remain undetected and unrecognized. In a study by Abuova G. et al. it was found that ultrasonography revealed oligohydramnios in 85% of cases, premature aging of the placenta and placental cysts in 27.5%, and impaired blood flow in utero-fetal-placental circulation in 12.5% of cases. [3]. Subsequently, more than half (51.4%) of the women gave birth at term. However, 48.5% of patients had preterm labor.

Pregnant women with COVID-19 infection are known to be at high risk not only because of an increased likelihood of severe infection and pneumonia, but also because of an increased incidence of placental-associated pregnancy complications [4].

Placental-associated complications of pregnancy are categorized as major obstetric syndromes that include conditions such as preeclampsia, preterm labor, and fetal growth retardation. [5]. To date, there are publications indicating that pregnant women with pneumonia are more likely than other groups to experience preterm labor and low birth weight preterm infants [6, 7].

Despite serious challenges, humanity has been able to adapt and develop measures to limit the spread of COVID-19 and prevent its negative consequences [8]. The pandemic emphasized the importance of global cooperation, scientific and medical progress, and emphasized the need to strengthen health systems and international crisis response mechanisms.

Humanity continues to face new COVID-19 challenges, including the emergence of new strains [9]. However, the development and introduction of vaccines and effective treatment methods have raised hope for overcoming the pandemic and creating a more sustainable health care system in the future. Our study was aimed at investigating the peculiarities of the course of the disease depending on the trimester of pregnancy.

Material and methods

The study was conducted on the basis of the city infectious disease hospital, infectious disease center and perinatal center of Shymkent city. It was a cohort, non-interventional clinical study.

The work was approved by the Ethical Committee of JSC "South Kazakhstan Medical Academy" on November 21, 2020 in accordance with the protocols of the Helsinki Declaration of 1964. The conclusion of the ethical committee is recorded in protocol #1 dated March 16, 2021. All study participants gave consent to participate after signing informed consent. The study was based on the protocols "Coronavirus infection in pregnant women, women in labor and delivery" and "Coronavirus infection in adults".

We retrospectively analyzed the medical histories of women with COVID-19 treated at the mentioned institutions between December 2020 and February 2022. The study examined parameters such as the number of previous pregnancies, age

groups, disease severity, and the presence of comorbidities depending on the trimester of pregnancy.

Statistics. The normality of the distribution was checked according to Kolmogorov-Smirnov with the Lilliefors correction. Since all data showed a normal distribution, the mean and standard deviation were subsequently used. Categorical variables are presented as absolute numbers, percentages, and frequencies. A $p < 0.05$ value was considered statistically significant. Statistical processing of the obtained data was carried out using the IBM SPSS Statistics 26.0 program.

Ethics

The study was approved by the Local Bioethical Committee of JSC "SKMA" (date: 03/16/2021). Written informed consent for publication in the article was obtained from patients or their legal representatives.

Results

Comparison of pregnancy parity according to trimester revealed, in the first trimester the median rate was 3.00 (Q -Q13 : 1-5), in the second trimester it was 3.00 (Q -Q13 : 2-4) and in the third trimester it was 3.00 (Q -Q13 : 2-5) (Table 1).

The patients were divided into age groups as shown in Figure 1: 18-20 years, 21-25 years, 26-30 years, 31-35 years, 36-40 years and 41-50 years. The largest number were women aged 26 to 35 years – 223 (54.4%). The smallest group consisted of pregnant women aged 41-50 years with only 10 (2.4%). The younger age group of 18-20 years was found in 21 cases (5.1%). The sample included all age groups, including both women of early and late reproductive age.

Table 2 shows the predominance of the age group between 26 and 30 years during the first two trimesters of pregnancy where this age range was 36.0% and 28.7% respectively. In the third trimester, pregnant women between 31 and 35 years of age accounted for 30.7%.

Table 1 Distribution of indicators by trimester of pregnancy

Indicator	Trimesters of pregnancy			p
	1 trimester n=50	2 trimester n=122	3 trimester n=238	
Pregnancy Parity Me (Q -Q)13	3 (1-5) Min=1 Max= 8	3 (2-4) Min=1 Max= 8	3 (2-5) Min=1 Max=9	0,685
Ages groups, abs.%	18-20 years old	4 (8,0)	7 (5,7)	0,565
	21-25 years old	14 (28,0)	31 (25,4)	
	26-30 years old	18 (36,0)	35 (28,7)	
	31-35 years old	7 (14,0)	29 (23,8)	
	36-40 years old	6 (12,0)	18 (14,8)	
	41-50 years old	1 (2,0)	2 (1,6)	
Severity abs.%	Light	1 (2,0)	5 (4,1)	0,000*
	Average	32(64,0)	64(52,5)	
	Heavy	7(2,9)	69(29,0)	
	Extremely difficult	0	2(1,6)	
Presence of comorbidities abs.%	Yes	27 (8,8)	82 (26,8)	0,005*
	No	23 (21,9)	40 (38,1)	
Number of bed days,abs.%	1-7 days	27 (13,8)	59 (30,1)	0,208
	8-15 days	18 (9,9)	49 (27,1)	
	16 or more	5(15,2)	14(42,4)	

* Differences of indicators are statistically significant ($p < 0.05$)

Table 2 Number of bed days spent by age groups of pregnant women with COVID-19

Number of bed days, abs. %	Age groups						P
	18-20 years old	21-25 years old	26-30 years old	31-35 years old	36-40 years old	41-50 years old	
1-7 days	9(4,6)	43(21,9)	55(28,1)	56(28,6)	29(14,8)	4(2,0)	p=0,04*
8-15 days	12(6,6)	46(25,4)	53(29,3)	43(23,8)	24(13,3)	3(1,7)	p=0,007*
16 or more	0	4(12,1)	6(18,2)	10(30,3)	10(30,3)	3(9,1)	

*Differences of indicators are statistically significant (p<0.05)

The next indicator we investigated was the severity of COVID-19 coronavirus infection in hospitalized pregnant women. As shown in Figure 2, mild COVID-19 accounts for a smaller proportion of the sample (3.2% or 13 cases), which is due to the fact that most of the patients were treated at home or as outpatients. More than half of hospitalized women (209, or 51.0%) were in severe condition at the time of admission.

Analysis of COVID-19 severity according to trimester of pregnancy showed statistical significance (p<0.05), indicating that the severity of the disease increased with increasing gestational age and progression to later trimesters.

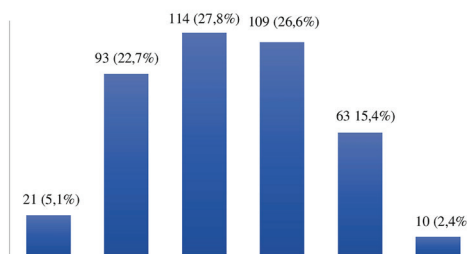


Figure 1 – Age groups of pregnant women with COVID-19 coronavirus infection

Table 3 Disease severity according to age groups in the studied subjects

Disease severity, abs. %	Age groups						P
	18-20 years old	21-25 years old	26-30 years old	31-35 years old	36-40 years old	41-50 years old	
Light	0	3(3,2)	4(3,5)	3(2,8)	2(3,2)	1(10,0)	p=0,04 *
Medium	14(66,7)	53(57,0)	53(46,5)	27(4,8)	15(23,8)	3(30,0)	p=0,02 *
Heavy	7(33,3)	36(38,7)	53(46,5)	72(66,1)	38(60,3)	3(30,0)	
Extremely heavy	0	1(1,1)	4(3,5)	7(6,4)	8(12,7)	3(30,0)	

*Differences of indicators are statistically significant (p<0.05)

Comorbidities were identified in 306 patients, accounting for 74.6% of the total number of patients studied. We found statistically significant differences in the presence of comorbidities depending on the trimester of pregnancy. Among the concomitant diseases, diseases of the circulatory system prevailed (50%), which is associated with a physiological decrease in hemoglobin during pregnancy. 21% of women had respiratory diseases, 13% – diseases of the circulatory and urinary system, 3% – diseases of the endocrine system.

For convenience in analyzing the length of hospital stay, bed days were divided into three categories: 1-7 days; 8-15 days; 16 or more days.

Table 2 shows that 196 pregnant women (47.8%) were medically treated in infectious diseases hospitals for 1-7 days. Of these, 27 (13.8%) were in the first trimester, 59 (30.1%) were in the second trimester, and 110 (56.1%) were in the third trimester. 181 patients (44.1%) spent 8 to 15 days in a health care facility with a diagnosis of COVID-19. Among them, 18 (9.9%) were between 1 and 12 weeks' gestation, 49 (27.1%) between 13 and 28 weeks' gestation, and 114 (63.0%) between 29 and 40 weeks' gestation. 33 pregnant women (8.1%) spent 16 or more days in hospital: 5 (15.2%) of them were in the first trimester, 14 (42.4%) in the second trimester and 14 (42.4%) in the third trimester. We analyzed nominal scales using Pearson's chi-square test. When comparing age groups according to the number of bed days, statistically significant differences were obtained (p=0.04). These differences were due to the absence of cases with 16 or more bed days in the 18-20 age group (p=0.007). A moderate association was recorded between the compared features (V=0.216).

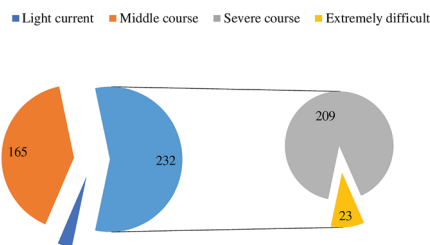


Figure 2 – COVID-19 severity in hospitalized pregnant women

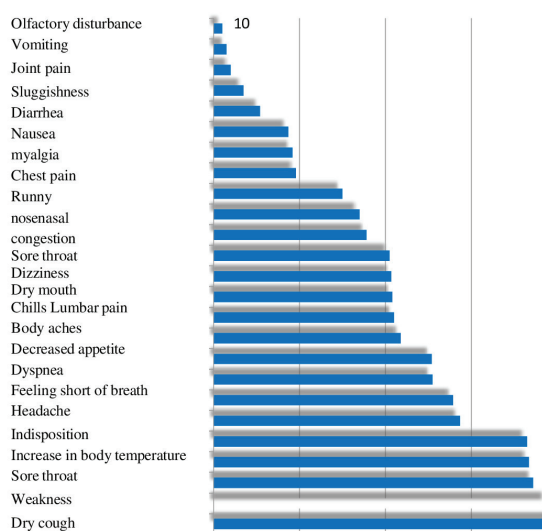


Figure 3 – Complaints at the time of examination in pregnant women with COVID-19

45% (9) of pregnant women in the age group of 16 to 20 years were admitted to hospital within the first three days after the onset of symptoms. At the same time, only 3.9% (4) of women over 31 years of age sought medical care 15 days after the onset of their first complaints. Under 30 years of age, the majority of pregnant women received inpatient care within the first three days of illness, while women in the older age group (31 years and older) sought medical care later, on the 4th day of illness.

The sample included patients with different degrees of disease severity: mild – 13 cases (3.17%), moderate – 165 cases (40.24%), severe – 209 cases (50.97%) and extremely severe – 23 cases (5.6%). Distribution by age groups is presented in Table 3.

During the study, nominal scales were analyzed using Pearson's chi-square criterion. Statistically significant differences ($p=0.000$) were found when comparing age groups according to disease severity. These differences were due to the fact that moderate severity was more common in patients between 16 and 30 years of age, while severe severity was more prevalent in women over 31 years of age ($p=0.02$). There was a fairly high correlation between the compared features ($V=0.516$). At the same time, cases of extreme severity were not registered in pregnant women of early reproductive age (18 – 20 years).

Figure 4 illustrates the symptoms characteristic of the patients during the disease. The most common complaints were dry cough (394 cases), weakness (388 cases), sore throat (372 cases), increased body temperature (367 cases), malaise (365 cases) and headache (287 cases). The least common symptoms were impaired sense of smell (10 cases), vomiting (15 cases), joint pain (20 cases), lethargy (35 cases) and diarrhea (54 cases).

Discussion

In our study, it was found that the number of bed days spent by patients in hospital decreases with increasing age. Pairwise comparison of groups revealed that COVID-19 coronavirus infection was more commonly reported in pregnant women at 28–40 weeks' gestation, especially those with a history of comorbidities. For example, one UK study showed that most of the 427 pregnant women hospitalized with COVID-19 between March 1 and April 14, 2021 were in the late second trimester or third trimester [10, 12, 13]. In pregnant women with COVID-19, it is possible for a critical condition to develop rapidly against the background of a relatively stable course of the disease. Pregnant women experience changes in the respiratory system, including an increase in lung volume and a decrease in respiratory function due to uterine growth. These factors can make it difficult for the body to fight respiratory infections such as COVID-19. In addition, pregnant women have an increased risk of complications, including preeclampsia and premature birth, which can worsen due to coronavirus infection. As a result of these circumstances, pregnant women may face a higher risk of developing severe symptoms requiring hospitalization and intensive care [11, 19, 23, 24].

The presence of comorbidities such as cardiovascular, hepatic and renal pathologies and diabetes mellitus affects the course of COVID-19 in pregnant women [11, 14]. The time of admission to hospital to receive specialized care is of paramount importance to achieve positive treatment outcomes, which is particularly important for both mother and child [15–19].

We also investigated the body mass index (BMI) of the women. The analysis showed that 20.7% of pregnant women had a normal BMI (18.5 to 24.9), while 79.3% were overweight

or obese. In our sample, obesity ($BMI>30$) was found in 29.3% of pregnant women. Previous studies confirm the significant impact of overweight and obesity on the increased morbidity and mortality of COVID-19 [20–22]. In another study, 19 (20.7%) out of 92 pregnant women had BMI within normal range, while 73 patients (69.3%) were overweight and 27 (39.3%) were obese, which is probably due to hypodynamia against strict quarantine measures and unbalanced diet [22]. Pregnant women who contracted COVID-19 at 1–12 weeks (13 – 26.0%) were more likely to recover compared to women at later gestation.

The presence of respiratory symptoms and the need for hospitalization increased significantly with later trimesters in pregnant women with COVID-19 [24].

Recruitment of pregnant women with COVID-19 during the pandemic has been rapid, which is one of the strengths of the study. However, the study was conducted in only one city, that was the limitation. In the future, we plan to conduct research in other cities. Another limitation was that this study is single center, which does not provide extended results. It should be noted that the sample size was relatively small.

Conclusions

Trimesters of pregnancy influence the course of the disease. The highest incidence of infection is observed in pregnant women in the third trimester, which is associated with increased diagnosis of women in this period. Associated diseases act as triggers for worsening of the patients' condition. Data analysis also showed that the severity of the disease increases with increasing gestational age or later trimesters.

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