Effect Of Termination Of Pregnancy On Pregnant Women With Covid

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Abstract

This descriptive analytic study was aimed to observe the clinical features and outcomes of pregnant women with COVID which has been confirmed through PCR or lung CT Scanning, and their pregnancy have been terminated because of mother's critical condition or obstetric indications, since the onset of COVID pandemic in Alzahra or EmamReza Hospitals in Tabriz. Before pregnancy termination, the enrolled mothers were categorized into four groups as mild, moderate, severe, and critical conditions, according to the percentage of lung's involvement in CT scan, SPO2 saturation, clinical symptoms, and delivery and paraclinical tests. These items were reassessed 24 and 48 hours after termination of pregnancy, and the changes of values were recorded and consequently compared through statistical methods in two phases of before and after delivery. The changes in the severity of disease during the measurement times (before termination of pregnancy, and 24 hours and 48 hours after delivery) were statistically significant ($P < 0.0001$). All 68 patients who were in the mild phase of the disease before delivery were discharged without any death. One case (2.8%) in moderate phase, 6(24%) in severe and 3(18.8%) in critical phase died. In conclusion, early termination of pregnancy in pregnancies complicated with COVID can improve the outcome.

Keywords: COVID Pandemic, Termination of Pregnancy, Computed Tomography Scan.

Introduction

Coronavirus disease (COVID) stands the second pandemic of the twenty-first century (1,2) affecting pregnant women significantly (3) with associated complications including pneumonia, acute respiratory distress syndrome, septic shock, cardiovascular disease (1), pre-eclampsia (4), intrauterine growth restriction, preterm birth, stillbirth, and developing defects in neonates (5), creating broad implications for obstetrical care and perinatal outcomes (6). Probably, pathophysiological changes caused by the virus cause severe adverse pregnancy outcomes and increase mortality (7).

Despite extensive research conducted on COVID, limited data are available about pregnant women with COVID pneumonia and its consequences in pregnant women (3,8,9). Also, the severe complications caused by COVID for mothers and newborns require careful screening during pregnancy and long follow-up (10).

We need more evidence to develop effective preventive and clinical strategies (11,12). Therefore, our purpose in this study was to investigate and report the relationship between clinical characteristics and the results of delivery tests obtained from pregnant women with COVID who are candidates for termination of pregnancy.

Materials and Methods

This descriptive analytic study conducted on pregnant women with COVID which has been diagnosed through PCR or chest CT Scanning (13) and their pregnancy have been terminated because of mother's critical condition or obstetric indications, since the onset of COVID pandemic in Alzahra or EmamReza Hospitals, related to Tabriz University of Medical Sciences. Before pregnancy termination, the enrolled mothers were categorized into four groups as *mild*, *moderate*, *severe*, and *critical* conditions, according to the national protocol and the following items: percentage of lung's involvement in CT scan, arterial blood oxygen saturation, clinical signs and symptoms (shortness of breath, sore throat, dry cough, chills, headache, loss of sense of taste and

smell, nausea and vomiting, diarrhea, anorexia, body pain, weakness and fatigue, chest pain and tension, consciousness level, fever, heart rate, respiration rate, blood pressure), results of delivery and paraclinical tests (CPK, SGPT, SGOT, CRP, ESR, CBC, ALP, BUN, Cr, BS, K, Na, Mg, P, LDH, Ferritin, D-dimer, Troponin, Fib, PT, PTT, INR, ABG) and ECG.

These items were reassessed 24 and 48 hours after termination of pregnancy and the changes of values were recorded and consequently compared through statistical methods in two phases of before and after delivery.

Ethical considerations: The study was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1400.691). This research is based on the information in the patients' records, and the studies and findings will be completely confidential. All patients signed the informed consent to confidential use of study findings at the beginning of hospitalization, and all pregnant women who underwent lung CT scan signed the informed consent. Also, the authors read the guidelines of ethic codes in research and followed them.

Statistical analysis: The data were analyzed using SPSS-22 software. The results were reported as frequency (percentage), standard deviation ± mean, and median (interquartile range) (due to the non-normal distribution of the data). Kolmogorov-Smirnov test was used to test the normality of data distribution. Also, other inferential statistics methods were used, including Chi-square tests, Fisher exact test, Marginal homogeneity test, and Friedman, Mann-Whitney U-test and Kruskal-Wallis test. P-values more than 0.05 were considered as the level of statistical significance.

RESULTS

This study conducted on 145 pregnant women with age range of 15 to 45 years. The demographic data of enrolled patients are demonstrated in table 1.

Table 1: Demographic characteristics of patients

Variable		Frequency (percent) n = 145
Patient’s age		30.26 ± 6.90*
Gestational age		36.86 (38.71 – 33.57)€
Cause of termination of pregnancy	Delivery pain	35 (24.3)
	Term pregnancy	22 (15.3)
	ROM	15 (10.4)
	Fetal distress	40 (27.8)
	Maternal indication	32 (22.3)
Termination method of pregnancy	NVD	27 (18.9)
	CS	116 (81.1)

* Mean ± Sd; ROM: premature rupture of membranes; NVD: normal vaginal delivery; CS: cesarean section

Duration of hospitalization was 1 to 30 days with an average of 4 days. Mechanical ventilation was applied in 18 cases (12.4%) with average duration of 7 days (2 to 20 days).

The stage of COVID disease before termination of pregnancy was *mild* in 68 (46.9%), *moderate* in 36 (24.8%) *severe* in 25 (17.2%), and *critical* in 16 (11%). Death was reported in 10 patients (6.9%) of the studied patients and the rest of the patients 135 (93.1%) were discharged from the hospital.

Comparison of the severity of COVID, 24 and 48 hours after, compared to before delivery: Friedman’s test showed that the changes in the severity of COVID disease in pregnant women during the measurement times (before termination of pregnancy, and 24 hours and 48 hours after delivery) were statistically significant (P<0.0001). Diagram 1 demonstrate the changes in the severity of COVID disease in pregnant women before termination of pregnancy, 24 hours and 48 hours after termination of pregnancy, as showed in diagram 1:

These changes for mile disease were 68 (46.9%), 89 (61.8%), and 45 (53.6%), respectively; the alterations fore moderate disease were 36 (24.8%), 20 (13.9%), and 9 (10.7%), respectively; the values for severe disease were 25 (17.2%), 18 (12.5%), and 14 (16.7%), respectively; and for critical disease were 16 (11%), 17 (11.8%), and 16 (19%), respectively.

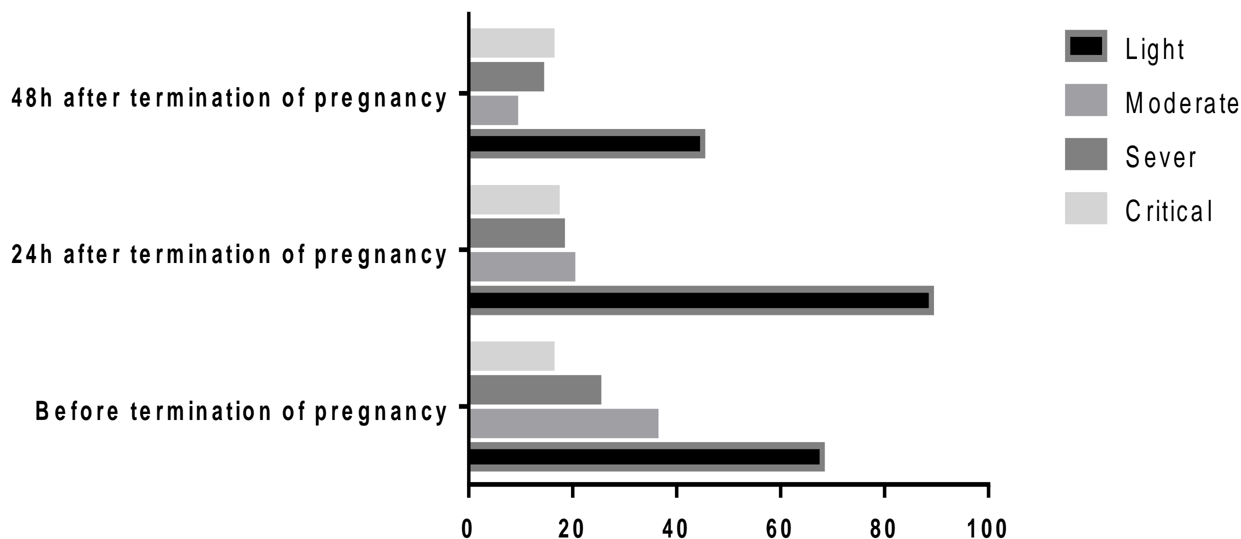

Diagram 1: Changes in the severity of COVID disease in pregnant women before termination of pregnancy, 24 hours and 48 hours after termination of pregnancy

Comparison of the severity of COVID, 24 hours after, compared to before delivery: Marginal homogeneity test showed statistically significant difference in the severity of COVID disease 24 hours after termination of pregnancy compared to before delivery (P = 0.001).

Of 68 patients who were in the *mild* phase before delivery, 24 hours after delivery, 64 (94.1%) remained in *mild* phase, 3 (4.4%) were in *moderate*, and 1 (1.5%) was in *severe* phase, and no case in *critical* phase.

Of 36 patients who were in the *moderate* phase before delivery, 24 hours after delivery, 24 (66.7%) were in *mild* phase, 10 (27.8%) remained in *moderate*, and 2 (5.6%) was in *severe* phase, and no case in *critical* phase.

Of 25 patients who were in the *severe* phase before delivery, 24 hours after delivery, 1 (4%) was in *mild* phase, 7 (28%) were in *moderate*, and 11 (44%) remained in *severe* phase, and 6 (24%) cases in *critical* phase.

Of 15 patients who were in the *critical* phase before delivery, 24 hours after delivery, no cases were in *mild* or *moderate* phase, and 4 (26.7%) cases were in *severe* phase, and 11 (73.3%) cases remained in *critical* phase.

Comparison of the severity of COVID, 48 hours after, compared to before delivery: Marginal homogeneity test showed statistically significant difference in the severity of the COVID disease in pregnant women 48 hours after termination of pregnancy compared to before delivery (P < 0.0001).

Of 68 patients who were in mild phase before delivery, 43 were discharged 48 hours after delivery, 24 (96%) remained in *mild* phase, 1 (4%) was in *moderate* phase, and none entered the *severe* or *critical* phase and no death was reported.

Of 36 patients who were in the *moderate* phase before delivery, 13 were discharged 48 hours after delivery, 16 (72.7%) were in the *mild*, 4 (18.2%) in *moderate*, and 2 (9.1%) were in *severe* phase and one case died.

Of 25 patients who were in *severe* phase before delivery, no case was discharged 48 hours after delivery, 5 (22.7%) were in *mild*, and 4 (18.2%) in *moderate* phase, and 6 (21.1%) entered *severe* and 7 (31.6%) entered *critical* phase, and 3 cases died.

Of 15 patients who were in *critical* phase before delivery, 6 (40%) entered *severe* phase and 9 (60%) remained in *critical* phase, but no death was reported.

The relationship between the severity of COVID disease and the outcome of the disease: Fisher exact test showed statistically significant relationship between the severity of COVID and the outcome in pregnant women, before and 24 hours and 48 hours after delivery (P<0.0001) (table 2):

Outcome and severity before delivery: All 68 patients who were in the mild phase of the disease before delivery were discharged without any death report. One case (2.8%) in moderate phase, 6(24%) in severe and 3(18.8%) in critical phase died.

Outcome and severity 24 hours after delivery: All patients who were in the mild and moderate phase 24 hours after termination of pregnancy were discharged. Three (16.7%) in severe and 6 (35.3%) in critical phase died.

Outcome and severity 48 hours after delivery: All patients who were in mild and moderate phase 48 hours after termination

of pregnancy, were discharged. One (7.1%) in severe phase and 7 (43.8%) in critical phase died (Table 2).

Table 2: Comparison of the outcome of the COVID disease and the course of the in different measurement times in pregnant women (Before, 24 h and 48h after termination of pregnancy)

COVID stage		Outcome of the COVID disease		P – Value*
		Discharged	Dead	
Before termination of pregnancy	Mild (n = 68)	68 (100)	0 (0)	<0.0001
	Moderate (n = 36)	35 (97.2)	1 (2.8)	
	Sever (n = 25)	19 (76)	6 (24)	
	Critical (n = 16)	13 (81.3)	3 (18.7)	
24h after termination of pregnancy	Mild (n = 89)	89 (100)	0 (0)	<0.0001
	Moderate (n = 20)	20 (100)	0 (0)	
	Sever (n = 18)	15 (83.3)	3 (16.7)	
	Critical (n = 17)	11 (64.7)	6 (35.3)	
48h after termination of pregnancy	Mild (n = 45)	45 (100)	0 (0)	<0.0001
	Moderate (n = 9)	9 (100)	0 (0)	
	Sever (n = 14)	13 (92.9)	1 (7.1)	
	Critical (n = 16)	9 (56.3)	7 (43.8)	

* Fisher exact test

Comparison of hospitalization period between discharged and deceased patients (based on the stage of COVID in patients before delivery): As showed in table 3 and analysis by Mann – Whitney U-test, there was no statistically significant difference in hospitalization period between patients who died and those who were discharged from the hospital in patients who were in the severe phase of the disease before delivery (P=0.687). However, the difference between died and discharged patients who were in critical phase before the delivery was significant (P=0.004). The median hospitalization period in patients discharged from the hospital was 20 days in patients who were in the mid-critical phase before termination of pregnancy and 6 days in 3 patients who died.

Table 3: Comparison of the hospitalization period between discharged and dead patients (based on the stage of COVID in patients before delivery)

COVID stage	Outcome of the COVID disease	hospitalization period (day) Median (Interquartile)	P – Value*
Mild	Discharged (n = 68)	3 (4.25 – 3)	---
	Dead (n = 0)	----	
Moderate	Discharged (n = 35)	6 (8 – 3)	---
	Dead (n = 1)	2	
Sever	Discharged (n = 19)	7 (13 – 3)	0.687

	Dead (n = 6)	6 (14.25 – 3.5)	
Critical	Discharged (n = 13)	20 (21 – 11.5)	0.004
	Dead (n = 3)	6	

* Mann – Whitney U-test

Comparison of gestational age (GA) between different stages of COVID disease in pregnant women before termination of pregnancy: GA of patients in mild, moderate, severe and critical phases were 37.5 (35.03-38.86), 36.42 (33-38.86), 35.78 (32.25-37.61), and 33.14 (28.03-35.53) weeks, respectively. Kruskal – Wallis test showed a statistically significant difference (P= 0.017). The average gestational age of patients in critical phase was lower than those in severe, moderate and mild phases. So, the younger the gestational age, the more intense of COVID disease.

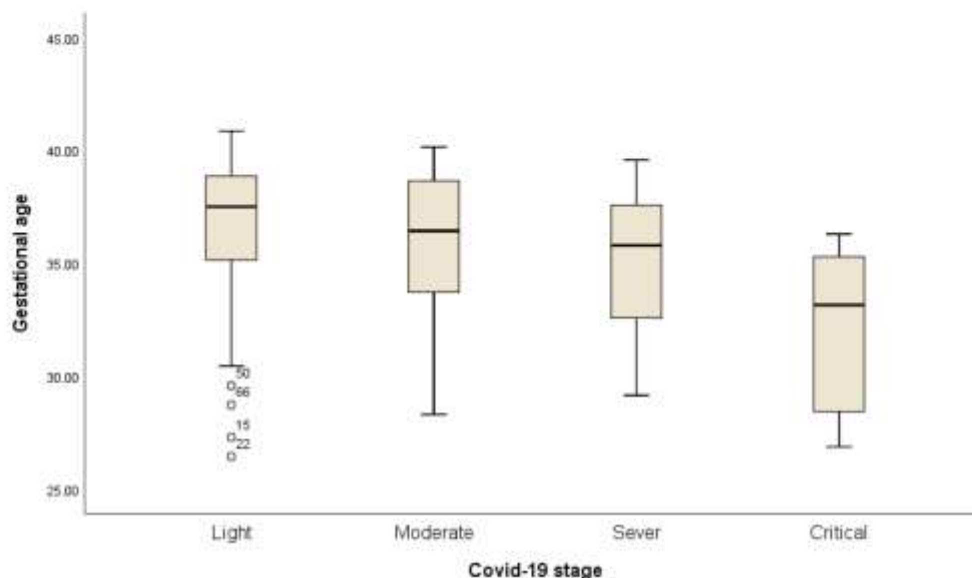

Diagram 2: Comparison of gestational age between different stages of COVID disease in pregnant women before termination of pregnancy

DISCUSSION

We studied the clinical features and outcomes of pregnant women with COVID underwent pregnancy termination, and concluded that early termination of pregnancy in pregnancies complicated with COVID can improve the outcome.

The emerging data from COVID-9 pandemic indicates increased risks of its complications during pregnancy (5). The SARS during pregnancy has been associated with a high incidence of adverse maternal and neonatal complications, such as need for endotracheal intubation, renal failure, ICU admission, and disseminated intravascular coagulopathy (12).

The immune system adjusts during pregnancy to growth of a semi allogenic fetus, resulting in an altered immune response to infections during pregnancy (14). Pregnant women are susceptible to respiratory pathogens and to affection by severe pneumonia, which possibly makes them more susceptible to COVID and other infections than the general population, especially if they have chronic diseases or maternal complications. Therefore, pregnant women and newborn babies should be considered as high-risk populations in approaches aiming to prevention and management of COVID infection (12).

The risk of severe COVID during pregnancy is higher than the general population (14). Considering the potential of SARS-CoV-2 to cause severe obstetric and neonatal adverse outcomes, close screening of suspected cases during pregnancy and long-term follow-up of confirmed mothers are necessary (9,15). However, there is rare information of assessment and management of pregnant women affected by COVID, and there is potential risk of vertical transmission (15).

Differences in current guidelines make challenges for maternal care clinicians during the COVID pandemic. Decisions on timing of delivery should be made by weighing the benefits versus the risks to the mother and fetus, and should be made by the maternal-fetal medicine specialist and the critical care team (16).

It is known that in the third trimester, uterine pressure can reduce inspiratory reserve volume, expiratory reserve volume, and functional residual capacity, which can increase the risk of severe hypoxemia in pregnant women, mainly those in critical condition. On the other hand, although the data about the time of delivery are limited, it is reasonable that the stress of delivery

plays a role in the deterioration of critically ill patients (14). Also, pregnant patients seemed more likely to undergo cesarean delivery during the emergence of COVID-19, and the main concern might be neonatal infection. Although it is unclear whether vaginal delivery or cesarean delivery is of greater benefit for these patients (9), it has reported that delivering the neonate benefited the recovery of these patients from COVID-19, since some antiviral remedies such as ribavirin are teratogenic during pregnancy (9).

We did not find a research about the clinical features and outcomes of pregnant women with COVID undergoing pregnancy termination for therapeutic goals. However, our study showed that the changes in the severity of disease during the measurement times (before termination of pregnancy, and 24 hours and 48 hours after delivery) were statistically significant ($P < 0.0001$). There was statistically significant difference in the severity of disease 24 hours after delivery compared to before delivery ($P = 0.001$), and between 48 hours after delivery and before delivery ($P < 0.0001$). In our survey, early termination of pregnancy in pregnancies complicated with COVID can improve the outcome. In our experience, it was especially efficient in early phases of disease, but was helpful in severe and critical phases.

Wang et al. studied 72 women (30 pregnant and 42 nonpregnant) with COVID-19. No patients affected by severe pneumonia. Compared with the nonpregnant women, pregnants were admitted earlier (0.25 vs 11.00 days; $P<0.001$), had milder symptoms, higher rate of asymptomatic infection (26.7% vs 0%), and shorter duration of hospitalization (14.5 vs 17.0 days; $P<0.01$). Values of inflammation markers including CRP, WBC count, neutrophil count, procalcitonin, and D-dimer were significantly more in pregnant women, whereas their mean lymphocyte percentage was significantly lower (9).

We used chest CT and PCR for disease confirmation, and findings of physical examination and deliveryatory tests for disease severity categorization. Pulmonary CT scan in combination with blood routine examination are preferred methods for finding pregnant women with asymptomatic or mild COVID, and can be used for screening COVID pregnant women (17).

Yang et al. (3) screened the suspected cases of COVID infection based on pulmonary CT scan and routine blood test and symptoms. Among the 55 cases, 13 patients were assigned into the confirmed COVID group for being tested positive severe and acute respiratory syndrome. All of the pregnant women confirmed with COVID were in mild or asymptomatic phase (17). They concluded that termination of pregnancy effort a stress for women with confirmed COVID pneumonias whatever undergoing cesarean or vaginal delivery (17).

Chen et al. studied 9 pregnant women with COVID pneumonia. None of the patients showed severe COVID pneumonia or died and finally all 9 patients had delivery in their third trimester (3). Another study showed that the number of abortions and ongoing pregnancies remained unchanged during the first wave of the COVID pandemic in 2020 in Sweden compared with before the start of the pandemic (18). Some literatures indicate that pregnancy does not increase the risk of COVID affection but the course of disease seems to be worse in pregnant women compared to nonpregnant females of the same age (19). Although more than 90% of pregnant women with COVID recover without serious morbidity, rapid deterioration of disease has been reported (19).

Dilek et al. showed that symptomatic pregnant women have a higher risk for severe disease compared to the symptomatic nonpregnant women with COVID. Also, severe disease is more common in cases with coexisting comorbidities like diabetes, obesity, asthma, more maternal age, or hypertension (19).

Maternal death rates range has reported between 0.14 and 0.80 (19). In our experience, all 68 patients who were in the mild phase of the disease before delivery were discharged without any death. Mortality was one case (2.8%) in moderate phase, 6(24%) in severe and 3(18.8%) in critical phase. The total mortality rate was 6.9%.

It has been long known that excessive inflammation, hypoxia, fever, and worsening in maternal condition may trigger premature delivery and can cause fetal distress. However, obstetric complications can also occur in mild COVID cases (19,20). The studies indicated that severe and critical disease was associated with increased rates of preterm and cesarean deliveries commonly due to the worsening in maternal health condition (21). Moreover, a higher rate of obstetric complications was observed in cases with higher viral load (19).

Timing of delivery should be decided based on maternal health condition, accompanying obstetric complications and gestational age (4,22). For asymptomatic cases and patients with non-severe COVID, delivery at <39 weeks of gestation should be avoided unless there is an obstetric complication that necessitates prompt delivery (22). For severe and critical cases, an individualized approach should be preferred. Delivery may be considered at >32–34 weeks of gestation for severe not intubated cases. The management of intubated cases should be performed according to maternal clinical characteristics. Prompt delivery may be considered in the presence of refractory hypoxemic respiratory failure or worsening critical illness (22). Acute decompensation in critical cases may also necessitate prompt delivery with cesarean section (19).

In our experience, timing of delivery was decided according the maternal health condition, obstetric complications and gestational age. Also, in severe and critical cases, an individualized approach was performed according to maternal clinical characteristics and weighing the benefits versus the risks to the mother and fetus, and the decision was made by the maternal-fetal medicine specialist and the critical care team.

CONCLUSION

The changes in the severity of disease during the measurement times (before termination of pregnancy, and 24 hours and 48 hours after delivery) were statistically significant ($P < 0.0001$). There was statistically significant difference in the severity of disease 24 hours after delivery compared to before delivery ($P = 0.001$), and between 48 hours after delivery and before delivery ($P < 0.0001$). All 68 patients who were in the mild phase of the disease before delivery were discharged without any death. One case (2.8%) in moderate phase, 6(24%) in severe and 3(18.8%) in critical phase were died. In conclusion, early termination of pregnancy in pregnancies complicated with COVID can improve the outcome. In our experience, it was especially efficient in early phases of disease, but was helpful in severe and critical phases.

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