The Effect of the Mode of Delivery on Probable Vertical Transmission in COVID-19-Positive Mothers

Original Article

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ABSTRACT

Background: Recent research indicates that human-to-human contact is the primary mode of transmission for SARS-coronavirus 2 (SARS-CoV-2), the disease-causing agent of COVID-19. However, information on the vertical spread of COVID-19 among newborns is scarce and contradictory. The study aims to assess the association between delivery methods and the risk of vertical transmission of COVID-19 to newborns.

Patients and Methods: This was a retrospective cohort study conducted at Misr El Gedida Military Hospital and El Obour Specialized Hospital of Ain Shams University on 100 pregnant women with confirmed COVID-19 infection, divided into two groups: Group A: those who delivered vaginally (n = 15); and Group B: those who delivered by cesarean section (n = 85) in the period between March 2020 and March 2022.

Results: Pregnancy outcomes did not vary significantly (*P-value > 0.05*) between groups A and B. There was no significant difference between both groups in stillbirth rate, viral status, APGAR score, or newborn weight (*p-value > 0.05*). In addition, there was no significant difference (*p-value > 0.05*) between groups A and B in the rates of admission to the NICU.

Conclusion: There was no association between the mode of delivery (vaginal vs. cesarean) and the rates of COVID-19 infection in newborns or neonatal mortality. These results do not lend credence to the idea that cesarean sections prevent the vertical transmission of COVID-19 from pregnant women to their newborn babies more effectively than vaginal births.

Key Words: Cesarean delivery, COVID-19, pregnancy, vaginal delivery, vertical transmission.

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INTRODUCTION

Several case reports or case series have demonstrated that infections are passed from mother to kid when the mother gets ill during the third trimester of pregnancy, and there is growing evidence that SARS-CoV-2 may be transmitted from sick pregnant women to their offspring[1]. The most researched method of vertical transmission of SARS-CoV-2 from an infected woman to her sick infant is through the placenta[2]. Results from previous pandemics suggest that pregnancy may increase a woman's risk of SARS-CoV-2 illness and mortality. To learn how the virus impacts pregnant women's immune systems, more study is needed.

Due to the heightened inflammation during the first and third trimesters of pregnancy to facilitate implantation and delivery (cytokine storm), SARS-CoV-2 infection may raise the risk of severe symptoms in pregnant women. Poor maternal COVID-19 results may be attributed to postpartum physiological changes, increased levels of stress and inflammation following delivery, and other factors. This is supported by clinical evidence because even pregnant women who presented with minimal symptoms upon admission for delivery frequently required additional hospitalization for respiratory problems[3].

In some cases, in addition to molecular confirmation of COVID-19, chest imaging may be beneficial. The periphery of the airways may appear shadowed on chest X-rays, and bilateral multi-lobar ground-glass opacities may be visible on chest CT scans. These characteristics appear to be constant throughout pregnancy[4].

Although there are multiple papers describing the analysis of various materials, nasopharyngeal swab analysis has been found to be the most reliable method for testing for SARS-CoV-2 in mothers and neonates. The reverse transcription polymerase chain reaction (RT-PCR) has revealed the presence of SARS-CoV-2 viral RNA in placental samples, breast milk, amniotic fluid, cord blood, and maternal vaginal secretions, illuminating the diverse

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vertical transmission routes of this virus. According to Jafari *et al*., SARS-CoV-2 was found in 12% of placental samples, 5% of samples taken from nursing mothers, 5% of samples taken from amniotic fluid, 6% of samples taken from cord blood, and 4% of samples taken from vaginal discharge[5].

According to preliminary studies, caesarean sections (CS) were done on 76.8% of newborns in order to reduce the risk of vertical transmission and the perception of risk by health care workers. Because they were exposed to diseased tissues for a shorter amount of time, newborns delivered via caesarean section may have had a lower risk of infection[6].

A review of case reports and research revealed no proof of vertical transmission of SARS-CoV-2 in pregnancy[7].

The data we have to work with is limited because this outbreak is so recent. Recent studies and reports frequently have tiny sample sizes. It is also uncertain whether the delivery method impacts the likelihood of the infant contracting SARS-CoV-2 during the perinatal period[8].

PATIENTS AND METHODS:

Research design and setting:

The retrospective cohort study was carried out at Misr El-Gedida military hospital and El Obour specialized hospital, Ain Shams University.

Participants:

All Between March 2020 and March 2022, pregnant women who had COVID-19 at the time of delivery or during the three weeks prior were recruited from Misr El-Gedida military hospital and El Obour specialised hospital at Ain Shams University. Those who had an infection that had been verified through laboratory testing and who had complete medical records were included, whereas those who declined to take part were excluded.

Two groups of pregnant women were created: group A included women who gave birth vaginally, and group B included women who gave birth through caesarean section.

Data Collection:

The lab archive was searched for patient records, follow-up forms, and laboratory results (including the RT-PCR swab for COVID-19). The viral status of the babies in both groups of women was monitored through their medical records (during the first 48 hours postpartum).

Age, gravidity, parity, gestational age at COVID-19 infection, and gestational age at birth were among the maternal characteristics that were recorded. Inflammatory markers such as lactate dehydrogenase (LDH), C-reactive protein (CRP), ferritin, and other laboratory tests were performed in addition to the complete blood count (CBC), serum alanine transaminase (ALT), aspartate aminotransferase (AST), kidney function tests, and coagulation profile tests. Results of the chest X-ray were also obtained.

The results of the pregnancy included the method of birth and any maternal difficulties brought on by the COVID-19 infection, such as the need for oxygen therapy, mechanical breathing, or hospitalization in the intensive care unit (ICU). Neonatal nasopharyngeal swab samples were tested for SARS-CoV-2 PCR to determine vertical transmission. The neonatal outcomes included birth weight, APGAR score, admission to the neonatal intensive care unit (NICU), and length of stay in the NICU.

Statistical analysis:

Data were entered in a Microsoft Excel spread sheet for Windows and analyzed using SPSS version 26 (**IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp**). Categorical variables were presented as frequency (n) and percentage (%) and analyzed using the chi-square test. Whereas quantitative variables were presented as mean, standard deviation (SD), median and interquartile range (IQR). Nonparametric data were analyzed with the Mann-Whitney U test, while parametric data were analyzed with the Student t-test. All statistical analyses were judged at a level of significance of 5% ($\alpha = 0.05$).

RESULTS:

In this study, 100 mothers with COVID-19 infection were included. Two groups of patients were created: group A, which included 15 vaginal deliveries (n = 15), and group B, which included 85 caesarean deliveries (n = 85).

When compared to women who delivered by C.S., those who delivered vaginally had considerably higher average ages and parities (*p-values* of *0.001* and *0.001*, respectively). Regarding gestational age at infection, there was no statistically significant difference between them ($P > 0.05$). (Table 1)

Table 1: Comparison between the two studied groups as regards basic characteristics.

	Group (A) (N=15)					Group (B) (N=85)					Mann- Whitney U test	
	Mean	SD	Median	Range		Mean	SD	Median	Range		Test value	*P-value*
Age (years)	34.57	3.63	36.0	26.0	36.0	28.83	6.98	32.0	18.0	37.0	3.268	*0.001*
Parity	2.80	0.41	3.0	2.0	3.0	1.99	0.98	2.0	0	3.0	3.215	*0.001*
GA at infection	32.29	0.73	32.0	32.0	34.0	25.76	10.44	27.0	10.0	38.0	1.195	*0.232*

There was no discernible difference between group A's and group B's heart rates (*P-value > 0.05*). While this was going on, group B's respiratory rate was considerably higher than group A's (*P-value 0.001*). On the other hand, group B had significantly lower O2 saturation than group A (*P-value 0.001*) did. (Table 2)

Table 2: Comparison between the two studied groups as regards vital signs. On admission

	Group (A) (N=15)					Group (B) (N=85)					Mann- Whitney U test	
	Mean	SD	Median	Range		Mean	SD	Median	Range		Test value	*P-value*
Heart Rate (beats/min.)	96.43	3.99	98.00	87.00	98.00	93.65	7.33	98.00	78.00	99.00	0.387	*0.699*
Respiratory Rate (beats/min.)	36.43	1.09	36.00	36.00	39.00	39.43	3.68	39.00	32.00	45.00	3.903	*<0.001*
O2 saturation	95.57	1.09	96.00	93.00	96.00	92.72	3.05	94.00	87.00	97.00	3.590	*<0.001*

Regarding WBCs and lymphocytes, there was no statistically significant difference between group A and group B (*P > 0.05*). In contrast, group B significantly had a greater red blood cell count and serum haemoglobin level than group A (*P values of 0.001* and 0.036, respectively). In comparison to group A, group B had considerably fewer platelets and neutrophils (*P values = 0.001* and 0.014, respectively). (Table 3)

Table 3: Comparison between the two studied groups as regards CBC.

	Group (A) (N=15)					Group (B) (N=85)					Mann - Whitney U test	
	Mean	SD	Median	Range		Mean	SD	Median	Range		Test value	*P-value*
Hb (gm/Dl)	10.3	0.2	10.2	10.2	10.8	12.5	1.9	12.2	9.9	16.1	4.60	*<0.001*
WBCs (10^3/uL)	7.6	2.2	7.8	3.6	10.6	7.8	2.1	8.2	3.8	11.4	0.33	*0.738*
Red cell count (10^6/uL)	4.9	0.2	5.0	4.6	5.0	4.7	0.5	4.9	4.0	5.3	2.10	*0.036*
Platelets (10^9/uL)	306.0	45.8	324.0	198.0	324.0	195.7	50.5	190.5	131.0	323.0	5.14	*<0.001*
Neutrophil	3.7	.4	3.9	2.8	3.9	3.2	1.0	3.1	2.1	5.1	2.46	*0.014*
Lymphocyte	3.2	.3	3.1	3.1	3.9	2.9	1.40	3.6	.9	4.7	0.46	*0.646*

There was no statistically significant difference between Groups A and B when comparing the AST and creatinine levels (*P > 0.05*). However, group A had significantly higher amounts of globulin and albumin than group B (*P-values* of *0.005* and *0.001*, respectively) However, group A had significantly higher amounts of globulin and albumin than group B (*P-values of 0.005* and 0.001, respectively). ALT and urea nitrogen concentrations in Group B were also noticeably greater than those in Group A (*P values* of *0.001* and *0.025*, respectively).Table (4)

Table 4: Comparison between the two studied groups as regards liver and kidney function tests.

	Group (A) (N=15)					Group (B) (N=85)					Mann- Whitney U test	
	Mean	SD	Median	Range		Mean	SD	Median	Range		Test value	*P-value*
Globulin (g/L)	48.14	2.18	49.0	43.0	49.0	43.18	7.71	44.0	31.0	54.0	2.779	*0.005*
Albumin (g/L)	42.29	1.82	43.0	38.0	43.0	32.67	8.15	33.0	20.0	47.0	4.032	*<0.001*
AST (IU/L)	35.29	3.27	34.0	34.0	43.0	40.61	12.89	43.0	12.0	55.0	1.895	*0.058*
ALT (IU/L)	23.71	1.82	23.0	23.0	28.0	35.24	11.65	34.0	16.0	65.0	4.124	*<0.001*
Serum creatinine (mg/dl)	1.10	0.0	1.10	1.10	1.10	1.33	0.48	1.10	0.89	2.30	0.369	*0.712*
Urea nitrogen (mmol/L)	6.10	0.25	6.20	5.50	6.20	7.57	1.94	6.80	4.80	10.20	2.242	*0.025*

As regard to the coagulation profile, group A had a considerably greater APTT and fibrinogen than group B (*P-value< 0.001*). Conversely, D-dimer was considerably higher in group B than in group A (*P = 0.007*). (Table 5)

Table 5: Comparison between the two studied groups as regards coagulation profile

	Group (A) (N=15)					Group (B) (N=85)					Mann- Whitney U test	
	Mean	SD	Median	Range		Mean	SD	Median	Range		Test value	*P-value*
PTs	19.14	.36	19.0	19.00	20.00	20.40	3.12	19.00	17.00	26.0	0.99	*0.318*
INR	1.10	.00	1.1	1.10	1.10	1.19	.21	1.20	1.00	1.7	0.97	*0.330*
APTT	38.71	.73	39.0	37.00	39.00	31.96	4.94	33.00	24.00	39.0	5.12	*<0.001*
D-dimer (ng\ml)	1.70	.25	1.8	1.10	1.80	1.99	1.78	1.00	.90	5.7	2.71	*0.007*
Fibrinogen (g/L)	5.86	.36	6.0	5.00	6.00	5.09	.92	5.00	4.00	7.2	3.77	*<0.001*

CRP did not significantly differ between groups A and B with regard to the inflammatory markers (*P-value > 0.05*). LDH and ferritin levels were similarly higher in Group B than in Group A (*P values of 0.05* and *0.022*, respectively). (Table 6)

Table 6: Inflammatory markers among the two studied groups

	Group (A) (N=15)					Group (B) (N=85)					Mann- Whitney U test	
	Mean	SD	Median	Range		Mean	SD	Median	Range		Test value	*P-value*
LDH, u/l	404.14	73.35	433.00	231.0	433.0	416.65	221.48	378.50	176.0	870.0	1.964	*0.05*
CRP, mg/L	20.86	5.45	23.00	8.0	23.0	33.21	28.91	20.0	12.0	96.0	1.591	*0.112*
Ferritin (ng/mL)	622.29	107.49	580.0	580.0	876.0	919.07	474.37	786.0	498.0	2111.0	2.284	*0.022*

Chest X-ray data showed that group B had considerably more pneumonia than group A did (*P-value = 0.017*), with more instances of ground glass appearance in group A. (Table 7)

Table 7: Comparison between the two groups regarding radiological findings.

Parameters		Group (A) (N=15)		Group (B) (N=85)		Chi-Square test	
		No.	%	No.	%	X2	P-value
Chest X-ray	Normal	2	13.3%	24	28.2%	8.12	0.017
	Ground glass appearance	13	86.7%	41	48.2%		
	Pneumonia	0	0.0%	20	23.5%		

Group B saw significantly higher rates of hospitalization, medical care, and oxygen therapy than did group A. There was no statistically significant difference between groups A and B in terms of admissions to the medical floor and intensive care unit (*P-value > 0.05*). (Table 8)

Table 8: Comparison between the two groups regarding management.

Parameters		Group (A) (N=15)		Group (B) (N=85)		Chi-Square test	
		No.	%	No.	%	X2	*P-value*
Hospitalization	No	15	100.0%	64	75.3%	4.691	*0.030*
	Yes	0	0.0%	21	24.7%		
Medical floor	No	15	100.0%	76	89.4%	1.75	*0.186*
	Yes	0	0.0%	9	10.6%		
ICU	No	15	100.0%	73	85.9%	2.406	*0.121*
	Yes	0	0.0%	12	14.1%		
Treatment given	Antibiotic therapy & Corticosteroids	12	80.0%	34	40.0%	8.59	*0.014*
	Antibiotic therapy, corticosteroids & antiviral	0	0.0%	12	14.1%		
	Antibiotic therapy & symptomatic treatment	3	20.0%	39	45.9%		
Oxygen therapy	No	15	100.0%	64	75.3%	4.69	*0.030*
	Yes	0	0.0%	21	24.7%		

Pregnancy complication in both groups did not differ significantly (*P-value > 0.05*). (Table 9)

Table 9: Comparison between the two groups regarding pregnancy outcome.

Parameters		Group (A) N=15)		Group (B) (N=85)		Test value	*P-value*
		No.	%	No.	%		
Pregnancy outcome	None	15	100.0%	65	76.5%	X2=4.412	*0.492*
	Antepartum hemorrhage	0	0.0%	1	1.2%		
	IUFD	0	0.0%	2	2.4%		
	IUGR	0	0.0%	7	8.2%		
	preterm labour	0	0.0%	4	4.7%		
	preterm labour and PROM	0	0.0%	6	7.1%		

The gestational age at birth was substantially older in Group A (*P-value = 0.002*) compared to Group B. (Table 10)

Table 10: Comparison between the two groups regarding gestational age at delivery

Parameters		Group (A) (N=15)	Group (B) (N=85)	Test value	*P-value*
GA at delivery (weeks)	Mean± SD	37.86 ± 0.36	35.30 ± 5.48	ZMWU=3.077	*0.002*
	Median	38.0	37.0		
	Range	37.0- 38.0	31.0- 38.0		

In terms of the stillbirth rate, viral positivity, APGAR score, or infant weight, there was no statistically significant difference between groups A and B (*p-value > 0.05*). Additionally, there was no statistically significant difference between groups A and B's NICU admission rates (*p-value > 0.05*). (Table 11)

Table 11: Comparison between the two groups regarding the neonatal outcome.

Parameters		Group (A) (N=15)		Group (B) (N=85)		Test value	*P-value*
		No.	%	No.	%		
Birth	Live birth	11	73.3%	74	87.1%	X2=0.961	*0.327*
	Stillbirth	4	26.7%	11	12.9%		
APGAR score (at 1 min.)	Mean ± SD	8.45 ± 0.71		8.57 ± 0.65		ZMWU=0.794	*0.427*
	Median	9.0		9.0			
	Range	7.0- 9.0		7.0- 9.0			
APGAR score (at 5 min.)	Mean ± SD	9.45 ± 0.71		9.57 ± 0.65		ZMWU=0.794	*0.427*
	Median	10.0		10.0			
	Range	8.0- 10.0		8.0- 10.0			
Birth weight (gram)	Mean ± SD	3086.83± 314.6		3023.59± 303.5		ZMWU=1.38	*0.168*
	Median	3213.0		2992.5			
	Range	2400.0- 3456.0		2100.0- 3456.0			
Viral status	Negative	15	100.0%	74	87.1%	X2=2.181	*0.140*
	Positive	0	0.0%	11	12.9%		
NICU	No	10	66.7%	72	84.7%	X2=0.045	*0.831*
	Yes	5	33.3%	13	15.3%		

DISCUSSION

A high level of viremia should be taken into account after the onset of symptoms. Pregnant women have a serious problem with the possibility of COVID-19 vertical transmission[9]. 100 pregnant women who had COVID-19 infections were included in this retrospective cohort study from Masr El Gdida Military Hospital and El Obour Specialised Hospital at Ain Shams University.

We discovered that, compared to women who underwent a caesarean section, those who gave birth vaginally were older and had more children. According to **Martnez-Perez *et al.***[10], vaginal delivery was strongly related to greater maternal age and higher nulliparity, which is consistent with the findings of the current study. Between Groups A and B, no statistically significant difference in heart rate was discovered. Group B's respiration rate was significantly higher than Group A's. Group B's oxygen saturation was significantly lower than Group A's. According to **Martnez-Perez *et al.***[10], who observed that adverse maternal outcomes were considerably higher among instances with CS compared to cases with normal delivery, these data revealed that caesarean birth patients were more likely to have poor maternal outcomes. Additionally, **Ferrazzi *et al.***[11] discovered a statistically significant link between CS and the requirement for oxygen support.

We found no significant difference between groups A and B in CRP. Group B also had greater levels of LDH and ferritin than Group A did. This was supported by **Ferrazzi *et al.***[11], who revealed that elevated C-reactive protein (>10 mg/l) was more prevalent among CS cases. The significant alteration of laboratory findings may be due to the infection with COVID-19 itself and not due to the difference in delivery mode. There was a strong correlation between the gestational age of the mother when she gave birth and the degree of COVID-19 infection[12].

Leukocytes, neutrophils, NLR, MLR, PLR, urea, creatinine, AST, LDH, and D-dimer levels were all higher in severe COVID-19 patients compared to mild to moderate COVID-19 patients, according to a study by **Bastug *et al.***[13]. The results of the current study showed a significant difference in radiological findings between groups A and B, with group B having a greater incidence of pneumonia and group A having a larger prevalence of ground glass appearance on chest X-rays. This was corroborated by **Martnez-Perez *et al.***[10], who found that women who gave birth via caesarean section tended to have more abnormal chest x-ray results than those who gave birth vaginally.

There was no noticeable difference in pregnancy problems between Groups A and B in the current study. This was corroborated by **Martnez-Perez *et al.***[10], who found no significant differences between the CS and control groups for preterm membrane rupture.

The gestational age at birth was another area where we found a significant difference between groups A and B. This concurs with a finding by **Ferrazzi *et al*.**[11] indicating CS babies were much younger than naturally born babies.

Birth weight, Apgar score, viral positivity, stillbirth, and other factors were not substantially different between Groups A and B. In terms of admission to the NICU, there was again no noticeable difference between groups A and B. This was consistent with the comprehensive study by **Cai *et al*.**[14], which found that 4% of live deliveries were confirmed cases of COVID-19, and 2.3% of infants delivered to moms who gave birth vaginally tested positive for the virus. Nine stillbirths (including a set of twins) and six neonatal deaths have occurred. The vaginal delivery group experienced no infant deaths, but the caesarean section group experienced approximately 1% mortality.

The study by **Ferrazzi *et al*.**[11] came to the conclusion that there is believed to be a low danger of the mother disseminating SARS-CoV-2 if the infant is delivered vaginally. Additionally, **Martnez-Perez *et al*.**[10] discovered that 3 (4.2%) of the 72 neonates whose COVID-19 status was examined in the first 6, 48, and 10 hours after birth were positive. The 48-hour follow-up test yielded unfavourable outcomes. No one showed signs of COVID-19 after ten days. Ten days after their births, two additional term caesarean babies showed signs of COVID-19. With just 3.3% of newborns having a positive RT-PCR test result, the multicenter study by **Oncel *et al*.**[15] also showed a high correlation between the delivery method and neonatal RT-PCR positivity. Additionally, the findings indicated that COVID-19 was linked to poorer perinatal and neonatal outcomes in pregnant women.

Limitations of the study

Future research should include larger, multicenter populations and larger sample numbers in order to reach more conclusive conclusions regarding the risk of COVID-19 vertical transmission. Additionally, no vaginal samples were analysed to determine whether COVID-19 was present during vaginal birth.

CONCLUSION

There is no evidence that vaginal delivery raises the risk of infection for newborns with COVID-19 or that it increases the risk of death for the baby. These results cast doubt on whether surgical delivery is superior to vaginal birth in terms of avoiding the vertical transmission of COVID-19 from a pregnant mother to her infant. Individual circumstances, including the nature and severity of the underlying medical illness and any obstetrical grounds for intervention, should inform the choice of delivery method. Specifically, studies that include extensive serial testing on many specimens are preferred.

ABBREVIATIONS

ALT: alanine transaminase

APTT: activated partial thromboplastin time

AST: aspartate amino transferase

Covid-19: coronavirus disease of 2019

CRP: c-reactive protein

ICU: intensive Care unit

INR: international normalized ratio

IUFD: intrauterine fetal demise

IUGR: intrauterine growth restriction

NICU: neonatal intensive care unit

PT: prothrombin time

RT-PCR: reverse transcription polymerase chain reaction

SARS-CoV-2: SARS-coronavirus 2

CONFLICT OF INTEREST

There are no conflicts of interest.

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