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Adverse Effects of COVID-19 Infection on Pregnant Females Admitted to Zagazig Isolation Hospitals

Amr Abd Al-Mohsen Alnemr, Khaled Baiomy Elsayed, Notaila Mohammed Shehata*, Mohammed Fathy Abo Hashem

Department of Obstetrics and Gynecology, Faculty of Medicine, Zagazig University, Egypt

***Corresponding author:** Notaila M. Shehata, **Mobile:** (+20)01006916595, **Email:** natylah011518@medicine.zu.edu.eg

ABSTRACT

Background: COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly across the world. As pregnant women are at greater risk of complications, they were advised to take additional precautions as the COVID-19 pandemic unfolded.

Objective: The aim of the present study was to provide an efficient and robust local database regarding the maternal and neonatal outcomes for the pregnant cases.

Patients and methods: An observational retrospective cohort study included 50 pregnant women, infected with COVID-19. They were admitted to Zagazig Isolation Hospitals during the study period, either aborted or in labor. All women were also subjected to detailed history taking, thorough investigations and medical examination. The patients were monitored during delivery and prior to it, with evaluating the respiratory symptoms. The maternal and neonatal outcomes were assessed.

Results: There was statistically significant relation between maternal outcome and duration of ICU stay. There was statistically significant relation between maternal outcome and result of CT chest. There was statistically non-significant relation between maternal outcome and neonatal gender or mode of delivery. There was statistically significant relation between maternal outcome and fetal weight, gestational age (higher with good outcome). There was statistically significant relation between need for NICU admission and fetal weight (lower in babies needed NICU admission).

Conclusion: Pregnant women, who are infected with COVID-19 doubly, require extra care. There was currently insufficient evidence on COVID-19 and pregnancy, with the majority of cases occurring late in pregnancy, which poses a really potential danger for the mother and her baby.

Keywords: Pregnant females, COVID-19, Adverse effects, Neonates.

INTRODUCTION

Since the early epidemic in Wuhan, China, the current age of Coronavirus illnesses, particularly (COVID-19) infection causes severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that has lasted from December 2019 to the present [(1)]. It posed a threat to public health and a significant strain on various health systems throughout the world, prompting the World Health Organization (WHO) to declare it a worldwide pandemic in March 2019 [(2)].

Pregnant women and their newborns are high-risk groups for COVID-19 virus infection [(3)]. They should be provided extraordinary care, as well as comprehensive research and study to prevent any substantial negative results that may occur at any moment during the infection period [(4)]. More comprehensive clinical trials have been completed and will be conducted in the future to demonstrate the safety and efficacy of the pharmaceutical regimen proved and represented by the WHO since the first wave of the pandemic, as well as the safety of the method of administration [(5)].

The aim of this work was to provide an efficient and robust local database regarding the maternal and neonatal outcomes for the pregnant cases admitted to Zagazig Isolation Hospitals.

PATIENTS AND METHODS

An observational retrospective cohort study included 50 pregnant women, infected with COVID-19 were admitted to Zagazig Isolation Hospitals during the study period.

Inclusion criteria: All pregnant females in labor, either preterm, near term or post-term who were admitted to Zagazig isolation hospitals with COVID-19 infection. All patients shared clinical and radiological signs of suspected or evident COVID-19 infection. The hospital records were also obtained to collect further data from them.

Exclusion criteria: Severe respiratory distress syndrome with known previous causes other than COVID-19 who were pregnant and admitted for delivery in Zagazig Isolation Hospitals.

Operational design:

data were collected from the hospital records regarding demographic data, gestational age at diagnosis, delivery characteristics as total number of deliveries and mode of delivery either cesarean or vaginal.

Clinical data included symptoms and signs as fever on admission, cough, malaise, dyspnea, myalgia, sore throat, diarrhea, loss of taste and smell, headache, vomiting, nausea and runny nose).

Laboratory and radiological characteristics: Lymphocytopenia, platelet count, elevated C-reactive

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protein (mg/L), chest X-ray (ground glass appearance) and CT chest (patchy shadowing)).

Maternal and Neonatal Outcomes included maternal ICU admission, maternal mortality, neonatal birth weight, neonatal ICU admission.

Ethical Consideration:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Written informed consents from all the participants were obtained. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data qualitative data were represented as number and percentage, quantitative continues group was represented by mean ± SD. Differences between quantitative independent multiple by ANOVA or Kruskal Wallis. P value was set at ≤ 0.05 for significant results & ≤ 0.001 for high significant result.

RESULTS

The current study showed a statistically non-significant relation between maternal outcome and maternal age, parity, or gravidity **(Table 1)**.

Table (1): Relation between maternal outcome and demographic and clinical data

	Maternal outcome		**Test**	
	Death(n=6) Mean ± SD	**Discharged (n=44) Mean ± SD**	**t**	**P**
Age (year)	25.5 ± 7.29	26.0 ± 6.53	-0.174	0.863
	Median (range)	**Median (range)**		
Parity	**1 (0 – 3)**	1 (0 – 4)	-0.371	0.710
Gravidity	2 (1 – 6)	3 (1 – 6)	-0.463	0.643

There was statistically non-significant relation between maternal outcome and placental site and the occurrence of PROM, or the fetal presenting part. There is statistically significant relation between maternal outcome and amount of amniotic fluid, larger percentage of those with bad outcomes had oligohydramnios because of the severity of infection in those cases, which resulted in dehydration and thus, decreased amniotic fluid amount and type of anesthesia (larger percentage of those with bad outcome received general anesthesia) (Table 2).

Table (2): Relation between maternal outcome and obstetric data

	Maternal outcome		**Test**	
	Death(n=6)	**Discharged(n=44)**	**t**	**p**
	(%)	**(%)**		
Placenta:				
Normal	6 (100)	43 (97.7)		>0.999
Previa	0 (0)	1 (2.3)		
Amniotic fluid				
Normal	1 (16.7)	32 (72.7)		
Oligohydramnios	5 (83.3)	9 (20.5)	4.631	0.031*
Polyhydramnios	0 (0)	2 (4.5)		
Meconium	0 (0)	1 (2.3)		
PROM:				
Yes	1 (16.7)	7 (15.9)		>0.999
No	5 (83.3)	37 (84.1)		
Type of anesthesia:				
General	5 (83.3)	2 (4.5)		
Local	0 (0)	6 (13.6)	20.617	<0.001**
Spinal	1 (16.7)	36 (81.8)		
Presenting part:				
Cephalic	5 (83.3)	40 (90.9)		
Breech	0 (0)	3 (6.8)		0.32
Transverse	1 (16.7)	0 (0)		
Twin	0 (0)	1 (2.3)		

There was statistically non-significant relation between maternal outcome and either of hemoglobin, red blood cells, white blood cells, lymphocyte, neutrophil count and platelet count or lymphocyte/neutrophil ratio **(Table 3)**.

Table (3): Relation between maternal outcome and hematological data

	Maternal outcome		Test	
	Death (n=6)	**Discharged (n=44)**	t	p
	Mean ± SD	**Mean ± SD**		
Hemoglobin	9.83 ± 0.95	10.45 ± 1.43	-1.022	0.312
RBCs	4.2 ± 0.73	4.5 ± 0.64	-1.047	0.3
WBCs	12.38 ± 2.75	10.92 ± 2.8	0.857	0.396
	Median (range)	**Median (range)**	Z	p
Lymphocytes	1.15 (0.39 – 2.4)	1.15 (0.2 – 8.3)	-0.03	0.976
Neutrophil	8 (5.3 – 17.2)	7.4 (2.1 – 17.4)	-0.58	0.562
Lymphocyte/neutrophil ratio	0.137 (0.07 – 0.22)	0.152 (0.03 – 0.76)	-0.442	0.658
Platelet count	231 (66 – 385)	199 (104 – 308)	-0.966	0.344

Z Mann Whitney test t independent sample t test

There was statistically non-significant relation between maternal outcome and either parity or gravidity. There was statistically significant relation between maternal outcome and oxygen saturation (SPO_2), GCS (both were higher among those with good outcome) and duration of hospital stay that was longer in those with poor outcome **(Table 4)**.

Table (4): Relation between maternal outcome and both clinical and obstetric history data

	Maternal outcome		Test	
	Death(n=6)	**Discharged(n=44)**	t	p
	Mean ± SD	**Mean ± SD**		
GCS	11.33 ± 2.5	14.98 ± 0.15	-3.565	0.016*
Oxygen saturation	70.83 ± 10.94	92.52 ± 3.47	-4.822	0.004*
	Median (range)	**Median (range)**		
Parity	**1 (0 – 3)**	1 (0 – 4)	-0.371	0.710
Gravidity	2 (1 – 6)	3 (1 – 6)	-0.463	0.643
Duration of hospital stay	7.5 (5 – 10)	3 (1 – 7)	-3.644	<0.001**

There was statistically significant relation between maternal outcome and duration of ICU stay **(Figure 1)**.

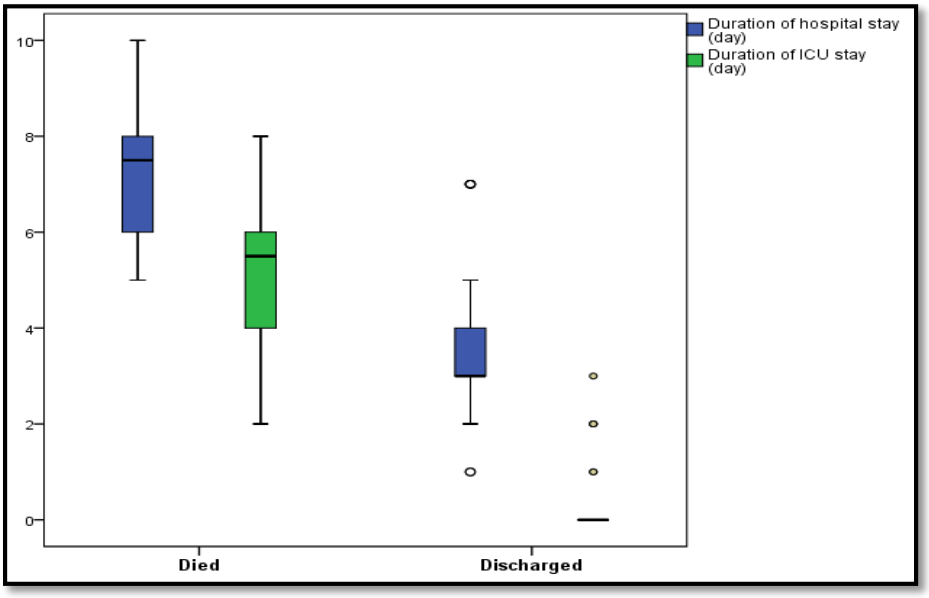

Figure (1): Boxplot showing relation between maternal outcome and duration of hospital and ICU stay

There was statistically significant relation between maternal outcome and result of CT chest (larger percentage of those with bad outcome had CORAD-5) **(Table 5)**.

Table (5): Relation between maternal outcome and chest CT

CT	Maternal outcome		P
	Death(n=6)	**Discharged(n=44)**	
	N=6 (%)	N=44 (%)	
GGO, CORDA-3	1 (16.7)	35 (79.5)	<0.001**
GGO, CORAD-4	0 (0)	7 (15.9)	
GGO, CORAD-5	5 (83.3)	2 (4.5)	

There was statistically non-significant relation between maternal outcome and neonatal gender or mode of delivery. There was statistically significant relation between maternal outcome and fetal weight (higher with good outcome), gestational age (higher with good outcome), need for NICU admission (66.7% born to mother with bad outcome and 20.5% born to mothers with good outcome need NICU admission) **(Table 6)**.

Table (6): Relation between maternal outcome and neonatal outcome

	Maternal outcome		
	Died (n=6)	**Discharged (n=44)**	**P**
	Mean ± SD	**Mean ± SD**	
Weight	1713.6 ± 471.32	2891.0 ± 517.19	<0.001**
Gestational age (week)	33.5 ± 2.07	37.55 ± 1.34	<0.001**
NICU admission Yes No	 4 (66.7) 2 (33.3)	 9 (20.5) 35 (79.5)	0.033*
Gender: Female Male	 5 (83.3) 1 (16.7)	 21 (47.7) 23 (52.3)	0.192
Mode of delivery CS NVD	 6 (100) 0 (0)	 37 (84.1) 7 (15.9)	0.292

There was statistically significant relation between need for NICU admission and fetal weight (lower in babies needed NICU admission) **(Figure 2)**.

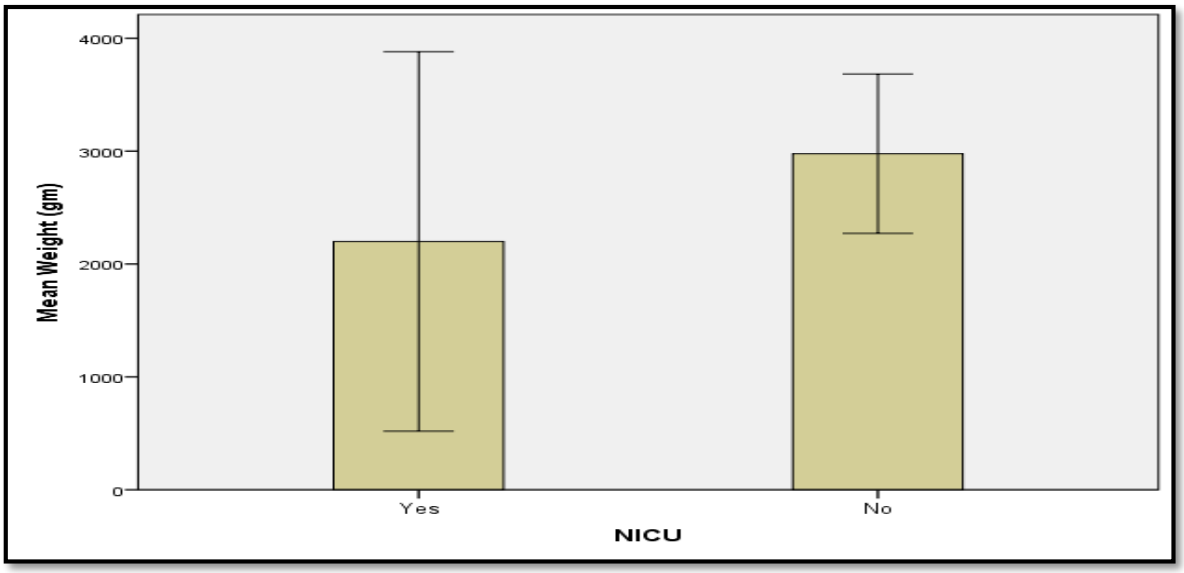

Figure (2): Simple bar chart showing relation between NICU admission and birth weight

DISCUSSION

Since the start of COVID-19 epidemic, there has been concern about how to safeguard vulnerable persons against the new SARS-CoV-2 illness. Regardless of the global epidemic, fatality rates are greater in pandemics. Pregnant women and their newborns are more vulnerable to infection than anybody else. During previous viral pandemics, such as SARS and H1N1, pregnant women were more vulnerable to serious sickness and mortality than the general population [(6)]. They were also at higher risk of poor perinatal outcomes because pregnancy has been linked to severe COVID-19 in a study of over 90,000 pregnant and non-pregnant women with COVID-19 in the United States based on the rate of critical care unit (ICU) admissions and mechanical ventilation is being used more frequently [(7)]. However, the fact that comprehensive reviews have begun to give information on maternal and pregnancy outcomes, knowledge of neonatal outcomes following maternal COVID-19 in pregnancy is still restricted to case studies and centre experiences. There has been a paucity of well-defined outcome measures recorded, as well as a lack of evidence to make clear conclusions concerning infant care, due to potential selection biases, a lack of denominators, a lack of recent comparators, and constrained and typically unspecific symptoms [(8)].

Most of the offspring of SARS-CoV-2-positive moms were asymptomatic, however a few developed neonatal morbidities. However, alternative causes of death could not be ruled out in any of the fatal patients that were discovered to be positive for SARS-CoV-2, and COVID-19 positivity did not contribute to the rising mortality risk. According to an examination of 77 articles from China, United States, and other nations, babies with the COVID-19 virus mothers were discovered to be infected [(9)]. Compared to negative moms, positive mothers passed away more frequently. Here, a little variation in fatality rates was seen, and no dead baby was determined to have COVID-19 infection according to existing definitions [(10)].

The current study revealed that admissions are on the rise. The patients who took general anaesthesia to perform the C.S had more mortality rates rather than the spinal ones. Also, women who admitted to the ICU had poorer prognosis and outcomes despite applying the full protocol, but the intubation and mechanical ventilation worsened the cases. The normal vaginal delivery had better outcomes than the caesarean ones as well. Especially in women who were reported with lesser symptoms or who were asymptomatic. Despite this, studies have shown that pregnancy may increase the risk of mortality, pneumonia, and ICU admission in SARS-CoV-2-infected women of reproductive age [(11)]. Additionally, a major risk factor for comorbidities in COVID-19 patients, such as advanced age, obesity, diabetes, and hypertension [(12)].

In order to achieve our aim this study was conducted on large scale in Zagazig Isolation Hospitals during the whole pandemic second and third waves, but only 50 pregnant women who were prior to labour completed the criteria and the follow-up period with a gestational age ranged from 31 to 41 weeks and aged from 18 to 42 years old with confirmed or suspected COVID-19 infection either by PCR or the CT chest.

On follow up of delivery outcomes of those patients and exclusion of those who lost to follow up, we found that 88% of patients showed recovery, whilst 12% died by the end. **Takemoto *et al.*** [(13)] studied 978 patients and reported higher maternal death rates, which was 12.7% of cases (124/978) in Brazil, and that deserves a real special attention.

We found that there was statistically non-significant relation between maternal outcome and past history of maternal illness or any drug intake. The survey found that pregnant women who died had greater comorbidities in a report included 385 patients as by **Elshafeey *et al.*** [(14)] where they mentioned more liability to develop maternal complications and higher death rates.

As for the mode of delivery, the majority was delivered by C.S although 90% of the foetuses had cephalic presentation and only 14% of cases required the transformation for general anaesthesia rather than spinal type. In the USA study of **Katz *et al.*** [(15)], reported that women with SARS-CoV-2 need neuraxial labour analgesia, which means that the presence or absence of maternal SARS-CoV-2 symptoms at the time of delivery should assist, stratify risk and care, and labour analgesia and potential hurdles during that serious pandemic should be investigated further.

In our study, patients with CO-RAD5 diagnosis in CT chest had the worst prognosis, with prolonged hospital stay and ICU admission for the need of close monitoring or the use of artificial mechanical ventilation with statistically significant relation between poor or good maternal outcome and oxygen saturation SPO_2 and GCS (both were higher among those with good outcome), duration of hospital stay, or duration of ICU stay (both were longer in those with poor outcome). Similar to our findings is **Khoury *et al.*** [(16)] in the group of women who died, ICU admission (72.3 vs. 17.5%) and invasive respiratory assistance (64 vs. 4.4%) were both greater than in the group of women who survived.

In our study, there was statistically significant relation between need for NICU admission and foetal weight (lower in babies need NICU admission). One mechanism implicated in this is related to the pre-placental hypoxia, which can occur as a result of maternal respiratory compromise with pneumonia/pneumonitis. This can perpetuate a cascade of anti-angiogenic and pro-inflammatory factors promoting endothelial dysfunction, end-organ damage, and placental insufficiency. Thereby, contributing to relative fetal hypoxemia and eventually hypoxia [(17, 18)]. Additionally, it was identified that nearly half of these neonates were symptomatic on the first day of life. Although none of the neonatal investigations at birth

were positive for COVID-19, **Dong *et al.* [19]** found that serial RT-PCRs for COVID-19 in neonates may appear negative with the neonate demonstrating delayed serological evidence of infection 3–7 days post-infection.

CONCLUSION

Pregnant women, who are infected with COVID-19 doubly, require extra care. There is currently insufficient evidence on COVID-19 and pregnancy, with the majority of cases occurring late in pregnancy, which poses a really potential danger for the mother and her baby.

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Author contribution: Authors contributed equally in the study.

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