Effect of COVID-19 Infection on Pregnancy

Ahmed T. Said-Elnaby *, Samy A. Saad, Tamer M. Assar and Sara T. Mostafa
Obstetrics and Gynecology Department, Faculty of Medicine, Benha University, Benha, Egypt
E-Mail:a7mdsyam1991@gmail.com

Abstract

Background: The COVID-19 pandemic has raised concerns about the impact of SARS-CoV-2 infection on pregnant women and their unborn babies. Understanding the clinical characteristics, laboratory findings, and outcomes of COVID-19 in pregnancy is crucial for providing appropriate management and care. This study aimed to describe clinical, laboratory characteristics and maternal and fetal outcomes of third trimesteric pregnant women confirmed to have SARS-CoV-2 infection. **Methods:** This prospective clinical study included 50 pregnant women aged 20 to 40 years, with gestational age ranging from 28 to 40 weeks. **Results:** The study population had a mean age of 29.74 years, with a majority being multipara. The most common clinical manifestations were fever (44 %), cough (64%), shortness of breath (32%), ICU admission in (22%) of cases in which (16%) needed mechanical ventilation, and (10%) were shocked. Laboratory findings revealed hematological abnormalities such as leukocytosis (52%), lymphopenia (60%), neutrophilia (52%), and thrombocytopenia (36%). Pregnancy outcome was bad in (8%) of cases with (2%) maternal mortality and (6%) neonatal mortality. As regard neonatal mortality statistics, according to UNICEF, it was 18 deaths per 1,000 live births in 2021(1.8%). As regarded maternal mortality statistics, according to UNICEF, it was 223 deaths per 100,000 live births at 2020 (0.233%). **Conclusions:** COVID-19 infection during pregnancy has a negative effect on maternal and neonatal outcome regarding both mortality and morbidity concerns.

Keywords: COVID-19; pregnancy; third trimester; clinical characteristics; laboratory findings; maternal outcomes; fetal outcomes.

1. Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has posed significant challenges to healthcare systems worldwide. With the rapid spread of the virus, it became essential to understand its impact on various populations, including pregnant women [1, 2].

Pregnancy is a unique physiological state that can influence the susceptibility and course of infectious diseases as pregnant women are known to be at increased risk of acquiring viral respiratory infections and developing severe pneumonia due to changes in their immune and cardiopulmonary systems [3]. Therefore, studying the clinical characteristics, laboratory findings, and maternal and fetal outcomes in pregnant women with COVID-19 infection is crucial for optimizing their

management and ensuring the well-being of both mother and child [4, 5].

Several studies have highlighted the potential risks associated with respiratory infections during pregnancy. Similar concerns have been raised regarding the impact of SARS-CoV-2 infection on maternal and fetal health [6]. Understanding the specific effects of COVID-19 on pregnant women is imperative for guiding clinical decision-making and developing appropriate preventive and therapeutic strategies [7, 8].

To date, a growing body of evidence has emerged on the clinical manifestations and outcomes of COVID-19 in the general population. However, there remains a need for a comprehensive evaluation of the impact of COVID-19 infection on pregnant women, particularly those in the third trimester. The third trimester is of particular interest as it represents a critical period of fetal development, and any adverse effects on the mother during this stage could have significant consequences for the fetus [9, 10].

Therefore, the aim of this study is to describe clinical, laboratory characteristics and maternal and fetal outcomes of third trimesteric pregnant women confirmed to have SARS-CoV-2 infection.

2. Methods

This prospective clinical study was conducted at Benha University Hospital, Kaha Central Hospital, and Benha Insurance Hospital. The study included 50 pregnant women who attended the Gynecology and Obstetrics departments of these hospitals from November 2020 to October 2021. The study protocol was approved by the hospital's research ethics board (ethical approval number MD 2.10.2020), and all study participants were counselled, and informed consent was obtained.

Inclusion criteria were women aged between 20 and 40 years with gestational age ranging from 28 to 40 weeks. Additionally, confirmed cases of COVID-19 were identified using PCR testing.

Exclusion criteria were pregnant women below 28 weeks of gestation, those with comorbidities such as diabetes mellitus (DM) and hypertension (HTN), as well as individuals with chronic chest diseases and haematological disorders.

In accordance with the New Coronavirus Pneumonia Prevention and Control Program (6th edition) published by the National Health Commission of China, laboratory evidence for confirmed COVID-19 cases included:

- Positive SARS-CoV-2 nucleic acid results by real-time reverse-transcription-polymerase-chain-reaction (RT-PCR).
- Viral gene sequencing showing high homogeneity to the known SARS-CoV-2.

Real-time RT-PCR assays were performed following the protocol established by the World Health Organization (WHO).

The clinical severity of COVID-19 was classified into four levels, as outlined in the New Coronavirus Pneumonia Prevention and Control Program (6th edition) published by the National Health Commission of China:

1. Mild: Presence of mild clinical symptoms such as backache, loss of taste or smell, headache, or sore throat.

2. Moderate: Presence of fever or upper respiratory symptoms.

3. Severe: Presence of one of the following conditions: i) shortness of breath and respiratory rate ≥ 30 breaths per minute, ii) resting oxygen saturation ≤ 93%, iii) partial pressure of oxygen/fraction of inspired oxygen ≤ 300 mmHg.

4. Severe acute: Presence of acute respiratory distress and need for mechanical ventilation, or presence of shock, or admission to the intensive care unit (ICU).

All cases were terminated by cesarean section, and the pregnancy outcomes were classified based on maternal deaths, fetal birth weight, Apgar score, tests for SARS-CoV-2, and neonatal death.

The primary composite endpoint was defined as the use of mechanical ventilation, admission to the ICU, or death, and its percentage was calculated.

Secondary outcomes included the percentage of pregnant women with mild, moderate, and severe symptoms, the percentage of newborns who developed acute respiratory distress syndrome (ARDS) and were admitted to the neonatal intensive care unit (NICU), as well as any mortalities among newborns.

Statistical analysis:

Version 26 of IBM SPSS Statistics was used to do statistical analysis (IBM Inc., Armonk, NY, USA). The normality of data distribution was examined using the Shapiro-Wilks test and histograms. Quantitative parametric data were presented as mean and standard deviation (SD) and analyzed using the unpaired Student's t-test. Non-parametric quantitative data were reported and analyzed as median and interquartile range (IQR) using the Mann-Whitney U test. When appropriate, qualitative data were provided as frequency and percentage (percent) and assessed using the Chi-square or Fisher's exact test. For the statistical comparison of different groups, analytical statistics were employed, including the ANOVA test (F value) to compare means of more than two groups for quantitative data. A p-value less than 0.05 was considered statistically significant (*).

3. Results

This was a prospective descriptive clinical study conducted at

Benha University Hospital, Kaha Central Hospital, and Benha Insurance Hospital. The study included 50 pregnant women who attended the Gynecology and Obstetrics departments of these hospitals from November 2020 to October 2021. These women were part of a group of 50 pregnant women who tested positive for COVID-19.

The study population had a mean age of 29.74± 4.0 years, with a median age of 30 years. Regarding parity, there were 20 primipara (first-time mothers) and 30 multipara (mothers with previous pregnancies). In terms of gestational age, the mean was 36.68± 2.29 weeks (range: 31-40), and the median was 37 weeks. **Table 1**

Table 1: The clinical characteristics of COVID-19 in 50 pregnant women

	No (50)	**%**
Age mean ±sd (range) Median (IQR)	29.74± 4.0 (23-40) 30.0 (27.0-33.0)	
Parity Primi para Multipara	20 30	40.0 60.0
GA mean ±sd (range) Median (IQR)	36.68± 2.29 (31-40) 37.0 (36.0-38.0)	

Among the clinical manifestations observed, fever was present in 22 cases (44% of the total), cough in 32 cases (64% of the total), and shortness of breath in 16 cases (32% of the total). Additionally, 11 cases (22% of the total) required admission to the intensive care unit (ICU), out of which 8 cases (16% of the total) required mechanical ventilation, and 5 cases (10% of the total) experienced shock. **Table 2**

Table 2: The clinical manifestations of COVID-19 in 50 pregnant women.

	Positive	
	No (50)	**%**
Fever	22	44.0
Cough	32	64.0
Shortness of breath	16	32.0
Mechanical ventilation	8	16.0
Shock	5	10.0
ICU	11	22.0

Regarding laboratory investigations, a complete blood count (CBC) was conducted for all cases. The results revealed leucocytosis in 26 cases (52% of the total), lymphopenia in 30 cases (60% of the total), neutrophilia in 26 cases (52% of the total), and thrombocytopenia in 18 cases (36% of the total). **Table 3**

Table 3: The laboratory and radiological investigations of COVID-19 in 50 pregnant women.

	NO	%
TLC (50) Elevated	26/50	52.0
Lymphocytes (50) Reduced	30/50	60.0
Neutrophils (50) Elevated	26/50	52.0
PLT (50) Reduced	18/50	36.0
Coagulation	NO	%
D-dimer (9) Elevated	9/9	100

PT (32) Prolonged	3/32	9.4
PTT (32) Prolonged	3/32	9.4
Inflammation	NO	%
CRP (17) Elevated	3/17	17.6
ESR (3) Elevated	3/3	100
Bioch	NO	%
LDH (9) Elevated	9/9	100
ALT (28) Elevated	9/28	32.1
AST (28) Elevated	9/28	32.1
Bilirubin (3) Elevated	3/3	100
Albumin (18) Reduced	6/18	33.3
Creatinine (41) Elevated	8/41	19.5
Ferrittin (9) Elevated	3/9	33.3
Radiological	NO	%
CT chest (21) Ground glass appearance	21/21	100

According to the guidelines outlined in the New Coronavirus Pneumonia Prevention and Control Program (6th edition) published by the National Health Commission of China, out of the total cases, 34 cases (68%) exhibited mild symptoms. Additionally, 9 cases (18%) had moderate symptoms, 4 cases (8%) experienced severe symptoms, and only 3 cases (6%) had severe acute symptoms. **Table 4**

Table 4: The severity of symptoms in 50 pregnant women with COVID-19 infection.

Severity of symptoms	No (50)	%
Mild	34	68.0
Moderate	9	18.0
Severe	4	8.0
Severe acute	3	6.0

Regarding the pregnancy outcome, it was favorable in 46 cases (92%) and unfavorable in only 4 cases (8%). The mean fetal weight was 2.98± 0.61 kg, with a median of 3 kg. APGAR scores ranged from 5-6 in 1 case to 10-10 in 1 case. Neonatal death occurred in only 3 cases (6%), and tests for SARS-CoV-2 were negative in 47 cases (94%). However, in 3 cases (6%), these tests could not be performed due to neonatal death. **Table 5**

There was a case of maternal mortality involving a 30-year-old woman who was at 34 weeks and 4 days of her second pregnancy. She was admitted to the emergency room due to accidental hemorrhage and fetal

distress. Additionally, the patient had exhibited chest manifestations a few days prior to admission. To address the situation, a termination of the pregnancy was performed through a cesarean section, resulting in the delivery of a single living fetus with APGAR scores of 8-8 after 1-5 minutes. However, due to the severity of the condition, the patient was subsequently admitted to the intensive care unit (ICU) for further monitoring. She required intubation, but unfortunately, multiple organ failure, shock, gastric bleeding, and disseminated intravascular coagulation (DIC) occurred in the following days, leading to her unfortunate demise. **Table 5**

Table 5: Complications of COVID-19 in 50 pregnant women.

	No (50)	%
Pregnancy outcome		
Bad	4	8.0
Maternal death		
+ve	1	2.0
FBW mean ±SD (range)	2.98± 0.61 (1.7-4.5)	
Median (IQR)	3.0 (2.5-3.5)	
Apgar score (47)		
5-6	1	2.1
6-7	1	2.1
6-9	1	2.1
7-8	6	12.8
7-9	10	21.3
8-8	1	2.1
8-9	10	21.3
8-10	3	6.4
9-10	13	27.7
10-10	1	2.1
Neonatal death		
+ve	3	6.0
Tests for SARS-COV-2		
Not done	3	6.0

No significant statistical difference was found in relation to age when analyzing the severity of symptoms (p-value = 0.077). **Figure 1**

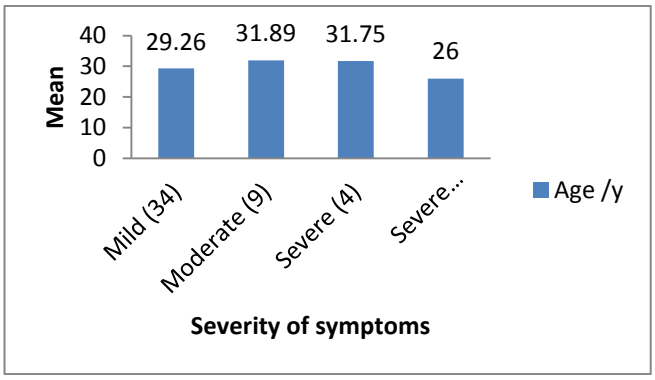

Figure 1: Distribution of the studied group according to age regarding severity of COVID-19 symptoms.

The analysis revealed no significant statistical difference in relation to gestational age when examining the severity of symptoms (p-value = 0.204). **Figure 2**

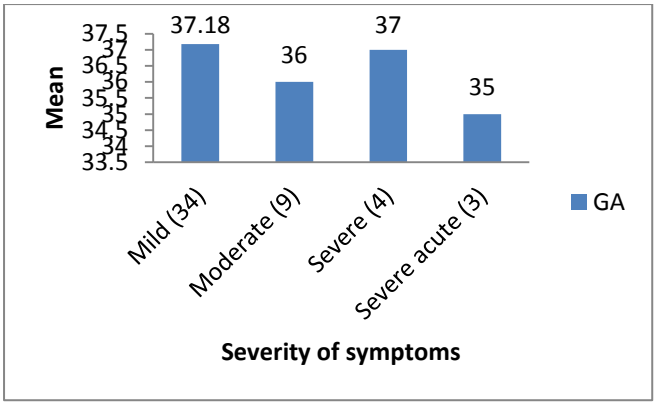

Figure 2: Distribution of the studied group according to gestational age regarding severity of COVID-19 symptoms.

There was no significant statistical difference between levels of severity of symptoms according to birth weight (p-value 0.164). **Figure 3**

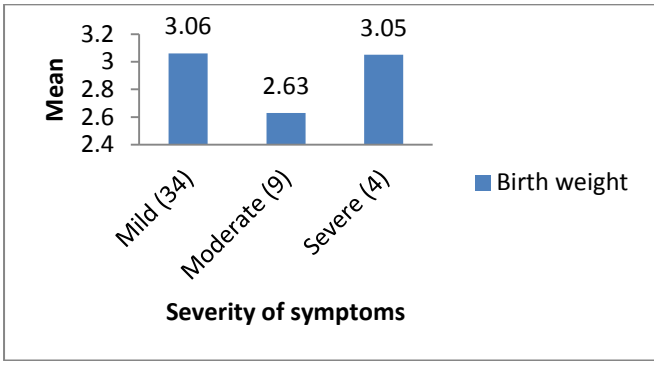

Figure 3: Comparison between levels of severity of symptoms according to Birth weight.

4. Discussion

Multiple studies have examined the effects of COVID-19 on pregnant women and their babies. **Schwartz et al. (2020)** studied 38 pregnant women with COVID-19, of whom 37 had RTPCR confirmed SARS-CoV-2 infection, there were no cases of either severe pneumonia or maternal deaths. Comorbid conditions did not increase the risk of virus transmission to the fetus [11]. Similarly, **Youssef et al. (2023)** reported that among 75 pregnant women with COVID-19, there were varying degrees of illness and complications. Some required intensive care and mechanical ventilation, resulting in a death rate of 15.9%. Prematurity was the most common outcome for newborns (13%) [12]. Overall, the studies provide valuable insights into the impact of COVID-19 on maternal and fetal health.

According to **Barbero et al. (2022)**, a study of 91 pregnant and postpartum women with SARS-CoV-2 infection found that 40 patients developed pneumonia, with a high rate of hospitalization and ICU admission (46.2%) [13]. Compared to non-pregnant women with similar characteristics, pregnant women had a higher risk of severe COVID-19. Obesity and Latin-American origin were identified as risk factors for hospitalization. Among the patients who delivered with active SARS-CoV-2, there was a high rate of cesarean section, especially in the hospitalized group. Prematurity was observed in both groups, but no maternal or neonatal deaths were reported. The study suggests that SARS-CoV-2 infection during pregnancy, particularly in the presence of obesity or Latin-American origin, may have more severe outcomes.

In another study by **Mullins et al. (2021)**, data from the PAN-COVID registry in the UK and the AAP-SONPM National Perinatal COVID-19 registry in the USA were analyzed [14]. A total of 4005 pregnant women with suspected or confirmed SARS-CoV-2

infection were included. The results showed low rates of maternal death, early neonatal death, and stillbirth in both the overall population and the confirmed infection group.

In pregnancies with SARS-CoV-2 infection, preterm delivery rates were higher than expected, but rates of stillbirth and small-for-gestational-age infants were comparable to historical data. Neonatal SARS-CoV-2 infection was reported in a small proportion of cases, and there was no significant impact on fetal growth or distress. Several studies explored treatment options, including Interferon-alpha, lopinavir-ritonavir, and chloroquine. Thromboembolic events were more common, suggesting the potential benefits of LMWH treatment. Continuous renal replacement therapy and hem-purification were effective in severe pneumonia cases. Our prospective clinical study included 50 pregnant women with confirmed COVID-19, following specific inclusion and exclusion criteria. The study was approved by the hospital research ethics board and followed the guidelines for confirming COVID-19 cases.

The study collected data on pregnant women with confirmed COVID-19, assessing their demographic information, medical history, clinical presentation, and laboratory findings. Clinical severity was categorized into mild, moderate, severe, and severe acute cases. Cesarean section was performed for all participants. Pregnancy outcomes showed overall positive results, with low maternal mortality and good fetal outcomes. Laboratory investigations revealed various abnormalities, while radiological findings exhibited a characteristic ground glass appearance. Most cases had mild symptoms, and there were no significant statistical differences between symptom severity and age, gestational age, or birth weight.

As regarded maternal mortality statistics, according to **UNICEF**, from 2000 to 2020, the global maternal mortality ratio (MMR) declined by 34 per cent – from 342 deaths to 223 deaths per 100,000 live births (0.233% in 2020), according to UN inter-agency estimates. And also, **as regard neonatal mortality statistics**, according to **UNICEF** Children face the highest risk of dying in their first month of life at an average global rate of 18 deaths per 1,000 live births in 2021, down by 51 per cent from 37 deaths per 1,000 live births in 1990 (1.8% in 2021).

As regard maternal morbidity statistics, according to (Kathryn R. Fingar et al, 2018) severe maternal morbidity at birth, per 10,000 U.S. births, 2015 included 5.9 cases with adult respiratory distress syndrome (0.059%), 1.2 cases needed mechanical ventilation (0.012%) and 4.3 cases in shoch state (0.043%). So, in comparison to the current study COVID-19 infection with pregnancy has higher incidence of maternal morbidity [15].

Maternal mortality rates globally have decreased over the years,

with the global maternal mortality ratio declining by 34% from 2000 to 2020 [16]. In Egypt, the maternal mortality ratio in 2020 was 17 deaths per 100,000 live births, showing a significant reduction from 76 deaths per 100,000 live births in 2001. However, the incidence of maternal mortality in pregnancies with COVID-19 infection appears to be higher than these rates [17]. Similarly, severe maternal morbidity rates are relatively low in general, but COVID-19 infection during pregnancy seems to increase the incidence of maternal morbidity. Neonatal mortality rates have also decreased globally, with the average rate being 18 deaths per 1,000 live births in 2021 [18]. In Egypt, the neonatal mortality rate in 2021 was 10 deaths per 1,000 live births, showing improvement from 60.3 deaths per 1,000 live births in 1972. However, the incidence of neonatal mortality appears to be higher in pregnancies affected by COVID-19 [19].

The study by **Schwartz et al. (2020)** analyzed 38 pregnant women with COVID-19 and found no severe pneumonia or maternal deaths, although some women had comorbid conditions such as preeclampsia and gestational diabetes. It also agreed with the current study that there were no risk factors for intrauterine transmission of the virus [11]. **Barbero P et al. (2022)** observed similar symptoms of COVID-19 in pregnant women, such as Bony-ache (71.7%), Fever (65.0%), Cough 30 (50.0%), and Loss smell (50.0%), as well as Loss taste (41.7%), Sore throat (30.0%), Loss of appetite (26.7%), Dyspnea (16.9%) and Diarrhea (6.7%) and found no increase in prematurity rates. However, they differed in terms of the type of delivery and identified obesity and Latin-American origin as risk factors [13]. **Mullins E et al. (2021)** disagreed with the current study, stating that COVID-19 in pregnancy did not significantly affect fetal growth, neonatal outcomes, or stillbirth rates. However, they agreed that maternal death rates were higher than expected based on population data in the UK and USA [14].

The study by **Youssef et al. (2023)** differs from the current study as it included the entire duration from conception to the end of the postpartum period and included confirmed cases with co-morbidities [12]. It observed a higher rate of C-sections due to concerns about the impact of COVID-19 on lung function and inflammation during labor. Prematurity was the most common outcome among newborns (13%), followed by fetal distress (10.9%) and respiratory distress syndrome (8.7%). However, it agrees with the current study in finding a significant rate of complications, including ICU hospitalization (37.2%), mechanical ventilation (5.2%), and a death rate among the participants (15.9%). The variation in results among these studies may be due to differences in study methods, duration of follow-up, sample size, and the presence of multiple study groups in other studies.

5. Conclusion

In conclusion, COVID-19 infection during pregnancy has a

negative effect on maternal and neonatal outcome regarding both mortality and morbidity concerns.

6. References

1. R. Filip, R. Gheorghita Puscaselu, L. Anchidin-Norocel, M. Dimian, W.K. Savage. Global Challenges to Public Health Care Systems during the COVID-19 Pandemic: A Review of Pandemic Measures and Problems. J Pers Med;12. 2022

2. M. Mihevc, D. Podgoršek, J. Gajšek, S. Mikuletič, V. Homar, M. Kolšek, et al. A remote care model for patients at high risk of hospital admission due to COVID-19 deterioration: who makes it at home? - a multicenter follow-up case from Slovenia. Croat Med J;64:170-8. 2023

3. A.J.M. Vale, A.C.L. Fernandes, F.P. Guzen, F.I. Pinheiro, E.P. de Azevedo, R.N. Cobucci. Susceptibility to COVID-19 in Pregnancy, Labor, and Postpartum Period: Immune System, Vertical Transmission, and Breastfeeding. Front Glob Womens Health;2:602572. 2021

4. M. Mirbeyk, A. Saghazadeh, N. Rezaei. A systematic review of pregnant women with COVID-19 and their neonates. Arch Gynecol Obstet;304:5-38. 2021

5. R. Matar, L. Alrahmani, N. Monzer, L.G. Debiane, E. Berbari, J. Fares, et al. Clinical Presentation and Outcomes of Pregnant Women With Coronavirus Disease 2019: A Systematic Review and Meta-analysis. Clin Infect Dis;72:521-33. 2021

6. D. Salem, F. Katranji, T. Bakdash. COVID-19 infection in pregnant women: Review of maternal and fetal outcomes. Int J Gynaecol Obstet;152:291-8. 2021

7. K. Narang, E.A.L. Enninga, M. Gunaratne, E.R. Ibirogba, A.T.A. Trad, A. Elrefaei, et al. SARS-CoV-2 Infection and COVID-19 During Pregnancy: A Multidisciplinary Review. Mayo Clin Proc;95:1750-65. 2020

8. K. Diriba, E. Awulachew, E. Getu. The effect of coronavirus infection (SARS-CoV-2, MERS-CoV, and SARS-CoV) during pregnancy and the possibility of vertical maternal–fetal transmission: a systematic review and meta-analysis. European Journal of Medical Research;25:39. 2020

9. A. Ciapponi, A. Bardach, D. Comandé, M. Berrueta, F.J. Argento, F. Rodriguez Cairoli, et al. COVID-19 and pregnancy: An umbrella review of clinical presentation, vertical transmission, and maternal and perinatal outcomes. PLoS One;16:e0253974. 2021

10. C. Daclin, M. Carbonnel, M. Rossignol, H. Abbou, H. Trabelsi, A. Cimmino, et al. Impact of COVID-19 infection in pregnancy and neonates: A case control study. J Gynecol Obstet Hum Reprod;51:102366. 2022

11. D.A. Schwartz. An Analysis of 38 Pregnant Women With COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes. Arch Pathol Lab Med;144:799-805. 2020

12. A.M. Youssef, S. EL-Gelany, M.H. Ibrahim, A.R. Gedawy. Maternal and Perinatal Outcomes in Pregnant Women with Covid-19: A Retrospective Egyptian Study. Annals of Neonatology Journal;5:79-96. 2023

13. P. Barbero, L. Mugüerza, I. Herraiz, A. García Burguillo, R. San Juan, L. Forcén, et al. SARS-CoV-2 in pregnancy: characteristics and outcomes of hospitalized and non-hospitalized women due to COVID-19. J Matern Fetal Neonatal Med;35:2648-54. 2022

14. E. Mullins, M.L. Hudak, J. Banerjee, T. Getzlaff, J. Townson, K. Barnette, et al. Pregnancy and neonatal outcomes of COVID-19: coreporting of common outcomes from PAN-

COVID and AAP-SONPM registries. Ultrasound Obstet Gynecol;57:573-81. 2021
15. K.R. Fingar, M.M. Hambrick, K.C. Heslin, J.E. Moore. Trends and disparities in delivery hospitalizations involving severe maternal morbidity, 2006–2015. 2018
16. R. Musarandega, J. Cresswell, T. Magwali, D. Makosa, R. Machekano, S. Ngwenya, et al. Maternal mortality decline in Zimbabwe, 2007/2008 to 2018/2019: findings from mortality surveys using civil registration, vital statistics and health system data. BMJ Glob Health;7. 2022
17. H. Wang, N. Li, C. Sun, X. Guo, W. Su, Q. Song, et al. The association between pregnancy and COVID-19: A systematic review and meta-analysis. Am J Emerg Med;56:188-95. 2022
18. J. Villar, S. Ariff, R.B. Gunier, R. Thiruvengadam, S. Rauch, A. Kholin, et al. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. JAMA Pediatr;175:817-26. 2021
19. W.H. Organization. Reaching the every newborn national 2020 milestones: country progress, plans and moving forward. 2017