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Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection: a single centre experience

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ABSTRACT

Objective. Aim of this study was to evaluate maternal and perinatal outcomes of pregnant women affected by COVID-19 during the first pandemic wave in a third level University Hospital of Southern Italy.
Materials and Methods. This was a single-centre, cohort study on SARS-CoV-2 in pregnancy. Pregnant women with laboratory-confirmed SARS-CoV-2 from August 1, 2020 to January 1, 2021 from University of Naples Federico II were included. A confirmed case of COVID-19 was defined as a positive result on real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay of nasal and pharyngeal swab specimens. The primary outcome was the incidence preterm birth.
Results. 249 singleton pregnancies were included in the study. Mean gestational age at diagnosis was 31.0 ± 6.7 weeks, with 2.4% of women being diagnosed in the first, 14.1% in the second and 83.5% in the third trimester of pregnancy. The majority of the women received therapy with low molecular weight heparin (88.8%). 47 women (18.9%) required oxygen. The rate of admission to maternal intensive care unit was 2.8%. There was one case of maternal death, accounting for a maternal mortality rate of 0.4%. Out of the 249 ended pregnancies, we reported two spontaneous abortions and two stillbirths. Among 245 live-born babies, no neonatal deaths were recorded. All babies were tested negative at RT-PCR nasal and pharyngeal swab. The incidence of preterm delivery before 37 weeks was 10%.
Conclusions. SARS-CoV-2 infection in pregnant women during the first pandemic wave in the South of Italy was associated with relative low rates of maternal and perinatal adverse outcome.

INTRODUCTION

The spread of COVID-19 in the last two years has had incalculable consequences [1, 2]. Initially, a lockdown was imposed by the government and all non-urgent medical treatments were stopped and postponed, while healthcare resources were reallocated to face this unprecedented health crisis. Guidelines and advices were soon released by experts and subspecialty societies to direct obstetrical and gynaecological management [3-15]. Interestingly, during the lockdown period, a significant decrease in admissions to the emergency units was also found for obstetric-gynaecological conditions [16-21], and even for important tests, such as invasive prenatal diagnosis, a drop in the number of procedures was noted [22], clearly showing that pregnant women were more concerned than others of contracting the infection and suffering from the COVID-19 disease [23, 24]. Moreover, reproductive medicine had to cease treatment unless for fertility preservation due to oncologic reasons, with consequences also on fertility and natality rates, opening a debate on the urgency to reduce time to pregnancy in women with poor prognosis [25-29]. Very soon, it appeared clear that pregnant women should have been considered a population at increased risk for severe forms of infection and therefore adverse maternal and perinatal outcomes [30-37]. One of the most dangerous complications of COVID-19 is pneumonia, which during pregnancy can have even more serious consequences due to the reduced lung excursion capacity [38, 39]. Furthermore, it was questioned how to diagnose and monitor lung involvement in pregnant women, since computed tomography (CT) scan raises the risk of foetal damage due to ionizing radiations, and therefore lung ultrasound has been largely proposed in this subset of the population, as a fast and easy procedure with apparently no risk for the foetus [40-45].
Italy was one of the first countries in Europe to be hit, initially in the northern regions, but few months later also the southern were reached by the pandemic wave. In this scenario, it is of striking importance to address the consequences of SARS-CoV-2 infection both on maternal and on foetal-neonatal health, and more data are needed also to help the management of future cases. The aim of this study was to evaluate maternal and perinatal outcomes of pregnant women affected by COVID-19 during the first pandemic wave in a third level university hospital of Southern Italy.

MATERIALS AND METHODS

Study design and participants

This was a single-centre, retrospective cohort study on SARS-CoV-2 in pregnancy. Clinical records and compiled data of all consecutive pregnant women with laboratory-confirmed SARS-CoV-2 from August 1st, 2020 to January 1st, 2021 from our institution (University of Naples Federico II) were included in a dedicated merged database.
Data before August 1st, 2020 were excluded for two reasons: first of all, data were partially included in our prior multicentre WAPM collaboration, where University of Naples was the coordinator centre [33]. In addition, before August 1st, 2020 the vast majority of patients were screened only in case of recent exposure history, or in case of clinical symptoms or signs. After August 1st, 2020 a policy of universal screening at the time of triage was applied [46]. COVID-19 was diagnosed on the basis of The World Health Organization (WHO) interim guidance [47]. A confirmed case of COVID-19 was defined as a positive result on real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay of nasal and pharyngeal swab specimens [1, 2]. Data on recent exposure history, clinical symptoms or signs, laboratory findings, maternal and perinatal outcomes were collected. Screening of neonates born from mothers infected by SARS-CoV-2 was performed with daily swabs during the 72 h of routine hospital neonatal stay.

Outcomes

The primary outcome was incidence of preterm birth at less than 37 weeks of gestations. Secondary outcomes were maternal admission to intensive care unit (ICU), maternal death, perinatal death, caesarean delivery, admission to neonatal ICU (NICU), and vertical transmission confirmed at neonate RT-PCR assay.

Study definitions

Abortion was defined as pregnancy loss before 22 weeks of gestations. Stillbirth was defined as intrauterine foetal death after 22 weeks of gestation. Neonatal death was defined as death of a live-born infant within the first 28 days of life. Perinatal death was defined as either stillbirth or neonatal death. Preterm birth was defined as delivery be-

fore 37 weeks of gestation. Fever was defined as an axillary temperature of 37.5 °C or higher.

Statistical analysis

Standard descriptive statistics (median with range, mean ± SD and frequencies with percentages) were used to describe the features of cases.

RESULTS

Characteristics of the included women

During the study period, 263 singleton pregnancies, positive to SARS-CoV-2 at RT-PCR nasal and pharyngeal swab, were referred to our centre. We did not have any twin pregnancy affected by SARS-CoV-2 infection during the first pandemic wave. Of them, 249 ended the pregnancy and were included in the study. The 14 women with an ongoing pregnancy were excluded from the study.

Mean gestational age at diagnosis was 34.2 ± 6.9 weeks, with 2.4% of women being diagnosed in the first, 14.1% in the second and 83.4% in the third trimester of pregnancy. The most common symptom at the time of triage was cough (27.7%), while anosmia was present in 28 women (11.2%). The vast majority of the women received therapy with low molecular weight heparin (LMWH) (88.8%) (**Table 1**). None of the included women were vaccinated against SARS-CoV-2, because the vaccine was not available yet at that time.

Table 1. *Characteristics of the included women.*

	n = 249
Demographics	
Age (years) Mean ± SD	31.0 ± 6.7
Healthcare workers n (%)	10 (4.0%)
Smoking n (%)	45 (18.1%)
Nulliparous n (%)	124 (49.8%)
Chronic disease pre-existing pregnancy n (%)*	105 (42.2%)
Obesity n (%)**	31 (12.4%)
Gestational age at infection (weeks) Mean ± SD	34.2 ± 6.9
Infection in the first trimester of pregnancy n (%)	6 (2.4%)
Infection in the second trimester of pregnancy n (%)	35 (14.1%)
Infection in the third trimester of pregnancy n (%)	208 (83.5%)
Flu vaccine	1 (0.4%)
Symptoms	
Fever n (%)	70 (28.1%)
Cough n (%)	69 (27.7%)
Rhinorrhea n (%)	8 (3.2%)
Anosmia n (%)	28 (11.2%)
Shortness of breath n (%)	18 (7.2%)
Diarrhea n (%)	1 (0.4%)
Conjunctivitis n (%)	2 (0.8%)
Asymptomatic n (%)	146 (58.6%)
Pharmacologic treatments	
Hydroxychloroquine n (%)	6 (2.4%)
Any antibiotics n (%)	77 (30.9%)
Azithromycin n (%)	48 (19.3%)
Antiviral drug	
Any	28 (11.2%)
Oseltamivir n (%)	3 (1.2%)
Lopinavir/Ritonavir n (%)	9 (3.6%)
Darunavir/Ritonavir n (%)	1 (0.4%)
Remdesivir n (%)	12 (4.8%)
LMWH n (%)***	221 (88.8%)
Steroids n (%)	77 (30.9%)

Data are presented as number (percentage) or as mean ± standard deviation (SD). *including diabetes, hypertension, or asthma; **defined as body mass index of 30 or greater; ***anticoagulants were used as prophylactic regimen. LMWH: Low molecular weight heparin.

Maternal and perinatal outcomes

47 women (18.9%) required oxygen therapy. There were three cases of intubation, and the rate of admission to ICU was 2.8%. There was one case of maternal death, accounting for a maternal mortality rate of 0.4%. The death occurred in a 34-year-old pregnant woman at 17 weeks of gestation. The woman presented with fever, shortness of breath, and thrombocytopenia with platelet count of 900 per cubic millimetre. The patient was therefore admitted to ICU, where developed multiorgan failure. Out of the 249 ended pregnancies, we reported two spontaneous abortion and two stillbirths. Among the 245 live-born babies, no neonatal deaths were recorded. Of them 15 (6.1%) were admitted to NICU. All babies were tested negative at RT-PCR nasal and pharyngeal swab. The incidence of preterm delivery before 37 weeks was 10% (**Table 2**).

DISCUSSION

Main findings

The rate of preterm birth in our cohort was 10%. Furthermore, the study showed that in pregnancies complicated by SARS-CoV-2 infection during the first pandemic wave in the South of Italy, the risk of maternal mortality was low (0.4%), as well as the rate of perinatal mortality (0.8%), and about

Table 2. *Maternal and perinatal outcomes.*

	n = 249
Maternal outcomes	
Use of oxygen, any type	47 (18.9%)
Admission to ICU n (%)	7 (2.8%)
CPAP n (%)	24 (9.6%)
Intubation n (%)	3 (1.2%)
Maternal death n (%)	1 (0.4%)
Perinatal outcomes	
Stillbirth n (%)	2 (0.8%)
Neonatal death n (%)	0
Admission to NICU n (%)	15 (6.1%)
Birth weight (grams) Mean ± SD	3098 ± 567
Preterm birth n (%)	25 (10.0%)
Gestational age at delivery Mean ± SD	38.2 ± 4.0
Caesarean delivery n (%)	213 (85.5%)
Possible vertical transmission n (%)	0

Data are presented as number (percentage) or as mean ± standard deviation (SD). CPAP: Continuous Positive Airway Pressure; ICU: intensive care unit; NICU: neonatal intensive care unit.

2.8% of the women required admission to ICU. The risk of vertical transmission was negligible, with no cases confirmed positive after the delivery.

Strength and limitations

Strength of our study is represented by the universal policy screening methods which allowed to recognize all infected pregnant women according to the WHO criteria. Limitations are given by the single centre design and the overall small sample size. Moreover, we did not perform a statistical analysis comparing our results to healthy pregnant women or other COVID-19 affected cohorts, but limited to describe the phenomenon in our main regional university hospital.

Implications

The burden of SARS-CoV-2 infection during pregnancy raises the importance of viral screenings, and the need for protection of this population during seasonal viral infections or viral epidemics. Historically, during the past influenza pandemic in the 20th century, there was increased risk for miscarriage and preterm birth, especially for women suffering from pneumonia [48]. Moreover, during seasonal influenza, the rate of visits for acute respiratory disease were significantly higher for pregnant women compared to non-pregnant [49]. Also, foetal defects have been associated to hyperthermia during the first trimester, and Central Nervous System (CNS) disease if this happens during more advanced gestational ages [50]. Furthermore, Zika virus infection during pregnancy has been associated to brain or eye defects when it affects pregnant women in the first trimester, but also to preterm birth and low birth weight during the second or third trimester [51].

Looking to SARS-CoV-2, another Italian study reported similar rates for asymptomatic pregnant women (57.6%) with lower rates of fever and cough (18.1% and 10.6%, respectively). Also, the rates of therapies administered were different: in particular, antibiotic use (24.1%) and LMWH (55.3%) were less commonly used in their population. Finally, our rates of caesarean delivery were sharply higher compared to them (29.15%), and there is a difference in the finding of neonatal positivity, given that we did not find any compared to their 2% [52]. Our population came mostly from women tested positive for SARS-CoV-2 at the time of triage using a policy of universal screening with RT-PCR nasal and pharyngeal swab. Therefore, the percentage of asymptomatic women in the study was high (58.6%). The WAPM working group on COVID-19 in pregnancy [33] published a large multicentre study including 388 pregnant women from 72 different centres in 22 different countries in Europe, the USA, South America, Asia and Australia, enrolled between February 1st, 2020 and April 30th, 2020. The included participants came mostly from women referred for suspected COVID-19, due to symptoms or exposure, and consequently tested with RT-PCR nasal and pharyngeal swab. Therefore, the percentage of asymptomatic women was lower (24.2%), and the maternal and perinatal outcomes worse (**Table 3**). Indeed, the presence of symptoms raises the risks of complications [53]. Our study did not report any cases of suspected vertical transmission and all live-born babies tested negative after delivery at RT-PCR test on nasopharyngeal swab. The possibility of mother-foetal vertical transmission of SARS-CoV-2 is still unclear [51, 54-56]. Testing for SARS-CoV-2 presence by reverse transcriptase PCR has repeatedly failed to identify the presence of the viral genome in maternal and neonatal specimens including placenta, umbilical cord blood, amniotic fluid or amniotic swab, maternal blood, vaginal secretions and breastmilk [34, 57]. The WAPM study [33] reported one case of suspected vertical transmission, with a neonate tested positive soon after birth. The newborn was asymptomatic and had negative RT-PCR

Table 3. *Maternal and perinatal outcomes comparing our cohort with the WAPM cohort study.*

Maternal outcomes		
	Naples study	**WAPM study (33)**
Asymptomatic n (%)	146/249 (58.6%)	94/388 (24.2%)
Use of oxygen, any type	47/249 (18.9%)	Not reported
Admission to ICU n (%)	7/249 (2.8%)	43/388 (11.1%)
CPAP n (%)	24/249 (9.6%)	Not reported
Intubation n (%)	3/249 (1.2%)	25/388 (6.4%)
Maternal death n (%)	1/249 (0.4%)	3/388 (0.8%)
Perinatal outcomes		
Stillbirth n (%)	2/249 (0.8%)	6/265 (2.7%)
Neonatal death n (%)	0/249	5/250 (2.0%)
Admission to NICU n (%)	15 (6.1%)	69/250 (27.6%)
Birth weight (grams) Mean ± SD	3098 ± 567	2921 ± 772
Preterm birth n (%)	25/249 (10.0%)	70/265 (26.4%)
Gestational age at delivery Mean ± SD	38.2 ± 4.0	37.2 ± 3.9
Caesarean delivery n (%)	213/249 (85.5%)	136/250 (54.4%)
Possible vertical transmission n (%)	0 /249	1/250 (0.4%)

Data are presented as number (percentage) or as mean ± standard deviation (SD.)
CPAP: Continuous Positive Airway Pressure; ICU: intensive care unit; NICU: neonatal intensive care unit.

test after 14 days of life. Another mother-foetal vertical transmission case of COVID-19 occurred in a pregnant woman with rectal and stool maternal swab positive for COVID-19 as reported by Carosso *et al*. [58]. The authors concluded that SARS-CoV-2 can enter the neonatal nasopharynx and potentially trigger neonatal infection. In a meta-analysis of 300 deliveries from mother with COVID-19 infection, only 9 newborns tested positive for SARS-CoV-2 with an average pooled incidence of vertical transmission of 16 per 1,000 newborns (95%CI 3.40-73.11) [59]. However, only one of the nine newborns were symptomatic at birth.
The different mortality rate in the different studies may be explained by the study location, *e.g*., low- *vs* high-income countries, and by the study design, *e.g*., study inclusion criteria [60-64]. In the WAPM study, the maternal mortality rate was reported to be 0.8% [33]. In a study conducted at the University of Washington, authors found that pregnant women who had an infection with COVID-19 were 3.5 times more likely to be hospitalized because of the virus, and that mortality rates in pregnant women were 13 times higher than people of similar ages who had the disease [62].
This evidence raised the question of the importance of COVID-19 vaccine in pregnant women even in absence of level-1 data on safety of vaccine in this population [65-67]. However, since the introduction of vaccinal programs against SARS-CoV-2 infection, pregnant women demonstrated that the anxiety of contracting the infection was not higher than the anxiety of possible adverse events linked to the novel mRNA-based vaccines, with low percentages of acceptance worldwide [68-82]. Indeed, so far reassuring data have been released and published on the importance of vaccine against SARS-CoV-2 during pregnancy, given that antibodies generate a robust humoral immunity in pregnant and lactating women and were also transferred to foetus and neonates through cord blood and breast milk [83-85]. Moreover, vaccination has been seen to not increase the risk of adverse maternal-foetal and perinatal adverse outcomes [86-88]. At the moment, we are facing another pandemic wave, with overcrowding of hospitals even more than what happened during previous waves, due to the increased infectiveness of the omicron-variant. In such a scenario, it is of fundamental importance that women get the vaccination and eventually the booster dose during pregnancy, to avoid the risk of worse infection and hospitalization. In the meantime, more data are still needed on SARS-CoV-2 during pregnancy, to uncover the mechanisms through which it determines adverse maternal and foetal-neonatal outcomes and counteract its action.

CONCLUSIONS

The rate of preterm birth in SARS-CoV-2 affected pregnant women during the first pandemic wave was 10%, with negligible risk of vertical transmission, and overall low rate of maternal and perinatal adverse outcomes. Further studies are needed to increase the knowledge of SARS-CoV-2 consequences on maternal and foetal-neonatal health. Vaccine against SARS-CoV-2 should be strongly counselled among pregnant women, given that the pandemic has not ended and protection is still needed, also for eventually future waves.

COMPLIANCE WITH ETHICAL STANDARDS

Authors contribution

M.G.: Conceptualization, supervision, writing - original draft. L.C., L.A., A.F., B.Z.: Investigation, data curation, writing - review & editing. C.F.: In-

vestigation, visualization, writing - review & editing. C.B., M.C.D.A., S.S.: Investigation, writing - review & editing. M.D.C.: Investigation, methodology, writing - review & editing. A.L., R.S., A.S., R.V.: Investigation, writing - review & editing. C.R.: Investigation, formal analysis, writing - review & editing. G.S.: Formal analysis, software, validation, writing - review & editing. M.L.: Conceptualization, methodology, validation, writing - review & editing. F.R.: Conceptualization, writing - review & editing. E.M.: Conceptualization, resources, methodology, writing - review & editing. G.B.: Resources, project administration, writing - review & editing.

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Study registration

N/A.

Disclosure of interests

The authors declare that they have no conflict of interests.

Ethical approval

Ethical approval for the study was obtained from the Ethical Committee of Federico II University of Naples (nr. 145/2020).

Informed consent

All patients signed an informed consent at the time of hospitalization.

Data sharing

Data are available under reasonable request to the corresponding author.

REFERENCES

1. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382:1708-20. doi: 10.1056/NEJMoa2002032.
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5.
3. Poon LC, Yang H, Kapur A, Melamed N, Dao B, Divakar H, et al. Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: Information for healthcare professionals. Int J Gynaecol Obstet. 2020;149(3):273-86. doi: 10.1002/ijgo.13156.
4. Rasmussen SA, Kelley CF, Horton JP, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) Vaccines and Pregnancy: What Obstetricians Need to Know. Obstet Gynecol. 2021;137(3):408-14. doi: 10.1097/AOG.0000000000004290.
5. Saccone G, Carbone FI, Zullo F. The novel coronavirus (2019-nCoV) in pregnancy: What we need to know. Eur J Obstet Gynecol Reprod Biol. 2020;249:92-3. doi: 10.1016/j.ejogrb.2020.04.006.
6. Boelig RC, Manuck T, Oliver EA, Di Mascio D, Saccone G, Bellussi F, et al. Labor and delivery guidance for COVID-19. Am J Obstet Gynecol MFM. 2020;2(2):100110. doi: 10.1016/j.ajogmf.2020.100110.
7. Boelig RC, Saccone G, Bellussi F, Berghella V. MFM guidance for COVID-19. Am J Obstet Gynecol MFM. 2020;2(2):100106. doi: 10.1016/j.ajogmf.2020.100106.
8. Saccone G. Get your obstetric inpatient and outpatient units ready for COVID-19. Minerva Ginecol. 2020;72(4):185-6. doi: 10.23736/S0026-4784.20.04560-8.
9. Franchi M, Bosco M, Garzon S, Laganà AS, Cromi A, Barbieri B, et al. Management of obstetrics and gynaecological patients with COVID-19. Ital J Gynaecol Obstet. 2020;32(1):6-19. doi: 10.36129/jog.32.01.01.
10. Breslin N, Baptiste C, Miller R, Fuchs K, Goffman D, Gyamfi-Bannerman C, et al. Coronavirus disease 2019 in pregnancy: early lessons. Am J Obstet Gynecol MFM. 2020;2(2):100111. doi: 10.1016/j.ajogmf.2020.100111.
11. Api O, Sen C, Debska M, Saccone G, D'Antonio F, Volpe N, et al. Clinical management of coronavirus disease 2019 (COVID-19) in pregnancy: recommendations of WAPM-World Association of Perinatal Medicine. J Perinat Med. 2020;48(9):857-66. doi: 10.1515/jpm-2020-0265.
12. Cavaliere AF, Vasarri PL, Scatena E, Vidiri A, Santicchia MS, Bordoni Vicini I, et al. SARS-CoV2 containment during pregnancy: single Center experience and the unique Chinese reality in

Prato. Ital J Gynaecol Obstet. 2020;32(3):163-5. doi: 10.36129/jog.32.03.02.
13. Vitale E, Canonico A. Obstetric nursing reorganization in pregnancy during the Covid-19 pandemic: a proposal integrative review of the literature. Ital J Gynaecol Obstet. 2021;33(3):190-6. doi: 10.36129/jog.33.03.07.
14. Marinelli E, Negro F, Varone MC, Trojano G, Del Rio A, Zaami S. Perinatal and post-partum infections in times of Coronavirus: are compliance with cautionary measures and safety protocols key factors in staving off litigation? Ital J Gynaecol Obstet. 2020;32(3):189-99. doi: 10.36129/jog.32.03.05.
15. Bitonti G, Palumbo AR, Gallo C, Rania E, Saccone G, De Vivo V, et al. Being an obstetrics and gynaecology resident during the COVID-19: Impact of the pandemic on the residency training program. Eur J Obstet Gynecol Reprod Biol. 2020;253:48-51. doi: 10.1016/j.ejogrb.2020.07.057.
16. Salsi G, Seidenari A, Diglio J, Bellussi F, Pilu G, Bellussi F. Obstetrics and gynecology emergency services during the coronavirus disease 2019 pandemic. Am J Obstet Gynecol MFM. 2020;2(4):100214. doi: 10.1016/j.ajogmf.2020.100214.
17. Abel MK, Alavi MX, Tierney C, Weintraub MR, Avins A, Zaritsky E. Coronavirus Disease 2019 (COVID-19) and the Incidence of Obstetric and Gynecologic Emergency Department Visits in an Integrated Health Care System. Obstet Gynecol. 2021;137(4):581-3. doi: 10.1097/AOG.0000000000004331.
18. Grandi G, Del Savio MC, Caroli M, Capobianco G, Dessole F, Tupponi G, et al. The impact of COVID-19 lockdown on admission to gynecological emergency departments: Results from a multicenter Italian study. Int J Gynaecol Obstet. 2020;151(1):39-42. doi: 10.1002/ijgo.13289.
19. Carbone L, Raffone A, Travaglino A, Sarno L, Conforti A, Gabrielli O, et al. Obstetric A&E unit admission and hospitalization for obstetrical management during COVID-19 pandemic in a third-level hospital of southern Italy. Arch Gynecol Obstet. 2022;305(4):859-67 . doi: 10.1007/s00404-021-06212-6.
20. Athiel Y, Civadier MS, Luton D, Ceccaldi PF, Bourret A, Sroussi J, et al. Impact of the outbreak of SARS-CoV-2 infection on urgent gynecological care. J Gynecol Obstet Hum Reprod. 2020;49(8):101841. doi: 10.1016/j.jogoh.2020.101841.
21. Dell'Utri C, Manzoni E, Cipriani S, Spizzico C, Dell'Acqua A, Barbara G, et al. Effects of SARS Cov-2 epidemic on the obstetrical and gynecological emergency service accesses. What happened and what shall we expect now? Eur J Obstet Gynecol Reprod Biol. 2020;254:64-8. doi: 10.1016/j.ejogrb.2020.09.006.
22. Carbone L, Raffone A, Sarno L, Travaglino A, Saccone G, Gabrielli O, et al. Invasive prenatal diagnosis during COVID-19 pandemic. Arch Gynecol Obstet. 2022;305(3):797-801. doi: 10.1007/s00404-021-06276-4.
23. Saccone G, Florio A, Aiello F, Venturella R, De Angelis MC, Locci M, et al. Psychological impact of coronavirus disease 2019 in pregnant women. Am J Obstet Gynecol. 2020;223(2):293-5. doi: 10.1016/j.ajog.2020.05.003.
24. Di Mascio D, Saccone G, D'Antonio F, Berghella V. Psychopathology associated with coronavirus disease 2019 among pregnant women. Am J Obstet Gynecol MFM. 2021;3(1):100290. doi: 10.1016/j.ajogmf.2020.100290.
25. Alviggi C, Esteves SC, Orvieto R, Conforti A, La Marca A, Fischer R, et al. COVID-19 and assisted reproductive technology services: repercussions for patients and proposal for individualized clinical management. Reprod Biol Endocrinol. 2020;18(1):45. doi: 10.1186/s12958-020-00605-z.
26. Picarelli S, Conforti A, Buonfantino C, Vallone R, De Rosa P, Carbone L, et al. IVF during coronavirus pandemic: who comes first? The POSEIDON viewpoint. Ital J Gynaecol Obstet. 2020;32(4):223-8. doi: 10.36129/jog.32.04.01.
27. Alviggi C, Borini A, Costa M, D'Amato G, Gianaroli L, Colacurci N. Sterility Special Interest Group position paper on ART treatments and COVID 19 pandemic. Ital J Gynaecol Obstet. 2020;32(3):154-62. doi: 10.36129/jog.32.03.01.
28. Rasmussen SA, Kelley CF, Horton JP, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) Vaccines and Pregnancy: What Obstetricians Need to Know. Obstet Gynecol. 2021;137(3):408-14. doi: 10.1097/AOG.0000000000004290.
29. Carbone L, Conforti A, LA Marca A, Cariati F, Vallone R, Raffone A, et al. The negative impact of most relevant infections on fertility and assisted reproduction technology. Minerva Obstet Gynecol. 2022;74(1):83-106. doi: 10.23736/S2724-606X.21.04870-3.
30. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, et al. Outcome of coronavirus spec-

trum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. Am J Obstet Gynecol MFM. 2020;2(2):100107. doi: 10.1016/j.ajogmf.2020.100107.
31. Schmid MB, Fontijn J, Ochsenbein-Kölble N, Berger C, Bassler D. COVID-19 in pregnant women. Lancet Infect Dis. 2020;20(6):653. doi: 10.1016/S1473-3099(20)30175-4.
32. Di Mascio D, Sen C, Saccone G, Galindo A, Grünebaum A, Yoshimatsu J, et al. Risk factors associated with adverse fetal outcomes in pregnancies affected by Coronavirus disease 2019 (COVID-19): a secondary analysis of the WAPM study on COVID-19. J Perinat Med. 2020;48(9):950-8. doi: 10.1515/jpm-2020-0355.
33. WAPM (World Association of Perinatal Medicine) Working Group on COVID-19. Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection. Ultrasound Obstet Gynecol. 2021;57(2):232-41. doi: 10.1002/uog.23107.
34. Di Girolamo R, Khalil A, Alameddine S, D'Angelo E, Galliani C, Matarrelli B, et al. Placental histopathology after SARS-CoV-2 infection in pregnancy: a systematic review and meta-analysis. Am J Obstet Gynecol MFM. 2021;3(6):100468. doi: 10.1016/j.ajogmf.2021.100468.
35. Gurol-Urganci I, Jardine JE, Carroll F, Draycott T, Dunn G, Fremeaux A, et al. Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study. Am J Obstet Gynecol. 2021;225(5):522.e1-522.e11. doi: 10.1016/j.ajog.2021.05.016.
36. Thornton JG. COVID-19 in pregnancy. BJOG. 2020;127(9):1122. doi: 10.1111/1471-0528.16308.
37. Stampini V, Amadori R, Bracci Laudiero L, Vendola N, Pires Marafon D, Gerbino M, et al. Covid-19 seroprevalence in a group of pregnant women compared to a group of non-pregnant women. Ital J Gynaecol Obstet. 2021;33(4):235-40. doi: 10.36129/jog.33.04.03.
38. Liu D, Li L, Wu X, Zheng D, Wang J, Yang L, et al. Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis. AJR Am J Roentgenol. 2020;215(1):127-32. doi: 10.2214/AJR.20.23072.
39. Moradi B, Kazemi MA, Gity M. CT Findings of Pregnant Women With Coronavirus Disease (COVID-19) Pneumonia. AJR Am J Roentgenol. 2020;215(1):W9. doi: 10.2214/AJR.20.23212.
40. Joob B, Wiwanitkit V. Lung ultrasound in pregnant women with suspicion of COVID-19. Ultrasound Obstet Gynecol. 2020;56(1):123-4. doi: 10.1002/uog.22091.
41. Quarato CMI, Venuti M, Lacedonia D, Simeone A, Sperandeo M. Diagnosis and monitoring of COVID-19 pneumonia in pregnant women: is lung ultrasound appropriate? Ultrasound Obstet Gynecol. 2020;56(3):467-8. doi: 10.1002/uog.22156.
42. Deng Q, Cao S, Wang H, Zhang Y, Chen L, Yang Z, et al. Application of quantitative lung ultrasound instead of CT for monitoring COVID-19 pneumonia in pregnant women: a single-center retrospective study. BMC Pregnancy Childbirth. 2021;21(1):259. doi: 10.1186/s12884-021-03728-2.
43. Moro F, Mascilini F, Buonsenso D, Inchingolo R, Smargiassi A, Soldati G, et al. Validation of the performance of "Fast Lung Ultrasound Teaching Program" for gynecologists/obstetricians dealing with pregnant women with suspicion of COVID-19 infection: an Italian prospective multicenter study. Ital J Gynaecol Obstet. 2021;33(1):52-6. doi: 10.36129/jog.33.01.06.
44. Buonsenso D, Pata D, De Rose C, Morello R, Moro F, Franchi M, et al. Clinical application of Lung Ultrasound for the management of pregnant women with suspicion of COVID-19: a review of literature. Ital J Gynaecol Obstet. 2020;32(3):182-8. doi: 10.36129/jog.32.03.04.
45. Carbone L, Esposito R, Raffone A, Verrazzo P, Carbone IF, Saccone G. Proposal for radiologic diagnosis and follow-up of COVID-19 in pregnant women. J Matern Fetal Neonatal Med. 2022;35(15):3002-3. doi: 10.1080/14767058.2020.1793325.
46. Zullo F, Di Mascio D, Saccone G. Coronavirus disease 2019 antibody testing in pregnancy. Am J Obstet Gynecol MFM. 2020;2(3):100142. doi: 10.1016/j.ajogmf.2020.100142.
47. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) is suspected: interim guidance. 13 March 2020. Available at: https://apps.who.int/iris/handle/10665/331446. Accessed on January 17, 2022.
48. Harris JW. Influenza occurring in pregnant women. JAMA. 1919;72:978-80.
49. Mullooly JP, Barker WH, Nolan TF Jr. Risk of acute respiratory disease among pregnant

women during influenza A epidemics. Public Health Rep. 1986;101(2):205-11.
50. Edwards MJ. Review: Hyperthermia and fever during pregnancy. Birth Defects Res A Clin Mol Teratol. 2006;76(7):507-16. doi: 10.1002/bdra.20277.
51. Ospina ML, Tong VT, Gonzalez M, Valencia D, Mercado M, Gilboa SM, et al. Zika Virus Disease and Pregnancy Outcomes in Colombia. N Engl J Med. 2020;383(6):537-45. doi: 10.1056/NEJMoa1911023.
52. Buonsenso D, Costa S, Giordano L, Priolo F, Colonna AT, Morini S, et al. Short- and mid-term multidisciplinary outcomes of newborns exposed to SARS-CoV-2 in utero or during the perinatal period: preliminary findings. Eur J Pediatr. 2022;181(4):1507-20. doi: 10.1007/s00431-021-04319-1.
53. Khan DSA, Hamid LR, Ali A, Salam RA, Zuberi N, Lassi ZS, et al. Differences in pregnancy and perinatal outcomes among symptomatic versus asymptomatic COVID-19-infected pregnant women: a systematic review and meta-analysis. BMC Pregnancy Childbirth. 2021;21(1):801. doi: 10.1186/s12884-021-04250-1.
54. Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, La Rosa M. Severe COVID-19 during Pregnancy and Possible Vertical Transmission. Am J Perinatol. 2020;37(8):861-5. doi: 10.1055/s-0040-1710050.
55. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, Abbasi H, Mirjalili SR, et al. Vertical Transmission of Coronavirus Disease 19 (COVID-19) from Infected Pregnant Mothers to Neonates: A Review. Fetal Pediatr Pathol. 2020;39(3):246-50.
56. Musa SS, Bello UM, Zhao S, Abdullahi ZU, Lawan MA, He D. Vertical Transmission of SARS-CoV-2: A Systematic Review of Systematic Reviews. Viruses. 2021;13(9):1877. doi: 10.3390/v13091877.
57. Facchetti F, Bugatti M, Drera E, Tripodo C, Sartori E, Cancila V, et al. SARS-CoV2 vertical transmission with adverse effects on the newborn revealed through integrated immunohistochemical, electron microscopy and molecular analyses of Placenta. EBioMedicine. 2020;59:102951. doi: 10.1016/j.ebiom.2020.102951.
58. Carosso A, Cosma S, Borella F, Marozio L, Coscia A, Ghisetti V, et al. Pre-labor anorectal swab for SARS-CoV-2 in COVID-19 pregnant patients: is it time to think about it? Eur J Obstet Gynecol Reprod Biol. 2020;249:98-9. doi: 10.1016/j.ejogrb.2020.04.023.
59. Goh XL, Low YF, Ng CH, Amin Z, Ng YPM. Incidence of SARS-CoV-2 vertical transmission: a meta-analysis. Arch Dis Child Fetal Neonatal Ed. 2021;106(1):112-3. doi: 10.1136/archdischild-2020-319791.
60. Gajbhiye RK, Sawant MS, Kuppusamy P, Surve S, Pasi A, Prusty RK, et al. Differential impact of COVID-19 in pregnant women from high-income countries and low- to middle-income countries: A systematic review and meta-analysis. Int J Gynaecol Obstet. 2021;155(1):48-56. doi: 10.1002/ijgo.13793.
61. La Verde M, Riemma G, Torella M, Cianci S, Savoia F, Licciardi F, et al. Maternal death related to COVID-19: A systematic review and meta-analysis focused on maternal co-morbidities and clinical characteristics. Int J Gynaecol Obstet. 2021;154(2):212-9. doi: 10.1002/ijgo.13726.
62. Lokken EM, Huebner EM, Taylor GG, Hendrickson S, Vanderhoeven J, Kachikis A, et al. Washington State COVID-19 in Pregnancy Collaborative. Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State. Am J Obstet Gynecol. 2021;225(1):77.e1-77.e14. doi: 10.1016/j.ajog.2020.12.1221.
63. Scheler CA, Discacciati MG, Vale DB, Lajos GJ, Surita F, Teixeira JC. Mortality in pregnancy and the postpartum period in women with severe acute respiratory distress syndrome related to COVID-19 in Brazil, 2020. Int J Gynaecol Obstet. 2021;155(3):475-82. doi: 10.1002/ijgo.13804.
64. Mendez-Dominguez N, Santos-Zaldívar K, Gomez-Carro S, Datta-Banik S, Carrillo G. Maternal mortality during the COVID-19 pandemic in Mexico: a preliminary analysis during the first year. BMC Public Health. 2021;21(1):1297. doi: 10.1186/s12889-021-11325-3.
65. Saccone G, Zullo F, Di Mascio D. Coronavirus disease 2019 vaccine in pregnant women: not so far! The importance of counseling and the need for evidence-based data. Am J Obstet Gynecol MFM. 2021;3(3):100324. doi: 10.1016/j.ajogmf.2021.100324.
66. Craig AM, Hughes BL, Swamy GK. Coronavirus disease 2019 vaccines in pregnancy. Am J Obstet Gynecol MFM. 2020;3(2):100295. doi: 10.1016/j.ajogmf.2020.100295.
67. Stafford IA, Parchem JG, Sibai BM. The coronavirus disease 2019 vaccine in pregnancy: risks, benefits, and recommendations. Am J Obstet

Gynecol. 2021;224(5):484-95. doi: 10.1016/j.ajog.2021.01.022.
68. Carbone L, Mappa I, Sirico A, Girolamo RD, Saccone G, Mascio DD, et al. Pregnant women's perspectives on severe acute respiratory syndrome coronavirus 2 vaccine. Am J Obstet Gynecol MFM. 2021;3(4):100352. doi: 10.1016/j.ajogmf.2021.100352.
69. Mappa I, Luviso M, Distefano FA, Carbone L, Maruotti GM, Rizzo G. Women perception of SARS-CoV-2 vaccination during pregnancy and subsequent maternal anxiety: a prospective observational study. J Matern Fetal Neonatal Med. 2022;35(25):6302-5. doi: 10.1080/14767058.2021.1910672.
70. Ceulemans M, Foulon V, Panchaud A, Winterfeld U, Pomar L, Lambelet V, et al. Vaccine willingness and impact of the COVID-19 pandemic on women's perinatal experiences and practices-a multinational, cross-sectional study covering the first wave of the pandemic. Int J Environ Res Public Health. 2021;18(7):3367. doi: 10.3390/ijerph18073367.
71. Geoghegan S, Stephens LC, Feemster KA, Drew RJ, Eogan M, Butler KM. "This choice does not just affect me." Attitudes of pregnant women toward COVID- 19 vaccines: a mixed-methods study. Hum Vaccines Immunother. 2021;17(10):3371-6. doi: 10.1080/21645515.2021.1924018.
72. Goncu Ayhan S, Oluklu D, Atalay A, Menekse Beser D, Tanacan A, Moraloglu Tekin O, et al. COVID-19 vaccine acceptance in pregnant women. Int J Gynaecol Obstet. 2021;154(2):291-6. doi: 10.1002/ijgo.13713.
73. Hailemariam S, Mekonnen B, Shifera N, Endalkachew B, Asnake M, Assefa A, et al. Predictors of pregnant women's intention to vaccinate against coronavirus disease 2019: A facility-based cross-sectional study in southwest Ethiopia. SAGE Open Med. 2021;9:20503121211038454. doi: 10.1177/20503121211038454.
74. Levy AT, Singh S, Riley LE, Prabhu M. Acceptance of COVID-19 vaccination in pregnancy: a survey study. Am J Obst Gynecol MFM. 2021;3(5):100399. doi: 10.1016/j.ajogmf.2021.100399.
75. Mohan S, Reagu S, Lindow S, Alabdulla M. COVID-19 vaccine hesitancy in perinatal women: a cross sectional survey. J Perinat Med. 2021;49(6):678-85. doi: 10.1515/jpm-2021-0069.
76. Nguyen LH, Hoang MT, Nguyen LD, Ninh LT, Nguyen HTT, Nguyen AD, et al. Acceptance and willingness to pay for COVID-19 vaccines among pregnant women in Vietnam. Trop Med Int Health. 2021;26(10):1303-13. doi: 10.1111/tmi.13666.
77. Skjefte M, Ngirbabul M, Akeju O, Escudero D, Hernandez-Diaz S, Wyszynski DF, et al. COVID-19 vaccine acceptance among pregnant women and mothers of young children: results of a survey in 16 countries. Eur J Epidemiol. 2021;36(2):197-211. doi: 10.1007/s10654-021-00728-6.
78. Sutton D, D'Alton M, Zhang Y, Kahe Ka, Cepin A, Goffman D, et al. COVID-19 vaccine acceptance among pregnant, breastfeeding, and non-pregnant reproductive-aged women. Am J Obst Gynecol. MFM 2021;3(5):100403. doi: 10.1016/j.ajogmf.2021.100403.
79. Riad A, Jouzová A, Üstün B, Lagová E, Hruban L, Janků P, et al. COVID-19 Vaccine Acceptance of Pregnant and Lactating Women (PLW) in Czechia: An Analytical Cross-Sectional Study. Int J Environ Res Public Health. 2021;18(24):13373. doi: 10.3390/ijerph182413373.
80. Tao L, Wang R, Han N, Liu J, Yuan C, Deng L, et al. Acceptance of a COVID-19 vaccine and associated factors among pregnant women in China: a multi-center cross-sectional study based on health belief model. Hum Vaccin Immunother. 2021;17(8):2378-88. doi: 10.1080/21645515.2021.1892432 .
81. Skirrow H, Barnett S, Bell S, Riaposova L, Mounier-Jack S, Kampmann B, et al. Women's views on accepting COVID-19 vaccination during and after pregnancy, and for their babies: a multi-methods study in the UK. BMC Pregnancy Childbirth. 2022;22(1):33. doi: 10.1186/s12884-021-04321-3.
82. Carbone L, Di Girolamo R, Mappa I, Saccone G, Raffone A, Di Mascio D, et al. Worldwide beliefs among pregnant women on SARS-CoV-2 vaccine: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2022;268:144-64. doi: 10.1016/j.ejogrb.2021.12.003.
83. Gray KJ, Bordt EA, Atyeo C, Deriso E, Akinwunmi B, Young N, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. Am J Obstet Gynecol. 2021;225(3):303.e1-303.e17. doi: 10.1016/j.ajog.2021.03.023.
84. Collier A-R, McMahan K, Yu J, Tostanoski LH, Aguayo R, Ansel J, et al. Immunogenicity of COVID-19 mRNA vaccines in pregnant and lactating women. JAMA. 2021;325(23):2370-80. doi: 10.1001/jama.2021.7563.

85. Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. N Engl J Med. 2021;384(24):2273-82. doi: 10.1056/NEJMoa2104983.
86. Rottenstreich M, Sela HY, Rotem R, Kadish E, Wiener-Well Y, Grisaru-Granovsky S. Covid-19 vaccination during the third trimester of pregnancy: rate of vaccination and maternal and neonatal outcomes, a multicentre retrospective cohort study. BJOG. 2022;129(2):248-55. doi: 10.1111/1471-0528.16941.
87. Trostle ME, Limaye MA, Avtushka V, Lighter JL, Penfield CA, Roman AS. COVID-19 vaccination in pregnancy: early experience from a single institution. Am J Obstet Gynecol MFM. 2021;3(6):100464. doi: 10.1016/j.ajogmf.2021.100464.
88. Bookstein Peretz S, Regev N, Novick L, Nachshol M, Goffer E, Ben-David A, et al. Short-term outcome of pregnant women vaccinated with BNT162b2 mRNA COVID-19 vaccine. Ultrasound Obstet Gynecol. 2021;58(3):450-6. doi: 10.1002/uog.23729.