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FULL PAPER

Impact of SARS-CoV-2 infection during pregnancy and persistence of antibody response

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SUMMARY

Background. Pregnant women may be at an increased risk of developing severe or critical disease associated with the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection causing severities during pregnancy. We performed a prospective study to describe the impact of SARS-CoV-2 infection on pregnancy outcomes and on the newborn, depending on the severity of the disease. The antibody response and persistence of SARS-CoV-2 anti-Spike (S) IgG, IgA and anti-Nucleocapsid (NCP) IgG, was investigated.

Methods. A total of 48 pregnant women with SARS-CoV-2 infection were enrolled, and sequential serum samples from 30 of them were collected until one year after infection. Outcomes of pregnancy and newborn parameters were evaluated in comparison with 200 uninfected controls.

Results. Asymptomatic infection was observed in 31/48 women (64.5%), mild COVID-19 in 12/48 women (25.0%), while 5/48 women (10.5%) developed pneumonia. Women with pneumonia mounted significantly higher levels of anti-S IgG, IgA and anti-NCP IgG between 1 and 3 months after onset of infection compared to asymptomatic women. Anti-S IgG persisted in the majority of women from 6 months to at least one year after infection, especially in those with symptomatic infection and pneumonia, while anti-S IgA and anti-NCP IgG declined earlier. Pregnancy complications and newborn parameters were not significantly different from those observed in uninfected controls.

Conclusion. Anti-SARS-CoV-2 antibody development and persistence was not impaired in pregnant women, while SARS-CoV-2 infection did not cause major pregnancy or newborn complications in asymptomatic or symptomatic women, nor in women with pneumonia receiving prompt clinical care.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was characterized as a pandemic by the World Health Organization on March 11, 2020 (Wu *et al.*, 2020). Data from previous pandemics, such as those caused by SARS, H1N1 (Rasmussen *et al.*, 2009) and MERS (Di Mascio *et al.*, 2020), show that pregnant women are more susceptible to serious illness with adverse outcomes and display greater mortality rates than the general population. Pregnancy causes physiological changes in the respiratory and circulatory systems as well as alterations in immune homeostasis. These are the primary factors that are likely to make pregnant women more vulnerable to viral infections (Zhao *et al.*, 2020). Pregnant women with SARS-CoV-2 infection are more likely to develop severe illness than non-pregnant women, with an increased rate of admission to the intensive care unit, need for invasive ventilation and death (Martinez-Portilla *et al.*, 2021; Breslin *et al.*, 2020). Some recent observational studies suggest that pregnant women with confirmed asymptomatic and symptomatic COVID-19, as well as mild and severe infections (Breslin N *et al.*, 2020; WAPM, 2020), may be at risk of both adverse pregnancy outcomes (miscarriage, preeclampsia, preterm birth and cesarean section at delivery) (WAPM, 2020, Wang *et al.*, 2021) and adverse neonatal outcomes (low birth weight, low gestational age at birth) (Wei *et al.*, 2021; Crovetto *et al.*, 2021). As reported by Dubey (2020) and colleagues (Dubey *et al.*, 2020), the rates of cesarean section, premature birth, low birth weight

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and adverse pregnancy events (such as fetal vascular malperfusion and premature rupture of membranes), were estimated to be as high as 72%, 23%, 7%, and 27%, respectively. The rates of pregnancy outcomes varied by location, type and size of the studies. Neonatal infection is rare, and the majority of infected newborns are asymptomatic, with few severe cases reported in the literature (Tsatsaris *et al.*, 2020). In this prospective study, we evaluated the impact of SARS-CoV-2 infection on pregnancy outcomes and in the newborn. Moreover, the development of antibody response to SARS-CoV-2 during pregnancy and its persistence over time were investigated.

METHODS

Study design

A prospective observational study was conducted to evaluate the kinetics of humoral immune response to SARS-CoV-2 infection occurring during pregnancy and the obstetrical and newborn outcomes among pregnant women with asymptomatic infection, mild COVID-19 or pneumonia. The study included 48 pregnant women with laboratory-confirmed SARS-CoV-2 infection, enrolled between April 2020 and February 2021 at the Obstetrics and Gynecology Clinics of Fondazione IRCCS Policlinico San Matteo, and a control group of 200 non-infected (i.e., negative for anti-SARS-CoV-2 Spike IgG) pregnant women frequenting the Obstetrics and Gynecology Clinics for routine ultrasound controls in the second and third trimester of pregnancy. Serum samples were obtained from all women at time of enrollment (i.e., within 90 days after diagnosis of infection) and at different gestational weeks after infection. Mother serum was collected in the first part of pregnancy (median of gestational weeks: 12; range 8-19), in the second part of pregnancy (median of gestational weeks: 23; range 20-27) and at peripartum/delivery (median of gestational weeks: 39; range 35-42). Sequential serum samples were obtained from 30 of the 48 SARS-CoV-2-infected women until one year after infection. In addition, serum samples from 22 non-pregnant women with SARS-CoV-2 infection were also analyzed and compared to women infected. Finally, all 49 newborns of infected mothers were tested at birth for SARS-CoV-2 in nasopharyngeal swabs. Of these, only seven cord blood samples collected at delivery were tested and analyzed. The newborn parameters were collected and compared to the characteristics of newborns of the non-infected women (control group). The study was approved by the local Ethics Committee and all subjects gave written informed consent.

Lymphocyte subsets

Total CD45, CD3, CD4, CD8, NK (CD56) and B cell (CD19) counts were determined by flow cytometry on whole blood (TruCount tubes, BD Biosciences; San Jose, CA, USA) using a FACS Canto II flow cytometer (BD Biosciences) and BD FACS CANTO software.

Antibody response

Serum samples were tested for SARS-CoV-2 anti-S IgG and IgA and anti-NCP IgG antibodies by ELISA (Euroimmun, Lübeck, Germany), according to the manufacturer's instructions. The semi-quantitative (IgG and IgA) results are expressed as a ratio (RU/ml) with respect to an internal calibrator: a ratio of <0.8 was considered negative, ≥1.1 was considered positive and intermediate results were considered borderline.

Data analysis

Numerical variables were expressed as median value with range and compared with the Mann-Whitney U test (for two-group comparison) or the Kruskall-Wallis test (for three-group comparison), while categorical variables were expressed as percentage and compared with Fisher's exact test. Persistence of antibodies was calculated with the Kaplan-Meier method. Analysis was performed with GraphPad Prism version 6 and a p-value <0.05 was considered statistically significant.

RESULTS

Clinical characteristics of the study cohort

In *Table 1* we report the clinical characteristics of the 48 SARS-CoV-2-infected pregnant women and of the 200 non-infected controls. Gravidity, delivery and abortion were not significantly different in the two groups, whereas a younger age (p=0.001) and a higher frequency of origin from Africa (p=<0.001) and Asia (p=0.036), but not from Europe (p=0.006), was observed in the group of infected pregnant women. Of the 48 SARS-CoV-2-infected women, 12 (25.0%) developed the infection during the first part of pregnancy (median gestational weeks at infection: 12, range 8-19), 8 (16.6%) during the second part of pregnant (median gestational weeks at infection: 23, range 20-27) and 28 (58.3%) at peripartum or at delivery (median gestational weeks at infection: 39, range 35-42).

Pregnant women were classified according to symptoms severity in three groups: asymptomatic women were defined by the presence of only SARS-CoV-2 RNA in nasal swab, but no history of COVID-19 symptoms. Mild COVID-19 women were defined by the appearance of symptoms such as fever, cough, rhinitis and/or weakness but without dyspnea and/or pneumonia. Finally, women with dyspnea and pneumonia requiring hospitalization characterized the third group (pneumonia).

Asymptomatic infection was observed in 31/48 wom-

Table 1 - *Clinical characteristics of pregnant women with SARS-CoV-2 infection and control group.*

Characteristics	*SARS-CoV-2 infected*	*Control Group*	*P value*
Number	48	200	na
Age, years (median, range)	28 (18-45)	33 (19-46)	0.001
Gravidity (median, range)	2 (1-6)	2 (1-7)	ns
Delivery (median, range)	0 (0-3)	0 (0-4)	ns
Abortion (median, range)	0 (0-2)	0 (0-5)	ns
Geographical areas, no. (%)			
Europe	34 (63.0)	182 (91.0)	0.006
Africa	9 (16.6)	2 (1.0)	<0.001
Asia	2 (3.7)	0 (0.0)	0.036
Middle East	5 (9.2)	8 (4.0)	ns
South America	2 (4.1)	8 (4.0)	ns

na: not applicable, ns: not significant.

Table 2 - *Symptoms and therapies of hospitalized pregnancy.*

			THERAPY					
Pregnant Code	*Symptoms*	*Chest x-ray findings*	*Remdesevir*	*Hydroxychloroquine*	*Azitromycin*	*Enoxaparin*	*Steroid*	*O_2*
#1	Cough, vomit, headache, fatigue, nausea	–	–	10 days	–	12 days	–	–
#2	Cough, rhinitis, vomit, fatigue, diarrhea, nausea	–	–	–	–	–	–	–
#3	Vomit, diarrhea, nausea	–	–	–	–	–	–	–
#4	Cough, rhinitis, vomit, fatigue, diarrhea, nausea	–	–	10 days	10 days	12 days	–	–
#5	Ageusia, anosmia, fatigue	–	–	–	–	–	–	–
#6	Cough, pharyngitis, astenia, dyspnoea	Thickening parenchymal	–	10 days	10 days	12 days	40 mg intravenous	–
#7	Fever, cough, pharyngitis, fatigue, dyspnoea	Mild thickening parenchymal	–	10 days	10 days	12 days	40 mg intravenous	3 L/min
#8	Fever, cough, pharyngitis, fatigue, dyspnoea	Interstitial pneumonia	5 days	10 days	10 days	12 days	–	5 L/min
#9	Fever, cough, pharyngitis, fatigue, dyspnoea	Thickening parenchymal	5 days	–	10 days	24 days	–	Venturi mask
#10	Fever, fatigue	Thickening parenchymal	–	–	–	10 days	–	2 L/min

en (64.5%) (median gestational weeks at infection: 39, range 8-42). Mild COVID-19 was observed in 12/48 women (25.0%) (median gestational weeks at infection: 27, range 9-40), who showed the following symptoms: fever, cough, anosmia and ageusia, arthralgia, and diarrhea, and 10 of them were hospitalized to monitor the course of pregnancy. Of five mild COVID-19 women, three received no therapy, whereas two women were treated with hydroxychloroquine, azithromycin for 10 days and anticoagulant therapy (enoxaparin). Finally, 5/48 women (10.4%) developed pneumonia (median gestational weeks: 33, range 22-39) and required hospitalization for oxygen therapy (2-5 L/min), although none of them needed mechanical ventilation. The five women with pneumonia were treated with hydroxychloroquine, azithromycin for 10 days, steroid (betamethasone) and enoxaparin; remdesivir was administered to two of them for five days (*Table 2*). Patient treatment was decided according to Guidelines for Management of SARS-CoV-2 infection.

Lymphocyte subsets

The frequency of CD3, CD4, CD8, NK and B cells were not different among the three groups of pregnant women with asymptomatic infection, mild COVID-19 or pneumonia (*Figure 1* and *Table 1* Supplement).

Antibody response

Anti-S IgG and anti-NCP IgG were detected at a median time of 28 days after infection (ranges 18-44 days and 3-44 days, respectively), while anti-S IgA were detected at a median time of 39 days (range 3-78) after infection. The antibody response varied depending on the severity of disease. At the peak (median time of 90 days, range 35-105), higher levels of anti-S and anti-NCP IgG, as well as anti-S IgA, were detected in pregnant women with pneumonia compared to women with mild COVID-19 (*Figure 1* and *Figure 2*). Asymptomatic women developed an earlier anti-S antibody response. Twenty asymptomatic women, six women with mild COVID-19 and four women with pneumonia were tested within 20 days after onset of infection: anti-S IgG and IgA were detected in 9 (45.0%, p<0.001) and 8 (40.0%, p=0.378) asymptomatic pregnant women, while 2 (33.3%) women with mild COVID-19 showed anti-S IgA but not IgG, and no women with pneumonia showed anti-S IgG or IgA (*Figure 2*). Anti-NCP IgG was detected in 4/20 (20%) asymptomatic women, in no women with mild COVID-19 and in 1/4 (25%) women with pneumonia. Conversely, at a later time interval (between 1 and 3 months after onset of infection), pregnant women with pneumonia mounted significantly higher levels of anti-S IgG (p=0.001) and IgA (p=0.03), as well as anti-NCP IgG (p=0.003), compared to asymptomatic women. In the same time interval, an-

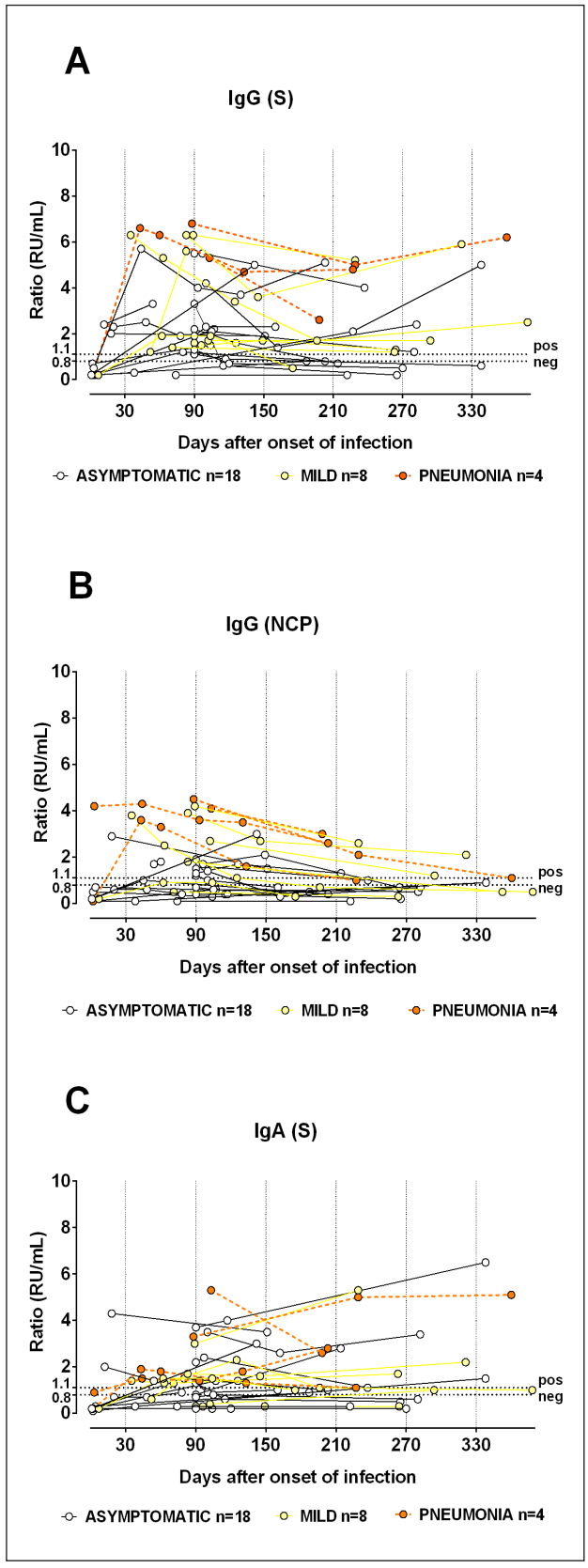

Figure 1 - *Kinetics of anti-Spike (S) IgG (A), anti-Nucleocapsid (NCP) IgG (B), and anti-S IgA (C) in pregnant women with asymptomatic SARS-CoV-2 infection, mild COVID-19 or pneumonia group.*

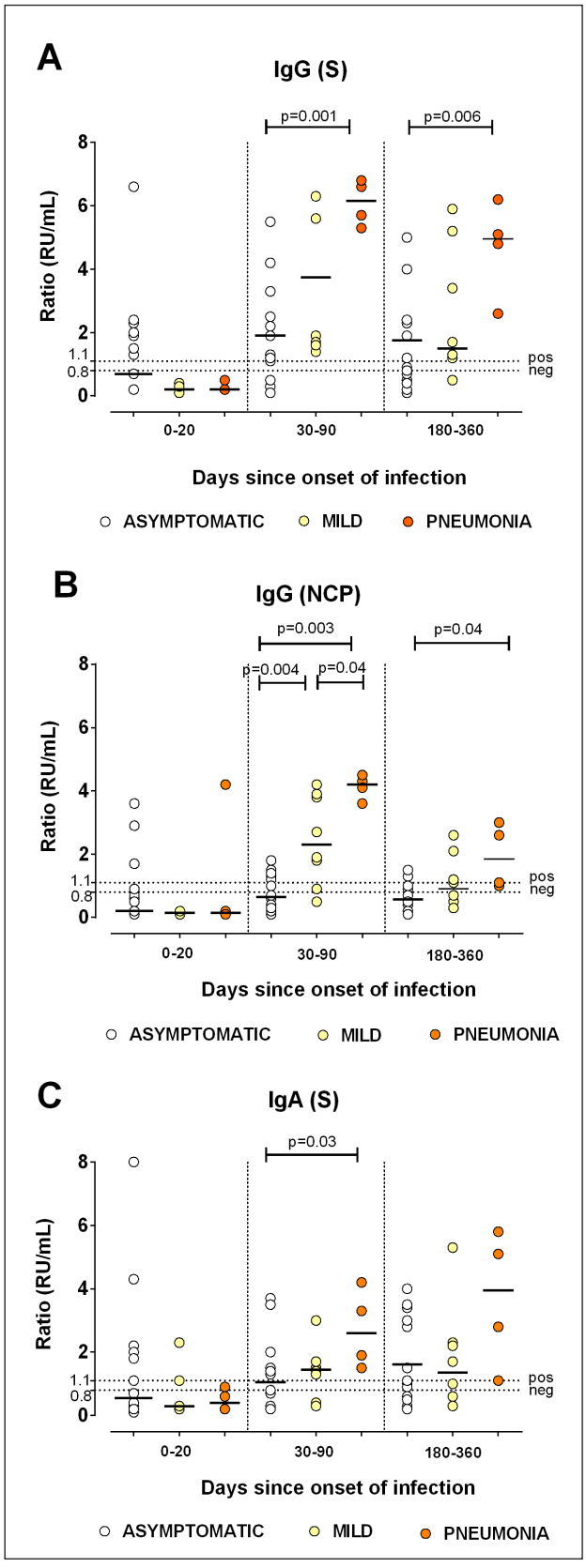

Figure 2 - *Anti-Spike (S) IgG (A), anti-Nucleocapsid (NCP) IgG (B), and anti-S IgA (C) levels in pregnant women with asymptomatic SARS-CoV-2 infection, mild COVID-19 or pneumonia.*

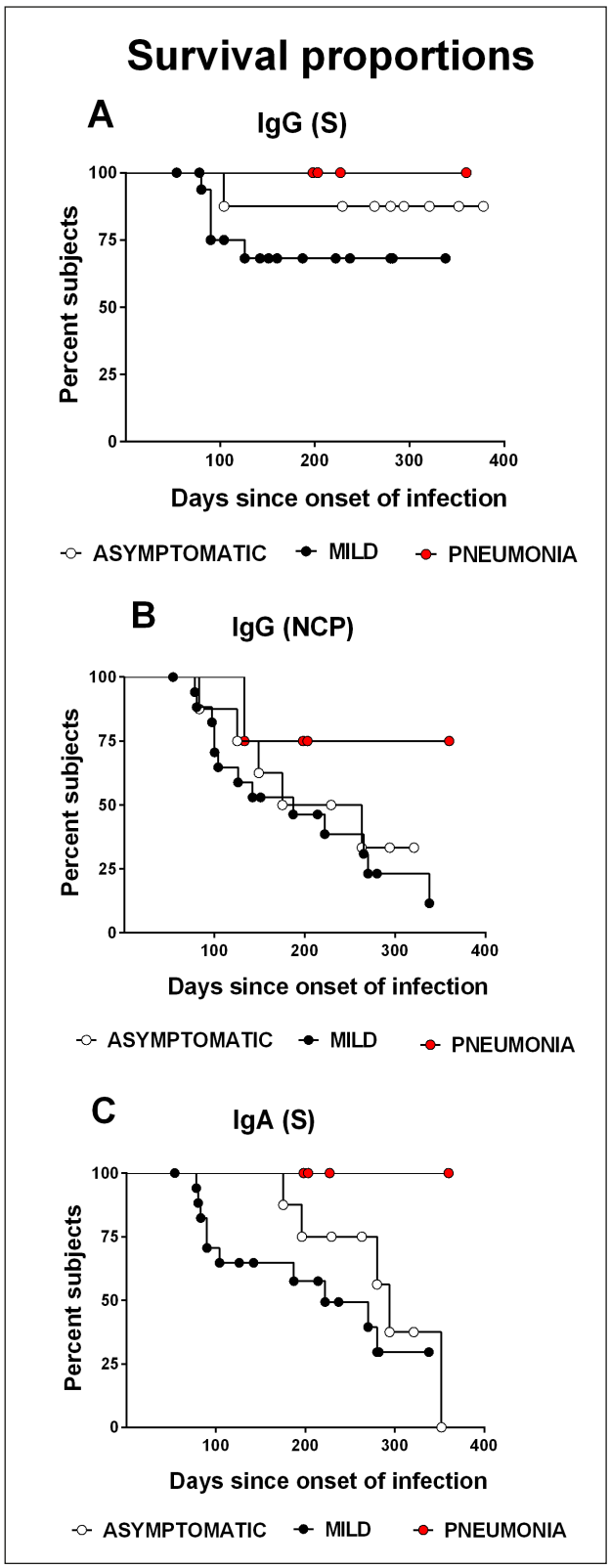

Figure 3 - *Persistence of anti-Spike (S) IgG (A), anti-Nucleocapsid (NCP) IgG (B), and anti-S IgA (C) in pregnant women with asymptomatic SARS-CoV-2 infection, mild COVID-19 or pneumonia. The percentage of subjects showing anti-SARS-CoV-2 antibodies at different times after infection is illustrated.*

ti-NCP IgG levels in the mild COVID-19 group were higher than in the asymptomatic (p=0.004) but lower than in the pneumonia (p=0.04) groups (*Figure 2*). From 6 months to one year after infection, higher levels of anti-S (p=0.006) and anti-NCP IgG (p=0.04) persisted in the pneumonia group compared to the asymptomatic group.

A susceptible condition such as pregnancy might be associated with partial immune suppression and more severe illness, and might increase the need for hospitalization. We compared mild COVID-19 and pneumonia pregnant women to a group of 22 non-pregnant women with the same characteristics (age, no comorbidities, mild or severe disease). In the two groups, we evaluated the possible differences in the development of antibody response to SARS-CoV-2, depending on the severity of disease and persistence over time. We observed that in the group of 17 non-pregnant women (median age 41 years old; range 21-51) with mild COVID-19, the anti-S IgG response determined at a median time of 63 days after infection (range 25-116) was not significantly different from that observed in pregnant women (median age 31 years old; range 23-35) with mild COVID-19. Higher anti-S IgG levels (p=0.016) were detected in non-pregnant (n=5) than in pregnant women (n=4) with pneumonia (*Figure 2* Supplement).

In the asymptomatic group, the anti-S IgG antibody response persisted until the last testing at one year after infection in 68.2% of mothers, the anti-NCP IgG in 11.6% and the anti-S IgA in 29.6%. In the mild COVID-19 group, the anti-S IgG antibody response persisted up to the last testing at one year in 87.5% of women, anti-NCP IgG in 33.3%, and anti-S IgA in 37.5%.

In the pneumonia group, the anti-S IgG and IgA antibody responses persisted until the last testing at one year after infection in all mothers, while anti-NCP IgG persisted in 75.0% of women (*Figure 3*).

Subsequently, we analyzed 7 cord blood serum samples from the newborns collected at delivery to evaluate efficient trans-placental transfer of anti-S IgG antibodies. Anti-S IgG, but no IgA, were detected in 6/7 (85.7%) newborns, while anti-NCP IgG were detected in 3/7 (42.8%) newborns. Nt titer developed in 5/7 (71.4%) newborn serum samples, although we observed Nt titer in serum of 7/7 of their mothers. This difference may be due to the additional contribution to neutralization in maternal serum of Spike-specific IgA, which are not transmitted to the fetus.

Pregnancy outcomes

To evaluate the effect of maternal infection on the newborn, the following parameters were compared between the 49 newborns of the 48 SARS-CoV-2 infected mothers and a control group of 200 newborns from the 200 non-infected mothers: term and mode of delivery, and newborn weight, length and head circumference. Infected mothers were analyzed according to the trimester at which the infection occurred or based on severity of the infection (asymptomatic, mild COVID-19 or pneumonia). The parameters analyzed were similar between pregnancies complicated

Table 3 - *Maternal and neonatal characteristics.*

Characteristics	*Period of infection*			*Severity of disease*			
	Period of infection	*Second part of pregnancy*	*Peripartum/ delivery*	*Asymptomatic*	*Mild*	*Pneumonia*	*Control group*
MOTHER, no. (%)	12 (25.0)	8 (16.6)	28 (58.3)	31 (64.5)	12 (25.0)	5 (10.4)	200
Gestational weeks at infection (median, range)	12 (8-19)	23 (20-27)	39 (35-42)	39 (8-42)	27 (9-40)	33 (22-39)	28 (12-37)
Miscarriage	0	0	0	0	0	0	0
NEWBORN, no. (%)	12 (24.4)	9 (18.3)	28 (57.14)	31 (63.2)	13 (26.5)	5 (10.2)	205
Weeks of gestation at birth (median, range)	40 (35-42)	40 (35-42)	40 (34-42)	40 (34-42)	40 (35-42)	40 (34-42)	40 (31-42)
Mode of delivery, no. (%) vaginal	11 (91.6)	5 (62.5)	22 (78.5)	28 (90.3)	8 (66.6)	2 (40.0)	144 (72.0)
Cesarean section	1 (8.3)	3 (37.5)	6 (21.4)	3 (9.6)	4 (33.3)	3 (60.0)	56 (28.0)
Sex (Male/Female), no. (%)	4/8 (8.1/16.3)	4/4 (8.1/8.1)	13/15 (26.5/30.6)	14/17 (28.5/34.7)	5/7 (10.2/14.3)	2/3 (4.1/6.1)	107/96 (57.2/47.3)*
Birth weight, g (median, range)	3090 (2585-4155)	3120 (1645-4030)	3272 (2320-4040)	3272 (1645-4155)	3212 (2400-3580)	3177 (2485-4030)	3200 (1455-4220)*
Birth length, cm (median, range)	50.0 (49.0-53.0)	50.0 (41.0-55.0)	50.5 (47.0-53.0)	50.5 (41.0-53.0)	50.0 (47.0-52.0)	50.0 (47.0-55.0)	51.0 (38.0-55.0)
Head circumference, cm (median, range)	34.0 (33.5-36.0)	34.0 (29.0-36.0)	34.0 (31.0-37.0)	34.0 (29.0-37.0)	34.0 (33.0-36.0)	34.0 (33.0-35.0)	34.0 (31.0-37.0)*

*not significantly different between control group and women with SARS-CoV-2 infection.

or not by SARS-CoV-2 infection, regardless of the gestational period at which the infection occurred or severity of the infection (*Table 3*). In addition, none of the 49 newborns was positive for SARS-CoV-2 in nasopharyngeal swabs collected at birth.

DISCUSSION

We evaluated:

1) the impact of the SARS-CoV-2 infection on pregnancy outcome and on the newborn and
2) the development of antibody response and its persistence, depending on the severity of the disease.

In the population of pregnant women analyzed, we observed a higher frequency of women from Africa and Asia compared to women from Europe in the infected group. This difference could be due to the fact that the European pregnant women accessed the Obstetrics and Gynecology outpatient ward for the routine monitoring of pregnancy more frequently than those from Africa and Asia and, consequently, are more represented in the control group. Alternatively, SARS-CoV-2 infection may actually have spread more easily in non-European groups because of different socio-economic or hygienic conditions, or because the hygienic information to reduce transmission of SARS-CoV-2 reached those communities less efficiently.

In our study, SARS-CoV-2 infection during pregnancy did not cause major damage to the fetus, regardless of severity of disease and weeks of gestation, and pregnancy status did not impair the development of the anti-SARS-CoV-2 antibody response. Importantly, the SARS-CoV-2-infected pregnant women with pneumonia develop a significantly higher and longer-lasting antibody response compared with the asymptomatic and mild COVID-19 group. The levels of antibody response in pregnant or non-pregnant women with mild COVID-19 were not significantly different. However, a significantly higher antibody level was observed in non-pregnant than in pregnant women with pneumonia.

Maternal immunization during pregnancy after infection or vaccine administration can protect the newborn by trans-placental antibody transfer (Marchant *et al*., 2017) and from SARS-CoV-2 infection during the first months of life (Carosso *et al*., 2020). As the average duration of human pregnancy is nine months, it is questionable whether the antibody response to SARS-CoV-2 infection is sufficient to ensure immunity for the entire length of gestation and to limit the risk of re-infection (Cosma *et al*., 2021). In a recent study, we found evidence of anti-S IgG and neutralizing antibodies in newborns from infected or vaccinated mothers (Cassaniti *et al*., 2021), in agreement with a previous study of newborn cord blood from infected mothers (Zeng H *et al.*, 2020; Joseph NT *et al*., 2021). In the present study, we correlated the magnitude and the persistence of anti-S IgG and IgA, and anti-NCP IgG with the severity of the SARS-CoV-2 infection. Recent studies showed that the antibody titers of patients with mild SARS-CoV-2 infection declined more quickly than those reported for SARS-CoV-infected patients (Zavaglio *et al*., 2021; Ibarrondo *et al*., 2020). However, as reported by Choe and colleagues, rates of antibody positivity in the general population were still high at 8 months after infection, even in asymptomatic or mildly symptomatic patients (Bölke *et al*., 2020; Choe *et al*., 2021). In the pregnant women cohort analyzed in this study, anti-S IgG persisted in the majority of women until at least one year after infection, especially in those with symptomatic infection and pneumonia, while anti-S IgA and anti-NCP IgG declined earlier, as observed in non-pregnant subjects (Choe *et al*., 2021). These results suggest that the anti-S IgG response developed during pregnancy may confer protection in both the mother and the newborn by trans-placental antibody transfer, as demonstrated by our results. We also observed that during the acute phase of infection, an earlier anti-S IgG response appears associated with asymptomatic infection, consistent with earlier, effective, immune responses, while women with pneumonia subsequently develop higher antibody levels than asymptomatic women, possibly explained by slower mounting of protective immune responses and exposure to higher viral replication and viral load. Another important end-point of this study was the occurrence of a pregnancy complication, defined by the presence of miscarriage, preterm birth and cesarean section at delivery and neonatal outcomes in comparison with non-infected pregnant women. Previous studies have shown that SARS-CoV but not SARS-CoV-2 infection during pregnancy can lead to high rates of spontaneous abortion, premature birth and intrauterine growth restriction (Selim *et al*., 2020). Furthermore, the maternal outcomes in SARS-CoV-2 compared to SARS-CoV and MERS-CoV infections were reported to be more favorable, with lower morbidity and mortality (Dashraath *et al*., 2020). However, a meta-analysis study reported preterm births, neonatal pneumonia and respiratory distress syndrome in infants born to SARS-CoV-2-positive mothers (Salem *et al*., 2021). As reported by Dubey and colleagues (2020), the rates of cesarean deliveries and adverse pregnancy outcomes were substantially higher in Chinese studies (91% and 21%) compared to American (40% and 15%) and European studies (38% and 19%). Similarly, the rates of preterm births were lower in American studies (12%) compared to Chinese and European studies (17% and 19%, respectively) (Dubey *et al*., 2020). Furthermore, as reported by Sacinti and colleagues, the miscarriage incidence appears to have increased 25% during the pandemic in their population (Sacinti *et al*., 2021). However, our

data in agreement with a recent report show that SARS-CoV-2 infection within the first trimester does not seem to predispose to early pregnancy loss (Zelini *et al*., 2021).

Moreover, in a recent study, it was observed that 77.4% (95% CI 76.2-78.6) of SARS-CoV-2 infections, 90.9% (95% CI 88.7-92.7) of SARS-CoV-2-associated hospital admission, and 98% (95% CI 92.5-99.7) of SARS-CoV-2 associated critical care admission, as well as all baby deaths, occurred in pregnant women who were unvaccinated at the time of COVID-19 diagnosis (Stock *et al*., 2022).

In our study, we analyzed the clinical outcome of pregnancies complicated by SARS-CoV-2 infection at different trimesters of pregnancy. SARS-CoV-2 infection has not led to congenital infection or negative results on newborns, as compared to controls, irrespective of gestational time or severity of infection. In addition, SARS-CoV-2 infection did not appear to be more serious during pregnancy compared to the overall population. However, we cannot exclude that the treatment administered to women with pneumonia may have avoided a severe pregnancy outcome in these subjects. Therefore, screening, early treatment and diagnosis during pregnancy may be helpful to reduce adverse outcomes in pregnant women with SARS-CoV-2 infection.

A limitation of our study derives from the relatively small number of women analyzed, and therefore we may have missed the occurrence of rare complications.

In conclusion, we demonstrated that SARS-CoV-2 antibodies are developed and persist throughout pregnancy. Maternal antibodies can also contribute to protection of the newborn via trans-placental transfer. Persistence over time of both natural and vaccine-induced anti-SARS-CoV-2 antibodies should be studied further to identify the most effective approaches to maternal immunization during or before pregnancy.

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Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee Area Pavia (protocol code 20200046007, date of approval 05/06/2020).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest:

The authors of this manuscript have no conflicts of interest to disclose.

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