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## Covid-19 seroprevalence in a group of pregnant women compared to a group of non-pregnant women

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### ABSTRACT

Pregnant women are an interesting population to study in the context of the current Coronavirus Disease 2019 (COVID-19); studies are still controversial in concluding if pregnancy is a protective condition or a risk factor for a more severe form of the illness.

We estimated rate of positive serology for SARS-CoV-2 in a population of healthy pregnant women, compared to a population of non-pregnant women of the same age and geographic area. We also made a comparison between the two groups in terms of previous symptoms and lifestyle.

This is a transversal study including pregnant women, above 18 weeks of gestation, aged between 18 and 40 years. The control group consisted of 588 non pregnant women from the same area and the same age group. A total of 344 pregnant women and 588 non pregnant women were recruited.

The rate of positive serology for SARS-CoV-2 was significantly lower in the pregnant group: 9/344 (2.6%) versus 75/588 (12.8%) in the non-pregnant group ( $p < 0.0001$ ). The two groups were similar in terms of occupation and in the self-reported habit to leave the house during the lockdown.

Our hypothesis to explain this result is that pregnant women might have adopted a more prudential lifestyle, due to their special condition, which may have led them to behave with more caution, *i.e.*, concerning the responsibility of wearing all the disposable personal protective equipment, and keeping the recommended 6 feet distance from other people.

### SOMMARIO

Le donne incinte sono una popolazione interessante da studiare nel contesto dell'attuale pandemia da Coronavirus 2019 (COVID-19); gli studi sono ancora controversi nel concludere se la gravidanza è una condizione protettiva o un fattore di rischio per una forma più grave della malattia.

Abbiamo stimato il tasso di sierologia positiva per SARS-CoV-2 in una popolazione di donne incinte sane, rispetto a una popolazione di donne non gravide della stessa età e area geografica. Abbiamo anche fatto un confronto tra i due gruppi in termini di sintomi precedenti e stile di vita.

Questo è uno studio trasversale su donne in gravidanza, con epoca gestazionale superiore a 18 settimane, di età compresa tra i 18 ei 40 anni. Il gruppo di controllo era composto da 588 donne non gravide della stessa area e della stessa fascia di età. Sono state reclutate 344 donne incinte e 588 donne non gravide.

Il tasso di sierologia positiva per SARS-CoV-2 è stato significativamente inferiore nel gruppo delle gravide: 9/344 (2,6%) contro 75/588 (12,8%) nel gruppo delle non gravide ( $p < 0,0001$ ). I due gruppi erano simili in termini di occupazione e nell'abitudine dichiarata di uscire di casa durante il lockdown.

La nostra ipotesi per spiegare questo risultato è che le donne in gravidanza potrebbero aver adottato uno stile di vita più prudente, a causa della loro condizione particolare, che potrebbe averle portate a comportarsi con maggiore cautela e responsabilità ad esempio nell'indossare tutti i dispositivi di protezione individuale e di mantenere la distanza consigliata di 6 piedi da altre persone.

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**Key words**

*Covid19; SARS-CoV-2; pregnancy; seroprevalence; pandemic.*

## INTRODUCTION

The year 2020 has been marked by the spread of the current Coronavirus Disease 2019 (COVID-19) pneumonia pandemic, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Pregnant women are an interesting population to study in this context. Pregnancy itself can be considered an immunological paradox: the woman must develop an immunological tolerance towards a semi-allogenic fetus, which has exposed pregnant women in history to an increased risk of infection, especially viral (*e.g.*, H1N1 in 2009, SARS epidemics of 2003, Ebola or Zika Virus), with maternal and neonatal unfavourable outcomes (1, 2). Physiological and mechanical changes in pregnancy might theoretically increase susceptibility to infections in general, particularly when the cardiorespiratory system is affected (3).

Concerning COVID-19 and its effect on pregnancy, studies are still speculative and controversial (4). Some theories support the hypothesis that, since COVID-19 is an immune condition marked by reduced lymphocytes and elevated selected proinflammatory cytokines, and similar immune expression has been demonstrated in pregnancy, pregnant women might be on higher risk for a severe form of the illness (5). According to other authors, immunomodulatory mechanisms employed by the pregnant status may mitigate violent immune response, may soften cytokine storm, tightly associated with severely ill COVID-19 patients, and potentially reduce SARS-CoV-2 transmission (6).

Even if it is too early to draw a conclusion, most evidences show that maternal and fetal outcomes do not seem to be unfavourable (7, 8) and, to date, the risk of vertical transmission is possible but very rare (9). Given the impossibility to accurately estimate the real incidence of the pathology, with all the possible limitations, serological tests for the measurement of immune response could represent an effective tool for the rapid monitoring of the population and

estimating the proportion of previous infections in a territory (10, 11).

Some other authors have already used this approach in pregnant women population, reporting data that necessarily need to be widened in order to obtain larger samples for further analysis (12, 13). The aim of this study is to assess the prevalence of positive serology in a population of pregnant women, compared to a control group of non-pregnant women. Both groups did not perform a baseline molecular oral/nose-pharyngeal swab at the time of enrolment because it is not yet foreseen in the hospital protocol.

## MATERIALS AND METHODS

This was a transversal study aiming to estimate the prevalence of immunological response in a population of healthy pregnant women at the time of enrolment. Primary outcome of the research was the rate of positive serology for SARS-CoV-2 in a population of healthy pregnant women, compared to a population of non-pregnant women. Secondary outcome was the comparison between the two groups in terms of previous symptoms and lifestyle.

We included 344 pregnant women attending the Obstetrical Clinic of the "Maggiore della Carità" Hospital (Novara, Italy). Inclusion criteria were: pregnant women,  $\geq 18$  weeks of gestation, aged between 18 and 40 years, willing to participate in the study.

The control group consisted of 588 non pregnant women from the same area and the same age group, chosen among those women performing the serological assay at the same time and laboratory used for our study population, and giving consent for an anonymous comparison of the results.

Recruitment period was from 27<sup>th</sup> April 2020 to 1<sup>st</sup> July 2020.

Women consented to participate in the study after being informed on the nature of the research and data managing and processing; an informed consent was therefore signed.

Data collection consisted of 1) demographics data, 2) serological results and 3) a short survey where they were asked questions on the presence of symptoms, about their lifestyle and about possible contacts with other people in the three months preceding the blood sample collection.

A single serum sample was collected from each participating woman and stored at  $-80^{\circ}\text{C}$  and subsequently tested for Sars-CoV-2 antibodies in Varella laboratory (Naples, Italy), blind to the study.

A chemiluminescent microparticle immunoassay (CMIA) (MAGLUMI 2019-NCov IgG/IgM, Snibe, China) was used to process the samples. This is a highly sensitive (95.6%) and specific (96.0%) assay that has been validated in usage with human serum sample (14-16).

All patients who tested positive to serology were confirmed with RT-PCR.

### Analysis

Statistical analysis was performed on frequency distributions of variables, expressed as absolute frequency and percentage. Proportions were compared by Chi-square test or Fisher's exact test, as appropriate. Quantitative variables, reported as medians and interquartile ranges (IQR), were analyzed using the Mann-Whitney U test for unmatched groups. All statistical tests were two sided; a  $p$  value  $< 0.05$  was considered as statistically significant. The analyses were performed using Stata 15.1 software (StataCorp LLC, College Station, Texas USA, 2017).

## RESULTS

A total of 344 pregnant women and 588 non pregnant women were recruited.

Nine of 344 (2.6%) in the pregnant and 75 of 588 (12.8%) in the non-pregnant group tested positive for IgG ( $p < 0.0001$ ).

In the non-pregnant women group 231/588 (39.3%) reported symptoms in the previous three months; symptoms were reported by 48 of the 75 IgG positive women (64.0%) and by 183 of the 513 IgG negative women (35.7%). In the IgG positive group, 18/75 (24.0%) had high-grade fever and 22/75 (29.3%) had low-grade fever. In the IgG negative group, 76/513 (14.8%) had high-grade fever and 71/513 (13.8%) had low grade fever. Overall fever was reported by 187/231 symptomatic non-pregnant women (80.9%). 94/231 (40.6%)

had high-grade fever and 93/231 (40.3%) had low-grade fever.

Cough was reported by 150/231 (64.0%) of symptomatic non-pregnant women. Cough prevalence in the IgG positive group was 27/75 (36.0%), and 123/513 (24.0%) in the IgG negative.

Ageusia was reported by 46/231 (19.9%) of symptomatic non-pregnant women. Ageusia prevalence in the IgG positive group was 27/75 (36.0%), and 19/513 (3.7%) in the IgG negative group.

Anosmia was reported by 53/321 (22.9%) of symptomatic non-pregnant women. Anosmia prevalence in the IgG positive group was 28/75 (37.3%), and 25/513 (4.9%) in the IgG negative group.

**Table I** summarizes the main characteristics of the non-pregnant group.

In the pregnant group 49/344 (13.9%) women reported symptoms in the previous three months.

Symptoms were reported by 5 of the 9 IgG positive women (55.6%) and by 44 of the 335 IgG negative women (13.1%).

Four of the 9 women with positive serology reported fever (44.4%): 3 (33.3%) with high grade and 1 (11.1%) with low grade. 23 of the 335 women with negative serology (6.9%) reported fever: 10 (3.0%) with high grade and 13 (4.0%) with low grade. Overall fever was reported by 27/344 (7.9%) pregnant women.

Cough was reported by 27/344 (7.9%) pregnant women: 5 of the 9 IgG positive women, and 22 of the 335 negative ones (6.6%). Six women reported ageusia and anosmia, but only one of them was IgG positive.

**Table II** describes the main characteristics of the pregnant group.

Considering the occupation of the pregnant women there are no evident differences between the two groups, pregnant and non-pregnant. No differences were evident even in the self-reported habit to leave the house during the lockdown.

The only difference we found in both groups was in the higher percentage of positive serology in women who got in contact with a person diagnosed with SARS COV2 disease: 5/9 (55.6%) *versus* 16/335 (4.8%) in the pregnant group and 12/27 (44.4%) *versus* 30/330 (9.1%). This difference was statistically significant within both groups ( $p < 0.001$ ).

The reduced incidence of IgG positivity in the pregnant group was found unrelated to the occupational status, indeed in the housewife or unemployed women subgroup 10/49 (20.4%) of the non-pregnant and 3/96 (3.1%) of the pregnant were IgG positive. In the employed subgroup,

**Table I.** Non pregnant women.

	Total (N = 588)	IgG <sup>+</sup> (N = 75)	IgG <sup>-</sup> (N = 513)	p-value (IgG <sup>+</sup> vs IgG <sup>-</sup> )
Age (year), median (IQR)	34 (29-37)	33 (26-38)	34 (29-37)	0.56
Comorbidities, n (%)	27 (4.6)	1 (1.3)	26 (5.1)	0.23
Symptoms				
Symptomatic, n (%)	231 (39.3)	48 (64.0)	183 (35.7)	<b>&lt; 0.0001</b>
Asymptomatic, n (%)	357 (60.7)	27 (36.0)	330 (64.3)	
If asymptomatic, recent contact with person affected by SARS COV2	42/357 (11.8)	12/27 (44.4)	30/330 (9.1)	<b>&lt; 0.0001</b>
Type of symptoms, n (%)				
Fever	187 (31.8)	40 (53.3)	147 (28.7)	<b>&lt; 0.0001</b>
High-grade Fever	94 (16.0)	18 (24.0)	76 (14.8)	<b>0.043</b>
Low-grade fever	93 (15.8)	22 (29.3)	71 (13.8)	<b>0.001</b>
Cough	150 (25.5)	27 (36.0)	123 (24.0)	<b>0.026</b>
Ageusia	46 (7.8)	27 (36.0)	19 (3.7)	<b>&lt; 0.0001</b>
Anosmia	53 (9.0)	28 (37.3)	25 (4.9)	<b>&lt; 0.0001</b>
Conjunctivitis	26 (4.4)	4 (5.3)	22 (4.3)	0.76
Diarrhea	68 (11.6)	14 (18.7)	54 (10.5)	<b>0.039</b>
Others	27 (4.6)	9 (12.0)	18 (3.5)	<b>0.004</b>
Occupation, n (%)				
Health worker	74 (12.6)	7 (9.3)	67 (13.1)	0.36
Employed	399 (67.9)	46 (61.3)	353 (68.8)	0.20
Housewife or unemployed	49 (8.3)	10 (13.3)	39 (7.6)	0.09
Student	66 (11.2)	12 (16.0)	54 (10.5)	0.16

**Table II.** Pregnant women.

	Total (N = 344)	IgG <sup>+</sup> (N = 9)	IgG <sup>-</sup> (N = 335)	p-value (IgG <sup>+</sup> vs IgG <sup>-</sup> )
Age (year), median (IQR)	32 (29-35)	30 (22-35)	32 (29-35)	0.36
BMI (Kg/m <sup>2</sup> ), median (IQR)	27 (23-29)	28 (24-29)	27 (23-29)	0.69
Comorbidities, n (%)	46 (13.4)	1 (11.1)	45 (13.4)	1.0
Symptoms				
Symptomatic, n (%)	49 (14.2)	5 (55.6)	44 (13.1)	<b>0.004</b>
Asymptomatic, n (%)	295 (85.8)	4 (44.4)	291 (86.9)	
If asymptomatic, recent contact with person affected by SARS COV2	12/295 (4.1)	3/4 (75.0)	9/291 (3.1)	<b>&lt; 0.0001</b>
Type of symptoms, n (%)				
Fever	27 (7.9)	4 (44.4)	23 (6.9)	<b>0.003</b>
High-grade Fever	13 (3.8)	3 (33.3)	10 (3.0)	<b>0.003</b>
Low-grade fever	14 (4.0)	1 (11.1)	13 (4.0)	0.33
Cough	27 (7.9)	5 (55.6)	22 (6.6)	<b>&lt; 0.0001</b>
Ageusia	6 (1.7)	1 (11.1)	5 (1.5)	0.15
Anosmia	6 (1.7)	1 (11.1)	5 (1.5)	0.15
Conjunctivitis	0 (0.0)	0 (0.0)	0 (0.0)	-
Diarrhea	7 (2.0)	0 (0.0)	7 (2.1)	1.0
Others	5 (1.5)	0 (0.0)	5 (1.5)	1.0
Occupation, n (%)				
Health worker	31 (9.0)	1 (11.1)	30 (9.0)	0.58
Employed	214 (62.2)	5 (55.6)	209 (62.4)	0.73
Housewife or unemployed	96 (27.9)	3 (33.3)	93 (27.8)	0.71
Student	3 (0.9)	0 (0.0)	3 (0.9)	-
Going out of home, n (%)	244 (70.9)	7 (77.8)	237 (70.8)	1.0
Housewife or unemployed	60/244 (24.6)	2/7 (28.6)	58/237 (24.5)	0.68
Partner health worker, n (%)	10 (2.9)	1 (11.1)	9 (2.7)	0.24
Partner crowded space, n (%)	156 (45.4)	6 (66.7)	150 (44.8)	0.31
Person affected by SARS COV2, n (%)	21 (6.1)	5 (55.6)	16 (4.8)	<b>&lt; 0.0001</b>

46/399 (11.5%) of non-pregnant women and 5/214 (2.3%) of pregnant women resulted IgG positive (p < 0.001). Between the health workers, the non-pregnant IgG positive were 7/74 (9.4%) while there was 1/31 pregnant woman IgG positive.

**Table III** shows the characteristics of women with positive serology, comparing 9 pregnant women versus 75 no pregnant women. The two groups report a similar amount and variability of symptoms.

**Table III.** Women with positive serology (IgG<sup>+</sup>).

	Pregnant (N = 9)	Non pregnant (N = 75)	p-value
Age (year), median (IQR)	30 (22-35)	33 (26-38)	0.20
Comorbidities, n (%)	1 (11.1)	1 (1.3)	0.20
Symptoms			
Symptomatic, n (%)	5 (55.6)	48 (64.0)	0.72
Asymptomatic, n (%)	4 (44.4)	27 (36.0)	
If asymptomatic, recent contact with person affected by SARS COV2	3/4 (75.0)	12/27 (44.4)	0.33
Type of symptoms, n (%)			
Fever	4 (44.4)	40 (53.3)	0.73
High-grade Fever	3 (33.3)	18 (24.0)	0.68
Low-grade fever	1 (11.1)	22 (29.3)	0.43
Cough	5 (55.6)	27 (36.0)	0.29
Ageusia	1 (11.1)	27 (36.0)	0.26
Anosmia	1 (11.1)	28 (37.3)	0.15
Congjunctivitis	0 (0.0)	4 (5.3)	1.0
Diarrhea	0 (0.0)	14 (18.7)	0.35
Others	0 (0.0)	9 (12.0)	0.59
Occupation, n (%)			
Health worker	1 (11.1)	7 (9.3)	1.0
Employed	5 (55.6)	46 (61.3)	0.73
Housewife or unemployed	3 (33.3)	10 (13.3)	0.14
Student	0 (0.0)	12 (16.0)	0.35

## DISCUSSION

Large-scale serology testing is critical for estimating how many individuals have been infected during a pandemic status such as the COVID-19 one. Due to widely imposed social distancing requirements, it is mainly difficult to collect serum from the whole population. Pregnant women represent an exception as they continue to have multiple interactions with the medical system for prenatal care and delivery, even during a pandemic, and they might represent a valid sample study of the general population to assess SARS-CoV-2 immunity.

The main and most important result of our study is the difference between the prevalence of positive serology between pregnant and non-pregnant women. This data itself implies two different conclusions: the former one is that the prevalence of positive serology in pregnant women cannot be used to estimate the prevalence of the disease in the general population, as suggested by some authors (17), the latter one is that the pregnant status might be protective towards SARS-CoV-2 infection.

Theoretically, to support this evidence we found that lifestyles did not influence the incidence of IgG positivity in the two groups, as a significative reduction was observed either in the unemployed or the employed subgroup; on the other hand, the media generated awareness in the general population (*i.e.*, for the high mortality of this infection) along with the overall reduced incidence of IgG positivity and symptom-

atology in the pregnant group might lead us to consider a more prudential lifestyle. Pregnant women may have behaved with more caution, *i.e.*, concerning the responsibility of wearing all the disposable personal protective equipment, and keeping the recommended 6 feet distance from other people. This interpretation can be enforced by the observed tendency of pregnant women to be particularly anxious and worried about their health, especially during the pandemic, as demonstrated in previous studies (18).

Data collected in this study support the idea that pregnant women are less infected than the equivalent female population. As previously speculated, this could be either a better immunological response or due to a more prudential lifestyle. Our data do not allow us to understand which of the two hypotheses is true.

Despite our results, we have to consider some limits of our study: low sample size; prevalent use of serological blood, currently not gold standard for diagnosis; and not having performed nasopharynx swab for confirmation.

Due to the lack of conclusive studies on this topic and of the importance of the contagion prevention, more research is necessary to confirm these findings.

## CONCLUSIONS

Pregnant women are less infected than the equivalent female population. This could be either a bet-

ter immunological response or due to a more prudent lifestyle. Furthermore, our study does not demonstrate important differences between pregnant and non-pregnant in symptomatology.

## ETHICS

This study has been approved by the local Ethical Committee. All women who participated in the study signed an informed consent.

## CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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