



Asymptomatic SARS-CoV-2 infections in pregnant patients in an Italian city during the complete lockdown

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Abstract

Data from both New York and London report a high prevalence of the asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in pregnant patients admitted for delivery, raising questions on the possible correlated dangers (ie, contacts with healthcare workers; the possible creation of an intrahospital outbreak at birth; and conflicting evidence on vertical transmission). For this study, results from SARS-CoV-2 screening via nasopharyngeal swab from maternity wards of the four hospitals of Genoa, Italy, were collected during a month of complete lockdown from 1 April to 30 April 2020. Out of 333 tested women, only 9 were symptomatic. Only one symptomatic patient (0.3%) and six asymptomatic ones (1.8%) tested positive. Out of the six positive asymptomatic patients, five were from the most disadvantaged neighborhood of the city (assessed by postal code). In conclusion, even if Italy was badly affected by coronavirus disease 2019 in the studied month, the reported prevalence of SARS-CoV-2 infections in asymptomatic pregnant patients at term was lower than the ones reported in the literature.

KEYWORDS

asymptomatic COVID-19, COVID-19 and pregnancy, maternal leave policies, SARS-CoV-2

1 | INTRODUCTION

Early detection and isolation of asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive patients is a crucial public safety action,¹ but a screening of the entire population is difficult to be organized and limited by test shortage. However, experiences of universal screenings in selected populations were reported, among them pregnant patients admitted for delivery. The incidence of positive SARS-CoV-2 nasopharyngeal swabs in asymptomatic pregnant women was 13.5% and 6.2% in two reported screened cohort in New York and London.^{2,3}

Genoa is an Italian metropolitan city with 852 009 inhabitants, situated in Liguria, directly neighboring Lombardy, the most affected Italian region. The first coronavirus disease 2019 (COVID-19) case in Genoa was reported on 1 March 2020. Italy imposed complete

lockdown to the entire population since mid-March. The first COVID-19 case in a symptomatic pregnant patient was diagnosed on 13 March 2020, followed by other 10 symptomatic cases in pregnancy during the same month. As a consequence, since 1 April 2020, a universal screening with real-time polymerase chain reaction (RT-PCR) on nasopharyngeal swabs was implemented in all maternity wards of the city hospitals (San Martino Hospital, G. Gaslini Hospital, Galliera Hospital, Villa Scassi—ASL3 Hospital).

2 | MATERIALS AND METHODS

Results from SARS-CoV-2 screening in all maternity wards were collected for this study from 1 April to 30 April 2020. Since the implementation of the universal screening, all pregnant women

admitted for delivery were tested for SARS-CoV-2. Women were initially triaged based on symptoms (fever and/or cough or other respiratory symptoms), contacts with positive patients, and travel history. They were asked also for their demographic data, current working situation, and observance of lockdown measures. All patients included signed written informed consent for the use of their anonymized data for clinical research. All nasopharyngeal swabs, collected by a nurse or a midwife, were then centralized in two laboratories. Total RNA was extracted from the swabs using QIAamp Viral RNA Kit (Qiagen) according to the manufacturer's procedure, the RNA was retrotranscribed and amplified using SuperScript III Platinum One-Step qRT-PCR Kit and a specific assay using a Mastercycler RealPlex2S system (Eppendorf, Hamburg, Germany). The screening was performed at two levels, the first level examined the presence of gene E (Envelope) using the following primers: 313241, 313242, and 313243 (TIB Molbiol s.r.l., Genoa); the second level examined the presence of gene RdRp (RNA polymerase RNA dependent) using the following primers: 313244, 313246, and 313250 (TIB Molbiol s.r.l.). As an internal control, RNaseP was used (313252, 313253, and 313254; TIB Molbiol s.r.l.) to examine the presence of human RNA. Positive control (as defined by ISS) and negative control (water as a template) were run simultaneously. The threshold was put beyond the noise of negative control. Tests were considered positive within 40 cq. The samples were labeled as "indefinite" if the internal control RNaseP was not amplified or if the quantitative PCR curve for gene E and/or RdRp was irregular.

The results are reported descriptively. Categorical data are expressed as number and frequency and continuous data as mean with standard deviation. Frequencies are compared through the χ^2 test. $P < .05$ is considered statistically significant.

3 | RESULTS

From 1 April 30 to April 2020, 333 pregnant women (mean age 35.02 ± 6.02 years) underwent the universal screening for SARS-CoV-2 infection. A total of 261 (78.4%) of them were at term, 61 (18.3%) were tested at admission for late premature delivery (34-36 weeks gestation), the remaining 11 (3.3%) between 30 and 34 weeks of gestation. All patients reported having stopped working and to have observed a complete lockdown. A total of 325 of all the screened patients were completely asymptomatic. Nine patients were febrile, but only one (0.3%) resulted positive to SARS-CoV-2 infection. The other eight had two negative nasopharyngeal swabs, and, accordingly, negative serology and were, therefore, treated as not infected. Out of the other 325 asymptomatic patients, 6 (1.8%) resulted positive, 2 had an indefinite result, and the others were negative. The two swabs without a definitive answer were repeated, together with SARS-CoV-2 serology, and found all negative. Out of the six asymptomatic positive women, no one developed clinical symptoms and no infection was reported in the newborns. On the note, five of the positive asymptomatic six patients were from the

most disadvantaged neighborhood of the city (assessed by postal code) and four of six were migrants (two from Ecuador, one from Nigeria, and one from Bangladesh), although all living in Genoa at least since the beginning of the pregnancy. Out of the asymptomatic negative patients, instead, only 70 of 319 lived in the most disadvantaged areas (21.9% vs 83.3%, $P < .001$) and 103 had not Italian citizenship (32.3% vs 66.7%, $P = .07$).

4 | DISCUSSION

COVID-19 transmission through asymptomatic carriers as described in literature during the early months of the pandemic^{4,5} and immediately raised great concern for the difficulties in identifying and isolating asymptomatic positive carriers. The experiences of universal screenings of pregnant people admitted to the hospital for delivery have great relevance for more than one reason. First of all, even if the vertical transmission from an asymptomatic carrier was never described,^{6,7} these infections are still particularly dangerous, because of the numerous contacts with health care workers and the possible creation of an intrahospital outbreak at birth. Awareness of the entity of the phenomenon is, therefore, an essential public health measure. Moreover, while pregnant women could never be entirely representative of the general population, especially because of the hypothesized protective role of estrogens,⁸ they are a subgroup in which such analysis is more feasible than in the entire population.

Our percentage of asymptomatic infected pregnant patients is considerably lower than previously reported, despite being in a region with high prevalence of the disease (+3508 new cases in April in Genoa).⁹ In our opinion, it could be the direct effect of the lockdown measures, which were implemented in all Italy by national law more than 2 weeks before the start of our universal screening. Indeed, lockdown and social distancing have been proved to be among the most efficacious measure for infection containment.¹⁰

The existence of paid antenatal maternity leave for the vast majority of the Italian population may have played a role too, but it is not possible to infer direct causation from this data. However, it is interesting to underline how none of the screened pregnant patients reported having continued to work near term during COVID-19 pandemic and they observed an almost complete lockdown. On the note, the few cases reported were among the most disadvantaged population, in neighborhoods where it is more likely to live in smaller houses, with a higher number of cohabitants.

Our results represent a snapshot of a month in a severely hit area and underline once again the relevance of public health measures like social distancing, mask wearing, and ultimately lockdown in the containment of the pandemic, reporting small numbers of symptomatic and asymptomatic positive pregnant patients in an Italian metropolitan city after the implementation of these measures.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

AF and PA had the research idea and designed the study. CM analyzed the data and wrote the manuscript. RP and MDL collected patients' data. MA, AC, FG, CG, and GV were responsible for the universal screening in the included hospitals. All authors commented on previous versions of the manuscript, contributed to clinical discussion, and read and approved the final submitted version.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Lo YMD, Chiu RWK. Racing towards the development of diagnostics for a novel coronavirus (2019-nCoV). *Clin Chem*. 2020; 66(4):503-504.
2. Sutton D, Fuchs K, D'Alton M, Goffman D. Universal screening for SARS-CoV-2 in women admitted for delivery. *N Engl J Med*. 2020; 382(22):2163-2164. <https://doi.org/10.1056/NEJMc2009316>
3. Khalil A, Hill R, Ladhani S, Pattison K, O'Brien P. SARS-CoV-2 in pregnancy: symptomatic pregnant women are only the tip of the iceberg. *Am J Obstet Gynecol*. 2020;223:296-297.
4. Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA*. 2020;323(14):1406-1407.
5. Yu X, Yang R. COVID-19 transmission through asymptomatic carriers is a challenge to containment. *Influenza Other Respir Viruses*. 2020; 14(4):474-475.
6. Lu D, Sang L, Du S, Li T, Chang Y, Yang XA. Asymptomatic COVID-19 infection in late pregnancy indicated no vertical transmission. *J Med Virol*. 2020;92:1660-1664. <https://doi.org/10.1002/jmv.25927>
7. Schwartz DA. 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*. 2020;144:799-805. <https://doi.org/10.5858/arpa.2020-0901-SA>
8. Cagnacci A, Xholli A. Age-related difference in the rate of coronavirus disease 2019 mortality in women versus men. *Am J Obstet Gynecol*. 2020. <https://doi.org/10.1016/j.ajog.2020.05.039>
9. <http://www.protezionecivile.gov.it/attivita-rischi/rischio-sanitario/emergenze/coronavirus>. Accessed June 12, 2020.
10. Lai S, Ruktanonchai NW, Zhou L, et al. Effect of non-pharmaceutical interventions to contain COVID-19 in China. *Nature*. 2020. <https://doi.org/10.1038/s41586-020-2293-x>

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