



Article type : Brief Communication

BRIEF COMMUNICATION

Assessing risk factors for severe forms of COVID-19 in a pregnant population: A clinical series from Lombardy, Italy

Daniela Di Martino^{1,*}, Francesca Chiaffarino¹, Luisa Patanè², Federico Prefumo^{3,4}, Patrizia Vergani^{5,6}, Sara Ornaghi⁶, Valeria Savasi^{7,8}, Arsenio Spinillo⁹, Antonella Cromi¹⁰, Francesco D'Ambrosi¹, Beatrice Tassis¹, Enrico Iurlaro¹, Fabio Parazzini^{1,11}, Enrico Ferrazzi^{1,11}

¹ Department of Mother, Child and Neonate, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

² Department of Obstetrics and Gynecology, Papa Giovanni XXIII Hospital, Bergamo, Italy

³ Division of Obstetrics and Gynaecology, ASST Spedali Civili, Brescia, Italy

⁴ Department of Clinical and Experimental Sciences, University of Brescia, Italy

⁵ Department of Maternal Fetal Medicine, Fondazione MBBM, San Gerardo Hospital, Monza, Italy

⁶ University of Milano Bicocca, Monza, Italy

⁷ Department of Woman, Mother and Neonate, Sacco Hospital-ASST-Fatebenefratelli-Sacco, Milan, Italy

⁸ Department of Clinical and Biological Sciences, University of Milan, Milan, Italy

⁹ Department of Obstetrics and Gynecology, IRCCS Foundation Policlinico San Matteo, Pavia, University of Pavia, Italy

¹⁰ Department of Obstetrics and Gynecology, University of Insubria, Varese, Italy

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1002/IJGO.13435](https://doi.org/10.1002/IJGO.13435)

This article is protected by copyright. All rights reserved

¹¹ Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

***Correspondence**

Daniela Di Martino, Via della Commenda 12, 20122, Milano, Italy.

Email: daniela.dimartino@policlinico.mi.it

Keywords

COVID-19; Pregnancy; SARS-CoV-2

Synopsis

In 250 pregnant women with either asymptomatic, non-severe, or severe SARS-CoV-2 infection, obesity turned out to be the main determinant of severe COVID-19 illness.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a global health emergency [1, 2], with Lombardy being the epicenter of this outbreak in Italy [3]. COVID-19 disease may be asymptomatic, or may manifest as more severe symptoms [4]. As of June 18, 2020 in Italy, the median age of infected patients was 60 years of age, and the median age of COVID-19-related death was 82 years of age (IQR 74–88) [1]. According to the largest population-based registry of COVID-19 in pregnancy [5], ethnicity, older maternal age, and obesity were significantly associated with hospital admission for pregnant women with SARS-CoV-2 infection. Conversely, available data do not suggest that pregnancy or the postpartum period are greater risk factors for severe COVID-19 [3, 5, 6]; however, ethnicity and comorbidities appear to play a significant role in heightening the risk of developing a severe clinical condition [5, 6]. The aim of the present study was to investigate whether these factors played a role in the severity of the outbreak in Lombardy. The study was an extended cohort of a previous prospective, multicenter study [3], which included women with SARS-CoV-2 infection who were admitted during pregnancy or in the immediate postpartum period to seven COVID-19 hub hospitals in Lombardy, Italy, between February 23 and May 20, 2020. Ethical approval for the study was granted by the Milano Area 2 Ethics Committee (#15408/2020).

Patients were admitted at any gestational age, or within the third postpartum day, with a diagnosis of SARS-CoV-2 infection which was diagnosed by reverse transcription polymerase chain reaction (RT-PCR) using nasopharyngeal swabs.

Data from electronic clinical records were collected for maternal demographic and anthropometric characteristics, medical or obstetric comorbidities, course of pregnancy, clinical signs and symptoms, and treatment for SARS-CoV-2 infection.

The study population was divided into asymptomatic, non-severe, symptomatic, and severe cases (requiring respiratory support or admission to the intensive care unit [ICU]). Descriptive statistics, frequency distribution, age-adjusted relative risks (RR), and 95% confidence intervals (CI) of severe and non-severe cases against asymptomatic cases of COVID-19 were calculated according to selected variables using unconditional multivariate logistic regression with maximum likelihood fitting.

The study included 250 pregnant patients with SARS-CoV-2 infection. Ninety-eight women (39.2%) were asymptomatic, 110 (44.0%) had mild symptoms, and 42 (16.8%) had severe COVID-19 infection requiring respiratory support, nine of whom (3.6%) were admitted to the ICU (Table 1). Interstitial pneumonia was diagnosed in 89 (35.7%) women upon admission; this was especially prevalent in the severe group. No maternal deaths were observed in our cohort. Of 250 patients, 67 (26.8%) had pre-gestational comorbidities.

Medical treatment during hospitalization included low-molecular-weight heparin prophylaxis (50.2%), empiric antibiotic therapy (27.5%), hydroxychloroquine (21.4%), antiviral therapy (8.7%), and combined therapies (31.2%).

The risk of severe COVID-19 disease was higher in obese women (RR 1.9; 95% CI 1.1–3.2) (Table 1). Obesity was significantly associated with non-white ethnic groups ($P<0.0005$). Women >35 years had an increased risk for non-severe/severe COVID-19 infection.

The present data show that obesity is the most important risk factor related to the severe form of the disease, understood as the need for oxygen support or ICU admission. Other comorbidities, including gestational diabetes and hypertension, were not statistically significant for severe infection in the population of pregnant patients. These findings underline the importance of a healthy lifestyle in pregnancy and highlight the issue of social inequality as a determinant for severe COVID-19 disease.

Author Contributions

DDM: manuscript writing, data analysis, literature analysis. FC: data analysis. LP: patient recruitment at Bergamo Hospital. FP: patient recruitment at Brescia Hospital. PV: patient recruitment at Monza Hospital. SO: patient recruitment at Monza Hospital. VS: patient recruitment at Sacco Hospital. AS: patient recruitment at Pavia Hospital. AC: patient recruitment at Varese Hospital. FDA: patient recruitment at Mangiagalli Hospital. BT: study design and planning at Mangiagalli Hospital. EI: patient recruitment at Mangiagalli Hospital. FP: supervision and correction of the draft manuscript. EF: design study, planning and supervision of manuscript writing.

Conflicts of interest

The authors have no conflicts of interest.

References

1. ISS: Characteristics of SARS-CoV-2 patients dying in Italy. Report based on available data on June 18, 2020. <https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-analysis-of-deaths>. Accessed Jun 18, 2020.
2. World Health Organization. Coronavirus disease 2019 (COVID-19) situation report–84. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200413-sitrep-84-covid-19.pdf?sfvrsn=44f511ab_2. Accessed April 13, 2020.
3. Savasi VM, Parisi F, Patanè L, et al. Clinical Findings and Disease Severity in Hospitalized Pregnant Women With Coronavirus Disease 2019 (COVID-19). [published online ahead of print, 2020 May 19]. *Obstet Gynecol*. 2020;10.1097/AOG.0000000000003979.
4. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA*. 2020 Apr 6;323(16):1574–81. doi: 10.1001/jama.2020.5394. Epub ahead of print. PMID: 32250385; PMCID: PMC7136855.
5. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ*. 2020;369:m2107. doi:10.1136/bmj.m2107.

6. Maraschini A, Corsi E, Salvatore MA, Donati S and the ItOSS COVID-19 working group. Coronavirus and birth in Italy: results of a national population-based cohort study. *medRxiv*. doi: <https://doi.org/10.1101/2020.06.11.20128652> medRxiv preprint.

TABLE 1 Relative risk of severe and non-severe COVID-19 infection in obstetric patients

	Asymptomatic n=98	Non-severe n=110	Severe n=42	RR: non- severe vs asymptomatic	RR: severe vs asymptomatic
	<i>n (%)</i>	<i>n (%)</i>	<i>n (%)</i>		
Ethnicity					
White	70 (71.4)	77 (70.0)	26 (61.9)	1+	1+
Other	28 (28.6)	33 (30.0)	16 (38.1)	1.2 (0.9–1.6)	1.6 (0.4–2.6)
Age					
≤29	43 (43.9)	28 (25.5)	13 (31.0)	1+	1+
30–33	21 (21.4)	36 (32.7)	10 (23.8)	1.6 (1.1–2.3)	1.4 (0.7–2.8)
≥34	34 (34.7)	46 (41.8)	19 (45.2)	1.5 (1.0–2.1)	1.5 (0.8–2.8)
Parity					
1	37 (38.5)	53 (48.2)	16 (38.1)	1+	1+
2	59 (61.5)	57 (51.8)	26 (61.9)	0.8 (0.7–1.1)	1.0 (0.6–1.7)
BMI					
≤24.99	64 (66.0)	61 (57.6)	23 (56.1)	1+	1+
25–29.99	23 (23.7)	31 (29.3)	8 (19.5)	1.2 (0.9–1.5)	1.0 (0.5–1.9)
≥30	10 (10.3)	14 (13.2)	10 (24.4)	1.2 (0.8–1.7)	1.8 (1.1–3.2)
Comorbidity*					
No	88 (89.8)	94 (85.5)	34 (81.0)	1+	1+
Yes	10 (10.2)	16 (14.6)	8 (19.1)	1.1 (0.8–1.5)	1.5 (0.8–2.7)

Abbreviations: BMI, body mass index; RR, relative risks.

*Obesity is excluded among the following co-morbidities and analysed in the BMI classes: Diabetes (13.4%), endocrinopathies (13.4%), respiratory diseases (11.9%), hypertension (5.9%), and autoimmune disorders (4.4%).