**Obstetrics**

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

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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 unsymptomatic, 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]).

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

| | Asymptomatic n = 98 n (%) | Non-severe n = 110 n (%) | Severe n = 42 n (%) | RR: non-severe vs asymptomatic | RR: severe vs asymptomatic |
|---|---|---|---|---|---|
| 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[a] | | | | | |
| 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.

[a]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%).

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.

## CONFLICTS OF INTEREST

The authors have no conflicts of interest.

## 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.

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## Obstetrics

# Ischemic uterine necrosis following Hayman suture for postpartum hemorrhage

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Uterine compression sutures (UCS) are immensely useful for the conservation of the uterus in cases of postpartum hemorrhage (PPH) which are refractory to medical management. However, the various complications associated with UCS include uterine necrosis, pyometra, hematometra, postpartum endometritis, uterine synechiae, intra-abdominal adhesions, and uterine rupture in subsequent pregnancy.[1] Ischemic uterine necrosis is an extremely rare complication which is usually diagnosed through Doppler ultrasound and CT/MRI imaging with or without contrast studies/angiography.[2]

The present study reports the case of a 34-year-old, G4P3L1A1 patient at 38 weeks of gestation who was referred to our hospital in obstructed labor with intrauterine fetal demise (IUFD). We performed an emergency lower segment cesarean section (LSCS) which was complicated by atonic PPH after closure of the uterus. The hemorrhage did not respond to medical management with syntocinon, methylergometrine, and carboprost, or uterine artery ligation. A compression test was performed followed by Hayman stitch application with Vicryl no.1 suture (Ethicon Inc., New Jersey, USA), which stopped the bleeding. The patient underwent transfusion of 2 units of packed red blood cells and was subsequently treated with broad-spectrum antibiotics. She developed gaseous abdominal distension on the third postoperative day due to hypokalemia, which was resolved with potassium chloride supplementation. Following on from this, she started developing high-grade fever from the seventh postoperative day. There was no sign of