Management of gestational diabetes in women with a concurrent severe acute respiratory syndrome coronavirus 2 infection, experience of a single center in Northern Italy

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Abstract
Objective: In this study we describe the management of women with gestational diabetes (GD) and an ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The aim of the study is to evaluate whether coronavirus disease 2019 (COVID-19) can further complicate pregnancies, and if the protocol we usually use for GD pregnancies is also applicable to patients who have contracted a SARS-CoV-2 infection.

Methods: This is a retrospective study analyzing all pregnant women with GD and concomitant COVID-19 admitted to our institution for antenatal care between March 1 and April 30, 2020.

Results: Among pregnant women with GD and a concomitant SARS-CoV-2 infection, the mean age was 32.9 (SD 5.6) years. Two patients (33%) were of white racial origin and four (67%) were of non-white racial origin. All patients were diagnosed with COVID-19 during the third trimester of pregnancy. Two women were asymptomatic and four were symptomatic. Only two (33.3%) women received treatment with insulin. None of the patients required intensive care or mechanical ventilation. No complications were found among the neonates.

Conclusion: COVID-19 was not found to worsen the prognosis of patients with GD or of their offspring. Glycemic monitoring, diet therapy, and insulin, when needed, are sufficient for good metabolic control and favorable maternal and fetal outcomes.

KEYWORDS
Coronavirus disease 2019, Diet, Gestational diabetes, Insulin, International Association of Diabetes and Pregnancy Study Groups, Management: Northern Italy, Pandemic

1 INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has had a profound impact on health services worldwide, including antenatal care. In northern Italy, one of the first areas in Europe to be hit by the pandemic, the virus has spread significantly among the pregnant population.1 Repercussions on prenatal care, especially of high-risk pregnancies, are yet to be analyzed.1-3

Among women with high-risk pregnancies, those with gestational diabetes (GD) represent one of the largest subgroups.4,5 The prevalence of GD is estimated at around 18% of pregnancies.4

As far as its repercussions on pregnancy are concerned, GD increases the risk of maternal and perinatal complications, both in the short-term and in the long-term, including a higher prevalence of type 2 diabetes in mothers, and a greater likelihood of childhood obesity in the offspring.4,5
TABLE 1 Maternal and obstetric characteristics of 57 women with gestational diabetes and concomitant COVID-19.

| Maternal age (years) | Multiparous | BMI | GD therapy | Ethnicity | Gestational age at COVID−19 diagnosis (weeks) | COVID−19 Symptoms | COVID−19 therapy |
|---------------------|-------------|-----|------------|-----------|--------------------------------------------|-------------------|-----------------|
| 1                   | Yes         | 24  | Insulin    | Caucasian | 38°0                                      | No                | Heparin         |
| 2                   | Yes         | 30  | Diet       | Magreb    | 38°0                                      | No                | Heparin, hydroxychloroquine, azithromycin, oxygen |
| 3                   | Yes         | 29  | Diet       | Magreb    | 33°1                                      | Fever             | Heparin, hydroxychloroquine |
| 4                   | Yes         | 29  | Diet       | Hispanic  | 39°0                                      | Dyspnea           | Heparin, hydroxychloroquine, azithromycin, oxygen |
| 5                   | No          | 30.5| Diet       | Magreb    | 29°1                                      | Fever             | Heparin, oxygen  |
| 6                   | Yes         | 31  | Insulin    | Caucasian | 27°1                                      | Fever             | Heparin         |

BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); BW, birth weight; COVID−19, coronavirus disease 2019; CS, cesarean section; GD, gestational diabetes; HL, blood loss at delivery.

As of 2020, coronavirus disease 2019 (COVID-19) can be classified as a complication of pregnancy, especially in women with comorbidities such as GD.4−8

In this study we provide a detailed description of the management of pregnant women with GD and an ongoing SARS-CoV-2 infection who gave birth in our obstetric unit, the largest high-risk maternity unit in the metropolitan area of Milan, Italy.

2 | MATERIALS AND METHODS

This retrospective single-center study was carried out in our Institution Fondazione IRCCS Ca’ Granda, Ospedale Maggiore Policlinico, Milan, Italy, one of the six COVID−19 maternity hubs designated by the Regional Health Authority, between March 1 and April 30, 2020.9

All pregnant women with GD and concomitant COVID−19 admitted to our institution for prenatal care were eligible for the present study.

SARS-CoV-2 infection was diagnosed using a nasopharyngeal swab, which, in accordance with the Italian National Guidelines,9 is administered to all women, both symptomatic and asymptomatic, at the time of admission.

Screening for GD was carried out according to the International Association of Diabetes and Pregnancy Study Groups’ recommendations.8 During the first trimester, fasting plasma glucose was measured. Pregestational diabetes was diagnosed when fasting glucose levels were ≥126 mg/dL (7.0 mmol/L). Women with fasting plasma glucose ≥92 mg/dL (5.1 mmol/L) and <126 mg/dL (7.0 mmol/L) were diagnosed with first-trimester GD. Between 24 and 28 weeks of gestation, all women, excluding those with pregestational diabetes and first-trimester GD, underwent a 75-g oral glucose tolerance test following 72 hours of no dietary restrictions and 10 hours of overnight fasting. Plasma glucose levels were measured before and 1 and 2 hours after the administration of a 75-g glucose solution. Second-trimester GD was diagnosed according to the International Association of Diabetes and Pregnancy Study Group’s criteria as follows: when fasting glucose was ≥92 mg/dL (5.1 mmol/L) and/or glucose levels were ≥180 mg/dL (10.0 mmol/L) 1 hour after the administration of the glucose solution and/or when glucose levels were ≥153 mg/dL (8.5 mmol/L) 2 hours after the administration of the solution.

Initial treatment consisted of a diet prescribed by a nutritionist. Women were asked to fill in a daily blood sugar chart. Insulin therapy was introduced when basal and post-prandial plasma glucose levels exceeded 95 and 120 mg/dL, respectively, or 90 and 110 mg/dL when the fetal abdominal circumference exceeded the 75th centile of local reference values.10

Data were collected from electronic clinical records. All patients signed an informed consent to use their data anonymously for research purposes.

The study was approved by the Institutional Review Board of Fondazione IRCCS Ca’ Granda, Ospedale Maggiore Policlinico, Milan, Italy (No.1512; date: April 2020).

For the statistical analysis, we performed a descriptive analysis of variables; continuous variables are reported as mean and standard deviation (SD). Data were analyzed using the statistical package SPSS version 22.0 (IBM Corp., Armonk, NY, USA) and Excel for Windows 2010 (Microsoft Corp., Redmond, WA, USA).

3 | RESULTS

More than half of the patients admitted to our institution between March 1 and April 30, 2020 (51.1%) were aged 35 years and above, 80.3% were of white racial origin, and 144 (16%) were diagnosed with GD. Fifty (5.6%) tested positive for COVID−19, and among these, six (12%) had GD.

The characteristics of the women with GD and concomitant COVID−19 were the following (Table 1). The mean age was 32.9 (SD 5.6) years. Two patients (33%) were of Caucasian ethnicity and four (67%) were non-Caucasian. All patients were diagnosed with COVID−19...
during the third trimester of pregnancy. Two were asymptomatic and the other four were symptomatic. Only two patients (33.3\%) received treatment with insulin. In all cases, because of the coexistence of two risk factors for the pregnancy’s outcome (GD and COVID-19), induction of labor or an elective cesarean section were preferred to spontaneous onset of labor. Among these patients, no complications were observed in childbirth. Only one woman required hospitalization for more than 7 days and this was because her household was not deemed an adequate setting for her to quarantine. None of the patients required intensive care or mechanical ventilation. No complications were found in the neonates, who were all allowed to room-in with their mothers.

### 4 | DISCUSSION

Incidence of COVID-19 was not greater among the GD population. Moreover, the infection was not found to worsen the prognosis of patients with GD or their offspring. None of the women with GD and a concomitant SARS-CoV-2 infection required hospitalization in an intensive care unit or mechanical ventilation.

Monitoring of glycemic control and fetal growth according to the protocols of our Institution prevented the onset of pregnancy complications.

A possible limitation of the present analysis may be represented by the small number of cases analyzed. We expect to increase our study sample in the following months and to provide further results. The main strength of this study is that it was conducted in one of the six reference centers for the treatment of COVID-19 in women in Lombardy, the first region to be affected by the disease in Europe and one of the areas with the highest diffusion rates of infection.\(^1\)\(^-\)\(^10\)

In conclusion, glycemic monitoring, diet therapy, and insulin, when needed, are sufficient for obtaining good metabolic control and a favorable maternal and fetal outcomes even among women with GD and a concomitant SARS-CoV-2 infection.

### CONFLICTS OF INTEREST

The authors have no conflicts of interest.

### AUTHOR CONTRIBUTIONS

All authors contributed significantly to the conception, planning, performance and analysis of the study. FD, GR, and EF were the primary writers of the manuscript. All authors read, revised, and consented to the publication of the final manuscript.

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How to cite this article: D'Ambrosi F, Rossi G, Soldavini CM, et al. Management of gestational diabetes in women with a concurrent severe acute respiratory syndrome coronavirus 2 infection, experience of a single center in Northern Italy. *Int J Gynecol Obstet.* 2021;152:335-338. https://doi.org/10.1002/ijgo.13434