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## CLINICAL ARTICLE

### Management of gestational diabetes in women with a concurrent Sars-Cov-2 infection, experience of a single center in Northern Italy

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**Keywords:** Gestational diabetes, COVID-19, management, diet, insulin, pandemic, northern-Italy, IADPSG.

**Synopsis:** Our management of pregnancies complicated by COVID-19 and gestational diabetes ensures a good maternal and fetal outcome.

## **Abstract**

**Objective:** In this study we describe the management of women with gestational diabetes (GD) and an ongoing Sars-Cov-2 infection. The aim of the study is to evaluate whether the COVID-19 infection can further complicate pregnancies and thus if the protocol we usually use for GDM pregnancies is also applicable to patients who have contracted a Sars-Cov-2 infection.

**Methods:** This is a retrospective study analysing all pregnant women with gestational diabetes and a concomitant COVID-19 infection admitted to our Institution for antenatal care between March 1<sup>st</sup> and April 30<sup>th</sup> 2020.

**Results:** Among pregnant women with GD and a concomitant COVID-19 infection, the mean age was 32,9 (SD 5,6) years. Two patients (33%) were of Caucasian ethnicity while four (67%) were non-Caucasian. All patients were diagnosed with COVID-19 during the third trimester of pregnancy. Two women were asymptomatic while four were symptomatic. Only two patients (33,3%) received treatment with insulin. None of the patients required intensive care or mechanical ventilation. No complications were found among the newborns.

**Conclusion:** the COVID-19 infection was not found to worsen the prognosis of GD patients or of their offspring. Glycaemic monitoring, diet therapy and insulin, when needed, are sufficient for a good metabolic control and a favourable maternal and fetal outcome.

## **INTRODUCTION**

The 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 amongst the pregnant population [1]. Repercussions on antenatal care, especially that of high-risk pregnancies, are yet to be analysed [1-3].

Amongst women with high-risk pregnancies, those with gestational diabetes (GD) represent one of the largest sub-groups [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].

As of 2020, COVID-19 can be classified as a complication of pregnancy, especially in women with co-morbidities such as GD [4-8].

In this study we provide a detailed description of the management of the 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, Lombardy.

## **MATERIALS AND METHODS**

This retrospective single centre study was carried out in our Institution Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy, one of the six COVID-19 maternity hubs designed by the Regional Health Authority, between March 1<sup>st</sup> and April 30<sup>th</sup> 2020.

All pregnant women with GD and a concomitant COVID-19 infection admitted to our Institution for antenatal care were eligible for the present study.

Sars-Cov-2 infection was diagnosed by the means of a nasopharyngeal swab, which in accordance to the Italian National Guidelines [9] is administered to all women, both symptomatic and asymptomatic, at time of admission.

Screening for GD was carried out according to the International Association of Diabetes and Pregnancy Study Groups' (IADPSG) recommendations [8]. During the first trimester, fasting plasma glucose was dosed. Pre-gestational diabetes (DM) was diagnosed when

fasting glucose levels were  $\geq 126$  mg/dL (7.0 mmol/L). Women with fasting plasma glucose  $\geq 92$  mg/dL (5.1 mmol/L) and  $< 126$  mg/dL (7.0 mmol/L) were diagnosed with 1st trimester GDM. Between 24 and 28 weeks of gestation, all women excluding those with DM and 1st trimester GDM, underwent a 75-g oral glucose tolerance test (OGTT) following 72 hours of no dietary restrictions and 10 hours of overnight fast. Plasma glucose levels were measured before, 1 hour and 2 hours after the administration of a 75-g glucose solution. Second trimester GDM was diagnosed according to the IADPSG's criteria as follows: when fasting glucose was  $\geq 92$  mg/dL (5.1 mmol/L) and/or glucose levels were  $\geq 180$  mg/dL (10.0 mmol/L) 1 hour after the administration of the glucose solution and/or when glucose levels were  $\geq 153$  mg/dL (8.5 mmol/L) 2 hours after the administration of the solution.

Initial treatment consisted in 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 75 centile of local reference values [10].

Data was 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).

### Statistical analysis

We performed a descriptive analysis of variables and continuous variables are reported in terms of mean and standard deviation (SD). Data was analysed using the statistical package IBM SPSS 22.0 (New York, USA) and Excel for Windows 2010 (Microsoft Corp., Redmond, WA, USA).

## RESULTS

More than half of the patients admitted to our Institution between March 1<sup>st</sup> and April 30<sup>th</sup> 2020 (51.1%) were aged 35 years and above. 80.3% were of Caucasian ethnicity. 144

(16%) were diagnosed with GD. 50 (5.6%) were tested positive for COVID-19 and, amongst these, 6 (12%) had GD.

The characteristics of the women with GD and a concomitant COVID-19 infection were the following, as shown in table 1. The mean age was 32,9 (SD 5,6) years. 2 patients (33%) were of Caucasian ethnicity while 4 (67%) were non-Caucasian. All patients were diagnosed with COVID-19 during the third trimester of pregnancy. 2 were asymptomatic while the other 4 were symptomatic. Only 2 patients (33,3%) received treatment with insulin. In all cases, due to the coexistence of two risk factors for the pregnancy's outcome (GD and COVID-19 infection), induction of labour or an elective caesarean section were preferred to spontaneous onset of labour. Among these patients, no complications were observed in childbirth. Only one woman required hospitalization for more than 7 days and this was due to the fact that 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 newborns, who were all allowed to room-in with their mothers.

## **DISCUSSION**

Incidence of COVID-19 disease was not greater among the GD population. Moreover, the infection was not found to worsen the prognosis of GD patients or of 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 glycaemic 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 exiguous number of cases analysed. We expect to increase our study sample in the following months and thus provide further results. The main strength of this study is that it was conducted in one of the six reference centres 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 rate of infection [1-10].

In conclusion, glycaemic monitoring, diet therapy and insulin, when needed, are sufficient for obtaining good metabolic control and a favourable maternal and foetal outcome even amongst women with GD and a concomitant Sars-Cov-2 infection.

### **AUTHOR CONTRIBUTIONS**

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

### **CONFLICTS OF INTEREST**

None declared. Completed disclosure of interests form available to view online as supporting information.

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**Table 1** Maternal and obstetric characteristics of 57 women with gestational diabetes and a concomitant COVID-19 infection.

|   | Maternal age (years) | Multiparous | BMI (kg/m <sup>2</sup> ) | GD Therapy | Ethnicity | Gestational age at COVID-19 diagnosis (weeks) | COVID-19 Symptoms | Covid therapy                                     | Gestational age at deliver | Labour    | Deliver     | Neonatal BW (gr) | HL (cc) | Apgar at 5 min | Analgesia | Breast feeding | Radiological signs | Days of hospitalization |
|---|----------------------|-------------|--------------------------|------------|-----------|-----------------------------------------------|-------------------|---------------------------------------------------|----------------------------|-----------|-------------|------------------|---------|----------------|-----------|----------------|--------------------|-------------------------|
| 1 | 32                   | Yes         | 24                       | Insulin    | Caucasian | 38+0                                          | No                | Heparin                                           | 39+1                       | Induced   | Vaginal     | 3670             | 100     | 10             | Epidural  | No             | No                 | 6                       |
| 2 | 26                   | Yes         | 30                       | Diet       | Magreb    | 38+0                                          | No                | Heparin, hydroxychloroquine, azithromycin, oxygen | 39+2                       | No labour | Elective CS | 3000             | 400     | 10             | Spinal    | No             | Yes                | 7                       |



|   |    |     |      |             |               |      |             |                                                                        |      |                  |                    |          |         |    |              |     |     |    |
|---|----|-----|------|-------------|---------------|------|-------------|------------------------------------------------------------------------|------|------------------|--------------------|----------|---------|----|--------------|-----|-----|----|
| 3 | 27 | Yes | 29   | Diet        | Magr<br>eb    | 33+1 | Fever       | Heparin,<br>hydroxyc<br>hloroquin<br>e                                 | 39+1 | Indu<br>ced      | Vagi<br>nal        | 375<br>5 | 60<br>0 | 10 | Epidu<br>ral | Yes | No  | 6  |
| 4 | 37 | Yes | 29   | Diet        | Hispa<br>nic  | 39+0 | Dispn<br>ea | Heparin,<br>hydroxyc<br>hloroquin<br>e,<br>azithromy<br>cin,<br>oxygen | 39+2 | No<br>labo<br>ur | Elec<br>tive<br>CS | 339<br>5 | 20<br>0 | 10 | Spina<br>l   | No  | Yes | 11 |
| 5 | 32 | No  | 30,5 | Diet        | Magr<br>eb    | 29+1 | Fever       | Heparin,<br>oxygen                                                     | 37+2 | No<br>labo<br>ur | Elec<br>tive<br>CS | 209<br>5 | 20<br>0 | 10 | Spina<br>l   | No  | No  | 49 |
| 6 | 40 | Yes | 31   | Insuli<br>n | Cauc<br>asian | 27+1 | Fever       | Heparin                                                                | 38+2 | No<br>labo<br>ur | Elec<br>tive<br>CS | 364<br>0 | 50<br>0 | 10 | Spina<br>l   | Yes | No  | 7  |

BMI: body mass index; GD: gestational diabetes; BW: birth weight; HL: blood loss at delivery.