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# Prevalence and predictors of postpartum glucose intolerance in Italian women with gestational diabetes mellitus

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ABSTRACT

*Aims:* To determine the prevalence of both prediabetes and type 2 diabetes mellitus (T2DM) by postpartum oral glucose tolerance test (ppOGTT) in Italian women diagnosed with gestational diabetes mellitus (GDM), and identify antepartum predictors of glucose intolerance.
*Methods:* Retrospective study of 454 Caucasian women that underwent a 75 g OGTT between 6 and 12 weeks postpartum in Calabria (Southern Italy) between 2004 and 2012. Prediabetes and T2DM were diagnosed according to the American Diabetes Association (ADA) criteria. Data were examined by univariate analysis and multiple regression analysis.
*Results:* 290 women (63.9%) were normal, 146 (32.1%) had prediabetes (85 impaired fasting glycemia; 61 impaired glucose tolerance), and 18 (4.0%) had T2DM. Of the continuous variables, pre-pregnancy body mass index (BMI), age at pregnancy, fasting plasma glucose (FPG) at gravid OGTT, and week at diagnosis of GDM were associated with prediabetes and T2DM, whereas the parity was associated with T2DM only. For categorical traits, pre-pregnancy BMI $\geq$25 and previous diagnosis of polycystic ovary syndrome (PCOS) emerged as the strongest predictors of prediabetes whereas the strongest predictors of T2DM were FPG $\geq$100 mg/dl (5.6 mmol/l) at GDM diagnosis and pre-pregnancy BMI $\geq$25. Moreover, FPG at GDM screening was a good predictor of T2DM after receiver-operating-characteristic analysis.
*Conclusions:* Our findings confirm the high prevalence of glucose intolerance in the early postpartum period in women with previous GDM. PCOS emerges as a new strong antepartum predictor of prediabetes.



## 1. Introduction

In recent years, gestational diabetes mellitus (GDM), the most common metabolic complication of pregnancy, has acquired greater public health relevance [1,2], due to the fact that its incidence is increasing worldwide, as a consequence of increasing obesity prevalence and advancing maternal age [3,4], and because of the introduction of more rigorous diagnostic criteria for this disorder [5]. There is evidence that

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GDM confers a strong risk for short-term pregnancy complications, such as gestational hypertensive disorders, fetal macrosomia, shoulder dystocia, and cesarean delivery [6,7], in addition to an increase in the risk for future T2DM and cardiovascular disease [8–11]. It has been reported that women with previous GDM have up to 7.5-fold higher risk of developing T2DM compared with women with normoglycemic pregnancy [8–10,12]. Moreover, up to one-third of women with T2DM may have been influenced by former GDM [10]. The tight relationship between GDM and T2DM suggests that GDM may represent an early stage in the natural history of T2DM [13,14], in which pregnancy may constitute a paraphysiological condition of acquired insulin resistance. It is well known that the defect in beta-cell compensation that characterizes GDM is chronic and not acquired during pregnancy, and therefore may underlie the high risk of T2DM in women who have a history of previous GDM [15,16]. Also, GDM and T2DM share many of the same environmental and genetic risk factors [17]. Consistently, despite the delivery of the baby being usually accompanied by resolution of impaired glucose tolerance, a prevalence of upto 46% in persistent abnormal glucose homeostasis [prediabetes or T2DM] in the early postpartum period has been reported [18].

Thus, women with GDM represent a high-risk group for metabolic and reproductive derangements, in which early identification is critical to plan both prevention and intervention strategies that may improve health outcomes [19]. For this reason, it would be desirable to identify women at greatest risk of postpartum T2DM during their pregnancy. So far, many antepartum predictors of postpartum diabetes have been identified [20–28], although none of them has been considered fully satisfactory in terms of prediction of subsequent T2DM. In the current study, we sought to determine the frequency of prediabetes or overt T2DM in the early postpartum period in Calabrian women previously affected by GDM, and to identify antepartum predictors of abnormal postpartum glucose tolerance.

## 2. Subjects, materials and methods

### 2.1. Study population

This study was conducted in the ''Complex Operative Structure Endocrinology-Diabetology'', Hospital Pugliese-Ciaccio, Catanzaro, Italy, where a total of 1342 Caucasian women had been diagnosed with GDM during the period 2004–2012, using the Carpenter-Coustan criteria [29] during the period January 2004 to April 2010, and the International Association of Diabetes and Pregnancy Study Groups criteria (IADPSG) [5] from May 2010 onward. Diagnosis of GDM was performed using an oral glucose tolerance test (OGTT) at 24–28th week of gestation [30]. OGTT was perfomed earlier if one or more of the following conditions applied: severe obesity, strong family history of T2DM, previous GDM, impaired glucose metabolism, or glycosuria [31]. Of the 1342 affected women, we retrospectively enrolled 454 (33.8%) GDM subjects who performed a 2-h OGTT-75 g at 6–12th week postpartum [31]. All consecutive pregnant women with singleton gestation were included. Exclusion criteria were as follows: preexisting type 1 or type 2 diabetes, as defined by ADA criteria [30]; untreated endocrinopathies; use of medications at time of postpartum OGTT (ppOGTT) affecting glucose tolerance; pregnancy at the time of ppOGTT. Patients' age, family history of diabetes (first- or second-degree relatives), previous GDM, pre-pregnancy weight, parity, preexisting PCOS (as defined by ''The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group'' criteria) [32], were recorded at diagnosis of GDM. Relevant data of pregnancy included gestational age at the time of diagnosis of GDM, basal, 60- and 120-min glucose values of OGTT, and insulin requirement. At the time of ppOGTT, breastfeeding and postpartum BMI were also recorded (Table 1). All women with a diagnosis of GDM received nutrition counseling and individualized diet and/or insulin treatment, performed self-monitoring of their blood glucose daily (fasting, and 1 hr after breakfast, lunch and dinner) using a portable glucometer, and underwent periodical (every 2 weeks or more frequently, when appropriate) clinical and biochemical evaluations. The goals of treatment were those indicated by ADA recommendations [33].

**Table 1 – General characteristics of GDM women adherent to ppOGTT.**

| Features | N = 454 |
|---|---|
| Race | Caucasian |
| Age (yr) | 35 (30–38) |
| Family history of T2DM (N) | 330 (72.7) |
| Pregravidic BMI (kg/m$^2$) | 25.4 (22.5–28) |
| Previous GDM (N) | 94 (20.7) |
| Gravidity (N) | 2 (1–2) |
| FPG at OGTT (mg/dl) | 94 (87–99) |
| Week at diagnosis (N) | 27 (24.75–28) |
| Insulin treatment (N) | 188 (41.4) |
| PCOS (N) | 94 (20.7) |
| Postpartum BMI (kg/m$^2$) | 25.7 (23–25.7) |
| Breastfeeding (N) | 212 (46.7) |
| FPG at ppOGTT (mg/dl) | 93 (86–101.25) |

Data are medians (interquartile range), or N (%). FPG, fasting plasma glucose; PCOS, polycystic ovary syndrome.

### 2.2. Statistical analysis

Initially, each quantitative trait was tested for normality of distribution using the Shapiro–Wilk normality test and, when required, it was log-transformed. Continuous variables are expressed as median and interquartile range, and categorical variables as numbers and percentages. The non-parametric Mann–Whitney or Kruskall–Wallis tests were used for comparisons of continuous variables between two or more groups, respectively, whereas the 2-tailed Fisher exact test was used for comparisons of proportions. A significance level of 0.05 was set for a type I error in all analyses. Spearman rank correlation analysis was used to explore the correlations between antepartum continuous traits and postpartum prediabetes and T2DM. All variables were then forced in multivariable regression models with prediabetes or T2DM (yes/no) as the dependent variable. Logistic regression analysis was used to evaluate individual effects of each patient's categorical antepartum characteristic as possible predictor of glucose intolerance at ppOGTT, providing odds ratios (OR) with 95% confidence bounds. Instead, linear regression analysis was