

Universal versus risk factor screening for gestational diabetes mellitus

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Summary

Background: Despite a general consensus about the importance of diagnosis and treatment of gestational diabetes mellitus (GDM), there is no agreement on screening criteria. The aim is to compare the performance of universal versus risk factor-based screening for GDM. **Materials and Methods:** The authors reviewed the medical records of 894 pregnant women, who were screened throughout 75 two-hour 75-gram oral glucose tolerance test (OGTT) between 24 and 28 weeks of gestation, from May 2012 to May 2014 at a single University Hospital. Each patient was evaluated for the presence of risk factors for GDM (age ≥ 35 years old, BMI ≥ 25 kg/m², previous fetal macrosomia, a family history of type 2 diabetes mellitus, and high risk ethnicity). **Results:** Out of the 894 pregnant women, 150 (16.8%) were diagnosed with GDM according to the universal screening. Two hundred five women (22.9%) were at low risk for GDM, while 689 presented at least one or more risk factors. Using a risk factors based screening, 205 low-risk women would have skipped OGTT, but 19 of them (12.7% of women affected by GDM) received the diagnosis of GDM throughout OGTT. Nevertheless, risk factors showed a high strength as predictors of GDM diagnosis, with the exception of age ≥ 35 years. The comparison of maternal fetal outcomes between GDM women with or without risk factors presented no statistically significant differences. **Conclusions:** In the present authors' experience, the implementation of a risk factors based screening may lead to a reduction in the detection rate of GDM women.

Key words: Gestational diabetes mellitus; Pregnancy; Screening.

Introduction

Gestational diabetes mellitus (GDM) is defined as “any degree of glucose intolerance with onset or first recognition during pregnancy” and it is one of the most common medical complications of pregnancy [1]. The condition of hyperglycemia usually disappears within six weeks after delivery, but sometimes some degree of glucose intolerance may persist [2, 3].

According to 2013 WHO recommendations, that are consistent with the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, the diagnosis of GDM any time during pregnancy is established if just one glucose value results abnormal (fasting ≥ 92 mg/dl; one-hour 75-gram oral glucose tolerance test (OGTT) ≥ 180 mg/dl; two-hour 75-gram OGTT ≥ 153 mg/dl) [1, 4].

The detection of hyperglycaemia during pregnancy represents a risk factor for adverse pregnancy outcomes, such as macrosomia (birth weight > 4 or 4.5 kg), large for gestational age newborn (birth weight $> 90^{\text{th}}$ centile for gestational age), pre-eclampsia, and caesarean delivery [5, 6]. GDM seems to increase the risk of perinatal mortality of

about 1.5-fold, even if not statistically significant [6].

GDM is a risk factor of adverse outcomes for both mother and child. It “puts two generations at risk of developing future diabetes mellitus”. During fetal life, maternal hyperglycaemia causes fetal hyperinsulinaemia that increases the fat mass. The result is a greater risk of obesity and insulin resistance in childhood. On the other hand, GDM represents for the mother a risk factor for Type 2 diabetes mellitus [7, 8].

During pregnancy, there is a close correlation between maternal glucose levels and risk of adverse pregnancy outcomes. Indeed, treatment of hyperglycaemia halves the risk of macrosomia, large for gestational age, shoulder dystocia, and pre-eclampsia/hypertensive disorders in pregnancy. So, early diagnosis and therapy of GDM to improve maternal fetal outcome are considered essential [9].

Despite a general consensus about the importance of diagnosis and treatment of GDM, there is no agreement on the screening criteria. In the last years, the choice between universal screening or a risk factor-based screening has been a major issue of debate [10, 11].

The IADPSG developed new recommendations in 2008,

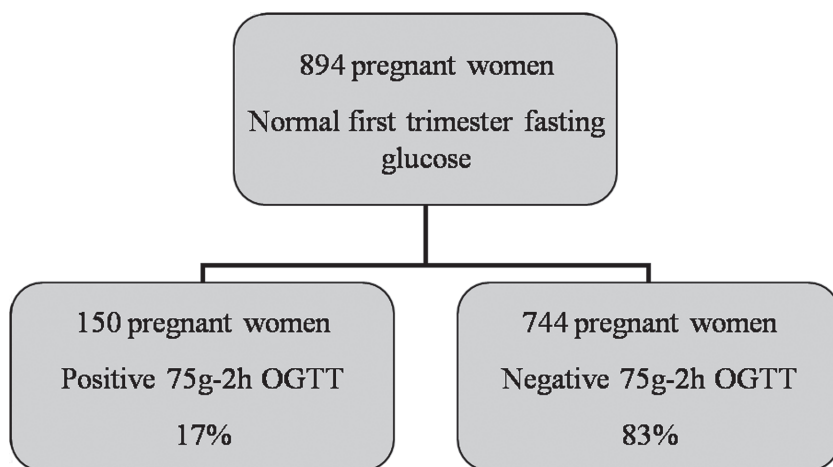


Figure 1. — Incidence of gestational diabetes mellitus in the study population.

based on the results of the HAPO study [5]. They proposed universal screening, offering a two-hour 75-gram OGTT to all pregnant women, between 24 and 28 weeks of gestation [1].

These recommendations were promptly adopted by scientific associations in several countries, including Italy, where the “National Consensus Conference for Recommendations and Implementation of the Guidelines for Screening and Diagnosis of Gestational Diabetes Mellitus” endorsed these new criteria of screening and diagnosis in March 2010 [12].

After few months, the Italian Institute of Health in the Guidelines of Physiological Pregnancy further modified the screening algorithm, introducing a risk factor-based selection of women who should undergo a two-hour 75-gram OGTT. In particular, the OGTT should be offered only to women with at least one of the following risk factors: age ≥ 35 years old, BMI ≥ 25 kg/m², previous fetal macrosomia, family history of type 2 diabetes mellitus or high risk ethnicity [13].

The aims of this study were to compare the diagnostic performance of the two different screening approaches (universal and risk factor-based) in identifying women affected by GDM, and to evaluate the impact on maternal fetal outcomes.

Materials and Methods

This study was carried out at the Operative Unit of Obstetrics and Gynecology of IRCCS San Martino University Hospital – National Institute for Cancer Research in Genoa, Italy.

The medical records of all pregnant women who underwent a two-hour 75-gram OGTT between 24 and 28 weeks of gestation, from May 2012 to May 2014 were reviewed throughout a computerized database.

According with the Italian Guidelines, each patient was evaluated for the presence of risk factors for GDM, such as age ≥ 35 years, BMI ≥ 25 kg/m², previous fetal macrosomia, a family his-

tory of type 2 diabetes mellitus or high risk ethnicity [13].

The diagnosis of GDM was made in presence of at least one altered plasma glucose values at the two-hour 75-gram OGTT. According to the IADPSG guidelines, the abnormal glucose values were: fasting ≥ 92 mg/dl, at one hour ≥ 180 mg/dl, and at two hours ≥ 153 mg/dl [1].

All the women, who received the diagnosis of GDM were followed up and treated according with a multidisciplinary care pathway, with multiple obstetrical and diabetes consultations. The obstetrical outcomes of all patients with GDM were reviewed, with particular attention to preterm delivery (before 37 weeks of gestation), caesarean section, large for gestational age newborn (birth weight $> 90^{\text{th}}$ centile for gestational age), fetal macrosomia (birth weight > 4.5 kg), and neonatal hypoglycaemia.

The study was approved by the Institutional Review Board of our Institution. Statistical analyses were performed using SPSS version 22.0.

Results

The present authors reviewed the medical records of 894 pregnant women, who underwent two-hour 75-gram OGTT between 24 and 28 weeks of gestation. All these women presented a normal first trimester fasting glucose. One hundred fifty of them (16.8%) received a diagnosis of GDM, according with the IADPSG criteria (Figure 1) [1].

Risk factors-based criteria to select women at high risk for GDM were used to the cohort of 894 pregnant women: 205 women (22.9%) resulted at low risk, while 689 presented at least one risk factor for GDM. In this way, according to the recommendation of Italian Institute of Health, 205 patients would skip OGTT [13]. Nevertheless, 19 out of them (2.1% of study population) were diagnosed with GDM and would have been lost to screening by applying the Italian guidelines (Figure 2).

The present authors analyzed the obstetrical outcomes of pregnant women who were diagnosed with GDM, while comparing the group of GDM patients without risk factors (19 women) with the group of women with at least one risk

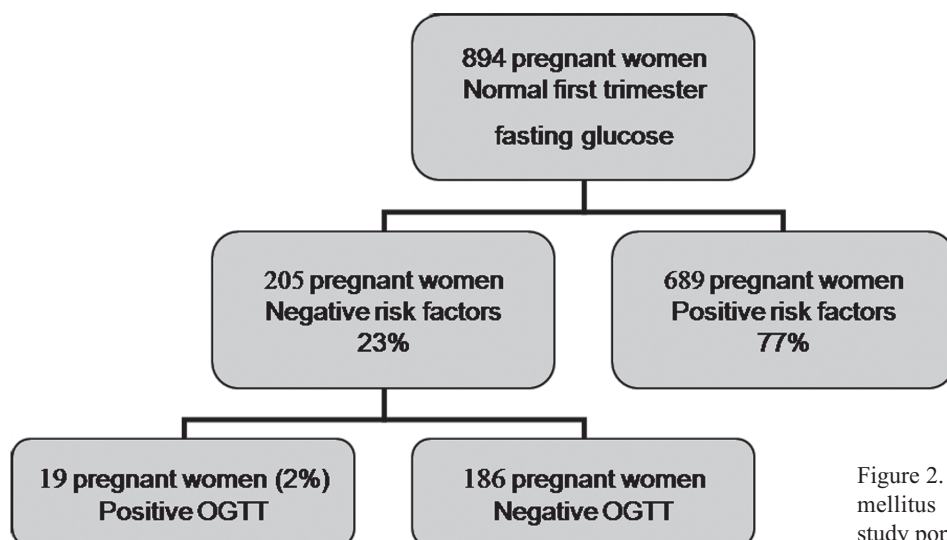


Figure 2. — Incidence of gestational diabetes mellitus and distribution of risk factors in study population.

Table 1. — The obstetrical outcomes of the pregnant women with gestational diabetes mellitus.

Outcome measures	Patients without risk factors (19 women)	Patients with risk factors (117 women)	<i>p</i> statistics
Preterm delivery ^a (frequency)	0	1	1.000
Gestational weeks at birth (mean ± SD ^b)	38.7 ± 1.4	38.8 ± 1.3	0.903
First caesarean section (frequency)	5	55	0.151
Birthweight (grams) (mean ± SD ^b)	3452.37 ± 395.37	3357.36 ± 470.84	0.541
Fetal macrosomia ^c (frequency)	1	10	0.793
Neonatal hypoglycemia (frequency)	2	8	0.922

^a Gestational age at birth < 37 weeks; ^b standard deviation;

^c Birthweight > 4,500 grams.

factor (117 women). Fourteen pregnant women with diagnosis of GDM were lost at follow-up and the pregnancy outcome was not available.

The two groups showed no significant differences about preterm delivery (0 vs. 1, *p* = 1.000), weeks of gestational age at birth (38.7 ± 1.4 vs. 38.8 ± 1.3, *p* = 0.903), first caesarean section (five vs. 55, *p* = 0.151), birthweight (3,452.37 ± 395.37 grams vs. 3,357.36 ± 470.84 grams, *p* = 0.541), fetal macrosomia (one versus ten, *p* = 0.793) and neonatal hypoglycemia (two vs. eight, *p* = 0.922) (Table 1).

The odds ratio (OR) of the risk factors, suggested by the new Italian guidelines, confirmed a close correlation between the diagnosis of GDM and the presence of at least one risk factor [13]. A high positive predictive value

Table 2. — The strength of risk factors, according with the Italian Guidelines, as predictors of GDM diagnosis.

Risk factors	Odds ratio (OR)	Confidence interval 95% (IC 95%)	<i>p</i> statistics
Fetal macrosomia	6.38	1.69-24.04	0.0018
Family history of type 2 diabetes mellitus	4.34	2.97-6.33	0.0001
High risk ethnicity	3.27	1.60-6.68	0.0006
BMI ≥ 25 kg/m ²	2.79	1.93-4.04	0.0001
Age ≥ 35 years	1.49	1.04-2.13	0.0274

was found for fetal macrosomia in previous pregnancy (OR=6.38, IC 95% = 1.69–24.04, *p* =0.0018), family history of type 2 diabetes mellitus (OR = 4.34, IC 95% = 2.97–6.33, *p* < 0.0001), high risk ethnicity (OR = 3.27, IC 95% = 1.60–6.68, *p* = 0.0006), and BMI ≥ 25 kg/m² (OR = 2.79, IC 95% = 1.93–4.04, *p* < 0.0001). Instead, age ≥ 35 years showed a poor correlation with the diagnosis of GDM (OR = 1.49, IC 95% = 1.04-2.13, *p* = 0.0274) (Table 2).

Discussion

The authors analyzed the incidence of GDM in the study population, accounting for 894 pregnant women who underwent two-hour 75-gram OGTT between 24 and 28 weeks of gestation. One hundred fifty of them were diagnosed with GDM, with an incidence of 16.8%. Considering only the Caucasian women (812 patients), the incidence was 15.8%. These data are comparable with the results of the HAPO study that reported an incidence of GDM of 17.8% and it is also similar to the incidence of

GDM in Italy, that ranges from 10.9% to 53.4% [5, 11, 14]. The high variability of the reported incidence of GDM may also depend on the screening methods.

In the study population, 77.1% of patients resulted at high risk for GDM, because of the presence of one or more risk factors [13]. Using the Italian risk factor-based screening, 22.9% of OGTT would have been spared, but 19 women affected by GDM would have been lost (12.7% of patients effectively diagnosed with GDM). In the present authors' experience, the Italian scheme showed a significant reduction of detection rate, although lower than that presented by previous studies [11, 14]. In a population of Southern Italian pregnant women, 25% of patients would not have been diagnosed with GDM for the absence of any risk factor, but sparing 22% of OGTT [11]. Corrado *et al.* reported a loss of 23% of patients effectively affected by GDM, saving 42% of OGTT [14].

In the present cohort of pregnant women, all the risk factors showed a high strength as predictors of GDM diagnosis, with the exception of age ≥ 35 years that showed a poor correlation with the diagnosis of GDM. These findings are in agreement with the study by Corrado *et al.* and the United Kingdom National Institute for Health and Clinical Excellence (NICE) guidelines [14, 15].

The comparison of maternal fetal outcomes between GDM women without risk factors and GDM women with at least one risk factor showed no statistically significant differences. This is in accordance with the HAPO study results [5]. Indeed, the maternal hyperglycemia and the occurrence of adverse pregnancy outcomes seem to be strictly associated, regardless of the presence of any risk factors. Thus, it is very important to early diagnose GDM for introducing an appropriate treatment, to prevent the hyperglycemia related complications for mother and child [16]. Therefore, the Italian risk factor-based screening of the pregnant women, who effectively should undergo a two-hour 75-gram OGTT, does not seem worthwhile. In fact, the sparing of OGTT does not justify the loss of the GDM diagnosis in women with no risk factors.

The present data suggest that the implementation of the new Italian guidelines could lead to a saving of OGTT (23%), but also to a significant proportion of undiagnosed cases of GDM, with the potential loss of benefits for mother and child from an appropriate therapy. In the present authors' opinion, the implementation of a risk factor-based screening should be revised, taking into account the evaluation of the maternal fetal outcomes in GDM women without risk factors, which in the current series did not present a better outcome than women with both GDM and risk factors.

Limitations of this study are its retrospective design and the lack of data about pregnancy outcome of the non diabetic women. Nevertheless, it compared two strategies for detecting GDM in a rather consistent number of women and showed significant differences between the two.

Moreover, the analysis of the present data confirmed the strength of risk factors as predictors of GDM diagnosis, while the lack of any differences between pregnancy outcomes of GDM patients with or without risk factors highlighted the risk of missing the diagnosis of GDM in women apparently at low risk.

In the present authors' opinion, future guidelines will have to consider some major issues: to optimize resources in order to be affordable for the health system, to avoid an excessive *medicalization* of pregnancy leading to anxiety and stress for the couple, and to reduce the risk of missing the GDM diagnosis in patients at low risk. Instead of excluding the universal screening with OGTT, it may be more worthwhile to evaluate the effectiveness of a lower number of obstetrical and diabetes consultations for women achieving an excellent blood glucose control only with diet.

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