

EDITORIAL

Early gestational diabetes: Is fasting glucose useful?☆

Diabetes Gestacional Precoz: ¿Es útil la glucemia en ayunas?

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It is well established that hyperglycemia worsens pregnancy outcomes. This occurs both when diabetes precedes pregnancy and with less severe degrees of hyperglycemia such as gestational diabetes mellitus (GDM). There is evidence that treatment of GDM, at least in women diagnosed after 24 weeks of pregnancy, decreases the occurrence of perinatal complications,¹ and detection and treatment of the condition are therefore fully justified. Less evidence is available on treatment efficacy in women diagnosed before 24 weeks of pregnancy because they are usually excluded from controlled studies.² Although diagnosis of GDM has been and continues to be controversial, debate has recently emerged on disease detection and treatment in this latter group and on the most adequate method for diagnosis. López del Val et al. in a study published in this journal, provided information on the value of fasting blood glucose levels at the start of pregnancy and subsequent diagnosis of GDM.³

GDM is characterized by an impaired carbohydrate metabolism of varying severity that is first diagnosed in pregnancy. Women who meet the criteria for diabetes outside

pregnancy at the start of pregnancy and are included in a separate category, overt diabetes, are now excluded from this group.⁴ Screening for GDM is therefore recommended in women with risk factors for type 2 diabetes mellitus T2DM.

GDM is one of the most common metabolic complications of pregnancy, and its prevalence has increased in recent years in parallel to the increase in incidence of obesity and T2DM, although this increase has been more marked in groups that have adopted the recommendations of the International Association of Diabetes and Pregnancy Study Groups (IADPSG), as shown in Spain by the San Carlos study.⁵ GDM is not only a risk factor for adverse events during pregnancy, but identifies a group of women who are more likely to develop diabetes, metabolic syndrome, and cardiovascular disease in the future. Moreover, exposure to hyperglycemia during intrauterine life appears to confer the offspring a greater risk of obesity, diabetes, and metabolic diseases in adult life. Diagnosis of this disease is therefore considered a public health problem.

Diagnosis of GDM is usually made in the second half of pregnancy, when the pancreatic beta cells are unable to compensate for the insulin resistance that develops during pregnancy, and hyperglycemia occurs. This would actually be pregnancy-induced diabetes. However, in some cases, alterations in carbohydrate metabolism precede pregnancy, with levels of hyperglycemia below frank diabetes and considered early GDM. This is a heterogeneous group, less well characterized and studied, despite the fact that women included in it usually have more severe degrees

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of hyperglycemia than those with GDM diagnosed later in life and that it has been associated to a greater number of complications in pregnancy,² even when treated according to clinical practice guidelines for GDM.⁶ Thus, although the benefits of treatment are assumed, no randomised, controlled studies have been reported showing that treatment of degrees of hyperglycemia less severe than frank diabetes in the first trimester is cost-effective.

Both IADPSG⁴ and the World Health Organization (WHO)⁷ have proposed use of basal blood glucose levels ≥ 92 mg/dL and < 126 mg/dL (≥ 5.1 mmol/L and < 7 mmol/L) for diagnosis of early GDM. The method most commonly used in Spain for screening GDM in the first trimester of pregnancy is the O'Sullivan test, followed by an oral glucose overload of 100 g if positive.⁸ This last strategy has been and continues to be the one recommended by the Spanish Group of Diabetes and Pregnancy (GEDE).⁹ Measurement of fasting blood glucose levels at the start of pregnancy has however become a widespread practice in women with risk factors for T2DM, and diagnostic doubts are sometimes raised. Measurement of basal blood glucose levels has a number of advantages: it is easier and faster to perform, allows for diagnosis of overt diabetes, and does not require administration of a glucose solution, which is often poorly tolerated and/or rejected by patients. On the other hand, the IADPSG decision to transfer the blood glucose cut-off point for GDM diagnosis between 24 and 28 weeks of pregnancy to the start of pregnancy, without taking into account the metabolic changes occurring during pregnancy, has been questioned. In fact, it has been noted that a non-negligible proportion of women who would be diagnosed with GDM based on fasting blood glucose levels at the start of pregnancy do not meet the criteria for GDM between 24 and 28 weeks of pregnancy,^{10,11} and it has even been proposed that the cut-off point is increased to 110 mg/dL (6.1 mmol/L) to increase diagnostic yield.¹¹ This lack of agreement has led some IADPSG members to suggest that fasting blood glucose levels are not used for diagnosis of early GDM,¹² but they have offered no alternatives. In this context, and despite the little evidence available, use of basal blood glucose levels for screening before 24 weeks of pregnancy would allow for integrating the preferences of pregnant women and for prioritizing diagnosis of overt diabetes.¹³

López del Val et al.,³ in their retrospective observational study on 1425 pregnant women measured fasting blood glucose levels in the first trimester of pregnancy, confirmed this lack of agreement. Of all study patients, 193 had fasting blood glucose levels of 92 mg/dL or higher (5.1 mmol/L), and when assessed after 24 weeks of pregnancy, 60% had a positive O'Sullivan test and only 20% were diagnosed with GDM, as compared to 31.7% with positive tests and 3.7% diagnosed with GDM in the group of patients with fasting blood glucose levels less than 92 mg/dL (5.1 mmol/L). When analyzing the results of this study, the low prevalence of GDM seen as compared to another study conducted in the same geographical area in a group of women with similar clinical characteristics and with the same diagnostic criteria should be considered.⁵ Another interesting aspect of this study is the potential impact of obesity on perinatal outcomes. Women who had been diagnosed with GDM based on basal glucose levels in the first trimester, but who did not meet the criteria between 24 and 28 weeks, had bigger

babies and higher rates of macrosomia and obstetric trauma than those who were diagnosed and treated. However, association to birth weight was lost after adjusting for maternal obesity, which suggests that factors other than blood glucose levels may be involved.

Based on these results, and on other previous/planned studies,^{10,11} fasting blood glucose levels before 24 weeks, at least with the cut-off point established by the IADPSG, do not appear to be a reliable tool to recognize patients who will develop GDM in the second half of pregnancy. However, they identify a group of women at increased risk for development of perinatal complications^{2,3} and with a profile similar to what would be a metabolic syndrome outside pregnancy, with greater insulin resistance, higher triglyceride, fatty acid and blood pressure levels, and greater waist circumference.¹⁴ For this reason, although it seems clear that these women could benefit from closer monitoring and probably from a therapeutic intervention, the type and intensity of treatment to be performed remains to be established, because dietary intervention appears to be insufficient.¹⁵ This is even more important knowing that some interventions during critical periods of life may lead to fetal programming that increases the risk of disease in adult life. For this reason, randomised controlled studies would be essential to establish which patients will benefit from detection and treatment of the condition.

Conflicts of interest

The author states that he has no conflicts of interest.

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