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Redefinition of gestational diabetes mellitus

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Abstract

Background: An ongoing epidemic of obesity and type 2 diabetes mellitus worldwide, as well as a more advanced maternal age has increased the number of women with undiagnosed gestational diabetes mellitus (GDM). International Association of Diabetes and Pregnancy Study Groups (IADPSG) has recently issued recommendations on the diagnosis and classification of hyperglicemia in pregnancy, and American Diabetes Association (ADA) and World Health Organization (WHO) have adopted them and revised the previous criteria. Therefore, the aim of the study was to evaluate the prevalence of GDM according to IADPSG recommendations and to compare them with the former WHO and ADA criteria.

Methods: The study included 208 women ages between 16 - 42 years who underwent a two-hour oral glucose tolerance test (OGTT) with 75 g glucose between 24 - 28 weeks of gestation, without previously diagnosed overt diabetes.

Results: Based on IADPSG criteria, GDM was diagnosed in 44 women (21.1%) who were significantly older than their healthy counterparts (33.2±5.42 vs. 29.4±5.12 years; p=0.0001). Only 12 women (27.3%) with GDM were younger than 30 years, whereas a total of 32 women (72.7%) were older than 30 years. On the other hand, using the previous WHO criteria, GDM was diagnosed in 10.1 % women, and only 2.4% of women were diagnosed with GDM based on the old ADA criteria.

Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with the onset or first recognition during pregnancy (1). An ongoing epidemic of obesity and type 2 diabetes mellitus (T2DM) worldwide, as well as a more advanced maternal age has increased the number of women with undiagnosed gestational diabetes mellitus (GDM) (2, 3).

There are two main pathways leading to GDM and T2DM: insulin resistance and chronic subclinical inflammation (4). Insulin resistance is caused by the inability of tissues to respond to insulin and the deficient secretion of insulin by pancreatic beta cells. On the other hand, the general low-grade chronic inflammatory state, closely related to obesity, by secreting adipokines from enlarged adipose tissue cells, and additional infiltration and accumulation of macrophages in adipose tissue, by secreting inflammatory cytokines can also affect insulin signaling.

Women with a history of GDM have an increased risk of developing diabetes after pregnancy compared to the general population, complicating further pregnancies (5). On the other hand, the relationship between decreased maternal insulin sensitivity and fetal overgrowth particularly in obese women and women with gestational diabetes may help explain perinatal morbidity and mortality and the increased incidence of adolescent obesity and related glucose intolerance in the offspring of these women (5). Furthermore, obesity in adolescence results in an increased risk of metabolic syndrome (6) and coronary artery disease (7).

In the light of all these facts, since GDM can have long-term pathological consequences for both mother and her child, it is of great importance to be promptly recognized and adequately treated. The large, prospective Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study (8) reported continuous association of maternal glucose levels even within ranges previously considered normal for pregnancy, with adverse pregnancy outcomes. Based on the results of the HAPO study, in 2010, International Association of Diabetes and Pregnancy Study Groups (IADPSG) has proposed a new set of diagnostic criteria for GDM (9). In addition, the American Diabetes Association (ADA) (1) in 2011, and World Health Organization (WHO) in 2013, have adopted these proposed criteria (10).

The primary purpose of addressing this issue is to raise awareness of the importance of adequate diagnosing and, thus, appropriate treating women with any form of diabetes in pregnancy. So, we aimed to evaluate the prevalence of GDM when applying the new diagnostic criteria, and compare these results with the previous WHO and the ADA criteria.

Methods

The study enrolled a total of 208 pregnant women between the ages of 16 and 42 years who underwent a two-hour oral glucose tolerance test (OGTT) with 75 g glucose, between 24 and 28 weeks of gestation, without previously diagnosed overt diabetes. Participants were recruited by the gynecologist in the Center of Laboratory Diagnostics, Primary Health Care Center in Podgorica for screening, in a period from November 2012 to

July 2013. Participants were instructed to fast for at least 8 hours before the phlebotomy, when scheduling the test the day before. Exclusion criteria were pregnant women who met overt diabetes criteria (fasting glucose ≥ 7.0 mmol/L or 2h glucose ≥11.1 mmol/L) (n=2), those who were not completed the test (n=8), as well as those who did not fast for at least 8 hours before the phlebotomy (n=5).

All the participants volunteered to participate in the study and provided written informed consent. The study protocol was approved by institutional ethics committee and the research was carried out in compliance with the Declaration of Helsinki.

Biochemical measurements

The first phlebotomy was performed between 7-9 hours a.m., after an overnight fast of at least 8 hours. Plasma glucose was measured using standardized enzymatic procedure (reference method with hexokinaze) by spectrophotometer (Roche Cobas 400, Mannheim, Germany) (11). The second and the third phlebotomy were performed one hour and two hours respectively, after loading a 75 g anhydrous glucose dissolved in 250 ml of water (OGTT). All participants were instructed to seat and were not allowed to eat or drink for the whole time of during the test. Blood samples were centrifuged at 3000 rpm for 10 minutes, separating plasma from the cells within 30 minutes from the time of sampling in order to avoid in vitro glycolysis (12).

According to IADPSG criteria, the diagnosis of GDM is made if at least one value of glucose concentration is equal or exceeds the thresholds of ≥5.1 mmol/L, ≥10.0 mmol/L, and ≥8.5 mmol/L (for fasting, one-hour and two-hour post load glucose values respectively), after performing a 75 g OGTT (9).

The old ADA criteria for GDM required two plasma glucose values ≥5.3 mmol/l (fasting), ≥10 mmol/l (1 h), and ≥8.6 mmol/l (2 h) after performing a 75 g OGTT (13).

The previous WHO criteria required a plasma glucose ≥7.0 mmol/l (fasting) or ≥7.8 mmol/l (2h) after performing a 75 g OGTT (14).

Statistical analyses

Statistical analyses were performed using SPSS statistical package (version 15.0 for Windows, SPSS, Chicago, IL, USA). Data are presented as mean ± standard deviation or counts and percentages. Differences between groups were evaluated with a Student's t test. A p value of < 0.05 was considered as statistically significant.

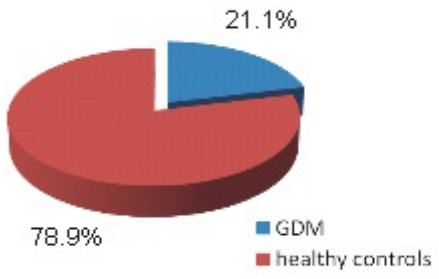

Figure 1 The prevalence of GDM according to the IADPSG criteria

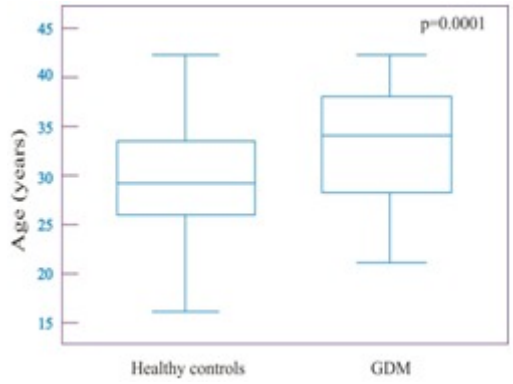

Figure 2 The mean age of the study participants

Results

Based on IADPSG criteria, GDM was diagnosed in 44 women (21.1%) (Figure 1).

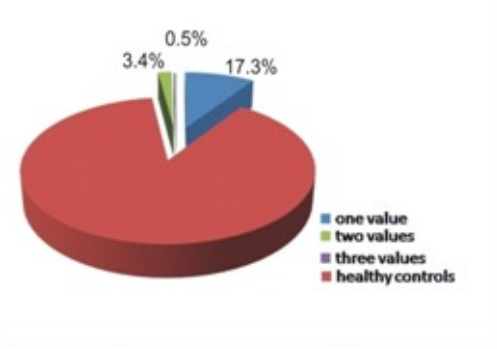

Figure 3 The prevalence of GDM according to the IADPSG criteria with one, two and three abnormal values of glucose level

Women diagnosed with GDM were significantly older than their healthy counterparts (33.2±5.42 vs. 29.4±5.12 years; p=0.0001) (Figure 2).

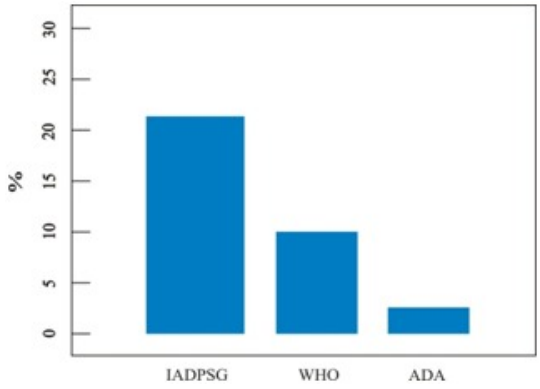

Figure 4 The comparisons of prevalence of GDM according

Only 12 women with GDM were younger than 30 years (27.3%), whereas a total of 32 women with GDM were older than 30 years (72.7%).

A total of 17.3% women had one value, 3.4% had two, and only 0.5% had all of the three values equal or exceeding the thresholds (Figure 3).

On the other hand, using the previous WHO criteria, GDM was diagnosed in 10.1 % of women, and only 2.4% of women were diagnosed with GDM based on the old ADA criteria (Figure 4).

Discussion

Hyperglycemia in pregnancy is an asymptomatic condition and diagnosis is dependent on some form of screening. However, due to differencies in screening programmes and diagnostic criteria, the comparisons of frequencies of GDM among various populations has been difficult, leading to serious controversies in epidemiological data and clinical practice (15). There has been a variety of OGTTs, with a different glucose loads (50 g, 75 g and 100 g glucose) and different durations (2h and 3h), as well as different approaches of whether to screen all, or only women at high risk for the development of GDM (13, 14, 16, 17, 18).

The first study to provide a solid evidence of a direct association between maternal glucose level and pregnancy outcome was the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study (8). The HAPO study was the largest multinational prospective study that included 25.505 women who underwent 75 g OGTT at 24-32 weeks of gestation. This study demonstrated that there was continuous, positive association of maternal glucose levels below diagnostic cut-offs for diabetes with adverse pregnancy outcomes: birth weight for gestational age and cord-blood serum C-peptide levels above 90th percentile, primary cesarean delivery, and neonatal hypoglycemia. Based on the incidence of adverse perinatal outcomes, as assessed in the HAPO study, International Association of Diabetes and Pregnancy Study Groups (IADPSG) has recently proposed a new set of diagnostic criteria for GDM (9). According to IADPSG criteria, the diagnosis of GDM is made if at least one value of glucose concentration is equal or exceeds the thresholds of ≥5.1 mmol/L, ≥10.0 mmol/L, and ≥8.5 mmol/L (for fasting, one-hour and two-hour post load glucose values respectively), after performing a 75 g OGTT. These arbitrary thresholds, when applied to the HAPO cohort, led to a GDM incidence of 17.8%. In addition to this, 11.1%, 3.95%, and 1.1% of pregnant women had one, two and three values of glucose above the threshold, respectively.

In 2011, ADA (1) has adopted the IADPSG criteria and revised the previous ones. Recently, their diagnostic criteria for gestational diabetes has also gained acceptance by WHO (10) in the interest of moving towards a universal standard recommendation for the diagnosis of GDM. Considering that the first step of screening for hyperglycemia in pregnancy involves fasting plasma glucose in the first trimester of gestation and diagnosis of either GDM or overt diabetes according to the IADPSG criteria, correct classification in the first place will not only improve pregnancy outcomes, but also reduce unnecessary OGTT, as only women with fasting plasma glucose in the first trimester of gestation below 5.1 mmol/L are eligible for testing at 24-28 weeks of gestation (12).

In our study the prevalence of GDM was 21.1%, which is significantly higher than when using the former WHO and ADA criteria. Women diagnosed with GDM were significantly older than their healthy counterparts, which is in accordance with previous results of advanced age of women with GDM (2, 3). Solomon et al. (3) reported that the risk rose by about 4% for every year after the age of 25. The incidence of GDM at < 20 years of age was <1%, 20-30 years, 2% and > 30 years, 8-14%. Moreover, the results of our study show that the prevalence of GDM is higher among women older than 30 years, accounting for 72.7% of all women diagnosed with GDM. However, we cannot exclusively confirm that either of our pregnant women had previously not-known pre-existing DM, or GDM in a previous pregnancy but nevertheless, this does not diminish the significance of our results, since the early diagnosis and appropriate management of both GDM and pre-existing diabetes in pregnancy are of paramount importance in avoiding adverse pregnancy outcomes. On the other hand, preventive care may decrease not only the risk for the woman, but also for her offspring. Moreover, it is of great importance to note that in 2 intervention studies (19, 20) that focused on women with more mild hyperglycemia than identified using older GDM diagnostic criteria, 80-90% of women could be managed with lifestyle therapy alone, showing encouraging results.

The limitations of our study must be emphasized. Unfortunately, this study, like others (2, 21), lacks data on maternal height and weight to assess maternal body mass index and the prevalence of obesity in the screened population. Furthermore, as our study was not based on general population, selection bias might have affected the outcome of the study. So, the utility of screening might have varied due to different baseline characteristics of the screened population. Thus, larger sample size in general population of pregnant women and prospective design with monitoring perinatal outcomes are required to confirm and extend the results of the present study.

Conclusion

The use of new diagnostic glucose cut-off values increases the prevalence of GDM as compared with the previous WHO and the ADA criteria, as would be expected primarily because only one abnormal value, but not two (the former ADA criteria), is sufficient to make the diagnosis. Moreover, the recommended glucose cut-off values for GDM proposed by IADPSG are lower than those recommended by earlier guidelines. Are these criteria good enough, it remains to be seen. Nevertheless, preventive measures should be aimed by Public Health Initiatives for reducing this trend, in the first place by assessing lifestyle interventions before and during pregnancy, such as healthier dietary pattern, with low-fat and low-carbohydrate nutrients, as well as physical activity, which may help in avoiding adverse pregnancy outcomes in women with GDM.

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