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Gestational diabetes mellitus prevalence: Effect of the laboratory analytical variation

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ABSTRACT

Aims: To highlight the effect of laboratory analytic variation, assessed by glucose (a) total analytic laboratory error (TAE_L) present in one index laboratory and (b) total recommended allowable error (TAEa) universally applicable to all laboratories, on the prevalence of gestational diabetes mellitus (GDM).
Methods: 2337 pregnant women underwent a 75-g oral glucose tolerance test (OGTT) for universal GDM screening. Since the true value of every laboratory result fluctuates within a range, the glucose TAE_L and TAEa were used to define a lower and an upper diagnostic threshold (95% confidence interval, CI) for the three glucose OGTT cut-offs of the criteria of the American Diabetes Association, ADA (2003); the Canadian Diabetes Association, CDA (2013) and the International Association of Diabetes and Pregnancy Study Groups, IADPSG (2010).
Results: For the ADA, CDA and IADPSG criteria, respectively, the GDM prevalence [95% CI, (glucose TAE_L) (glucose TAEa)] was 13.3% [(8.0–21.8) (6.3–25.9)], 30% [(17.3–53.1) (14.3–61.3)] and 45.3% [(27.0–71.0) (22.3–79.2)]. Using the lower and higher assigned OGTT glucose thresholds for TAE_L, respectively, among the different criteria, either 200 (8.6%)–601 (25.7%) additional or 122 (5.2%)–426 (18.3%) fewer women would be identified with GDM ($p < 0.0001$).
Conclusions: Independent of the diagnostic criteria, any reported GDM prevalence can potentially vary between one half to two times even for laboratories meeting recommended quality specifications. To avoid misclassifying women with GDM substantially, individual laboratories can significantly reduce this disparity by improving analytic performance. All physicians must ensure that their laboratory meets acceptable quality standards for optimal patient care.

1. Introduction

Gestational diabetes mellitus (GDM) or hyperglycemia first identified during pregnancy is associated with several maternal and fetal complications like preeclampsia, increased caesarean sections and birth injuries [1,2]. A diagnosis of GDM is confirmed by the oral glucose tolerance test (OGTT) with various health organizations recommending different glucose thresholds for diagnosis; as a result, many international diagnostic criteria are available for diagnosis. Depending on which one of these diagnostic criteria is used and the

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ethnicity of the population, the prevalence of GDM varies widely from 1.1 to 25.5% [3]. Generally, the laboratory quality (reflected by the glucose analytic variability) is not implicated as a cause for the variation of GDM prevalence. In analytical terms, quality of laboratory results is quantified by the degree of imprecision (reproducibility) and extent of bias (variation from the true value). Ideally, for good laboratory performance both the imprecision and bias should be minimal and meet specified analytic regulatory criteria; if not, the medical diagnosis may be compromised [4]. This is even more crucial for diagnoses which rely on fixed laboratory test thresholds, e.g., GDM (glucose), diabetes mellitus (HBA_1c) and myocardial infarction (troponin) [5].

The United Arab Emirates (UAE) is a multi-ethnic community with the prevalence (approximately 19.2%) of type 2 diabetes mellitus (DM) among the highest in the world [6]. The prevalence of GDM in the UAE varies from 7.9% to 37.7%, depending on the criteria used for the diagnosis [7,8]. In any country, the quality of laboratories varies and ideally every laboratory should be accredited for excellent patient care [9]. This accreditation is provided by a national regulatory body or an international organisation like College of American Pathologists (CAP) or International Organization for Standardization (ISO 15189); however, in the UAE many hospitals (both federal and private) have unaccredited laboratories—a situation analogous to many countries worldwide.

This study was done to document the effect of laboratory quality, assessed by the glucose (a) total analytic error (TAE_L) present in one specific laboratory and (b) total allowable error (TAEa) recommendation of the National Academy of Clinical Biochemistry (NACB) [10], applicable to all laboratories, on the prevalence of GDM as defined by three international expert panels.

2. Materials and methods

2.1. Patients

The pregnant women in this study were attending the routine antenatal clinics at Tawam Hospital (under aegis of Johns Hopkins International), Al Ain, United Arab Emirates. A total of approximately 2500 women are delivered annually at this hospital. During the 12-month study period (January 1, 2012–December 31, 2012), as part of a universal screening program, all the 2384 women registered for antenatal care underwent a diagnostic 2-h, 75-g OGTT. This OGTT was scheduled between 24 and 28 weeks gestation but performed at other gestations, if clinically warranted. Forty-seven women were not able to finish the OGTT due to vomiting, eating food during the test, refusal to undergo the test or other reasons. The data from the remaining 2337 pregnant women, who completed the 75-gm OGTT, were used for the study.

2.2. Glucose analysis and diagnostic criteria for GDM

A standard OGTT protocol was followed. After a 12-h overnight fast, venous plasma samples were collected for fasting (F), 1-h and 2-h post oral 75-gm glucose. The plasma glucose was estimated by the glucose oxidase method (DXC-800, Beckman-Coulter Instruments, Brea, California, USA). The hospital laboratory is accredited by the CAP and participates in their external proficiency testing program.

Since the prevalence of GDM is dependent on the diagnostic criteria used, in order to get a better estimate of the effect of glucose analytic laboratory variation, the prevalence was obtained by applying the diagnostic criteria of three different international expert panels (from the many available) to the results of the same OGTT (Table 1), i.e., American Diabetes Association (ADA) 2003 [11]; Canadian Diabetes Association (CDA) 2013 [12], International Association of Diabetes and Pregnancy Study Groups (IADPSG) 2010 [13]. The IADPSG approach was endorsed by the ADA in 2011, World Health Organization in 2013 [2] and the International Diabetes Federation in 2014 [6].

2.3. Analytical performance standards

Imprecision is the reproducibility of replicate measurements (expressed as coefficient of variation (%), CVa) while bias (B) is the difference of a laboratory result from its true value (expressed as a percentage of the true value). The imprecision and bias components of laboratory error are combined into the concept of total laboratory analytic error (TAE_L). At 95% confidence limits ($p < 0.05$) the TAE_L can be calculated using the following formula [14]:

$$TAE_L(\%) = 1.65 * CVa\,(\%) + B\,(\%)$$

Imprecision of glucose for the laboratory was calculated from three levels of commercial human liquid control material used over the study period. The laboratory bias of glucose was determined by the difference in the glucose results reported by the laboratory compared to the target reference values of glucose proficiency testing (PT) program of the College of American Pathologists during the study period.

The analytical performance of any laboratory can be judged against objective quality specifications, e.g., those proposed by the venerable NACB guidelines for total maximum allowable error (TAEa). For glucose, the NACB maximum permissible targets are as follows: imprecision <2.9%, bias <2.2% and TAEa <6.9%, which were used in this study [10].

Every laboratory test result ('the reported value') is not absolute and unequivocal, but it varies between a range (a low and a high value), which covers the 95% confidence interval (CI) of the reported value; this range depends on the laboratory performance for that analyte. Applying this concept glucose test variation to the diagnosis of GDM, based on the laboratory imprecision and bias, the diagnostic threshold range was calculated for each of the three cut-off glucose levels (of the OGTT) of the three selected international expert panel's GDM criteria, for (a) the laboratory (TAE_L) used in this study and (b) NACB recommended maximum allowable error (TAEa). The TAE_L documents the variation of GDM prevalence in one index hospital laboratory; the TAEa reflects the potential effect on GDM prevalence of the maximum allowed glucose variance and therefore applies to any hospital globally meeting the laboratory recommended standards. In general, better laboratories, generally accredited, consistently produce reproducible results with less imprecision and less bias resulting in better patient care [9]. Laboratory accreditation is a self-regulating