Letter to the editor

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A national survey of preanalytical handling of oral glucose tolerance tests in pregnancy

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To the Editor,

While the criteria for the diagnosis of gestational diabetes mellitus (GDM) continue to be mired in controversy with a lack of international consensus, many countries and the World Health Organization have adopted the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommendations [1]. In addition, revised stricter recommendations have also been produced and endorsed by the National Academy of Clinical Biochemistry (NACB) for laboratory standards in the analysis of maternal glucose measurements [2].

Glycolysis of samples leading to the underestimation of glucose levels is long established. Previously, the recommendation was for plasma to be separated from the cells within 60 min; if this was not possible, a tube containing sodium fluoride was recommended for sample collection [3]. Revised recommendations have introduced the placement of fluoride tubes on an ice-slurry. The interval to cell separation and analysis has been reduced from 60 to <30 min. If this is not possible, the use of a citrate buffer is recommended because with delayed separation and without an ice-slurry, it is a more effective glycolysis inhibitor than sodium fluoride [2, 3]. These laboratory standards have assumed greater importance for the diagnosis of GDM now that it can be made on the basis of one increased value with the IADPSG criteria, and not two as previously [4].

The importance of preananalytical inhibition of glycolysis in the diagnosis of GDM has been shown in two recent studies we have reported in women being screened using a one-step 75 g oral glucose tolerance test (OGTT) using the latest IADPSG diagnostic criteria [5, 6]. In 24 obese women, the incidence was 54% when the NACB recommendations (placement of fluoride sample tubes on an ice-slurry; separation and analysis within 30 min) for the OGTT were implemented compared to 17% when they were not (fluoride sample tubes kept at room temperature; transfer to laboratory for separation and analysis deferred until after all three samples were collected) ($p<0.01$) [5]. In a larger study of all women screened selectively with an OGTT (n=155), the incidence was 38% when the NACB recommendations were implemented compared with 14% when they were not ($p<0.001$) [5, 6].

The maternity services in Ireland are highly centralized with all 19 units around the country delivering >1000 women annually. Of the 19, 18 have a biochemistry laboratory on site within walking distance of the maternity outpatients department. In one unit, the samples have to be transferred a short distance by car from the maternity hospital to the laboratory in the acute general hospital. Like other countries, there are no national recommendations in Ireland for preanalytical laboratory standards in maternal glucose measurements. Furthermore, wide variations between maternity units in the incidence of GDM have been recently reported [7]. We therefore carried out a cross-sectional study of the preananalytical handling of glucose samples in all 19 units in the Republic of Ireland.

In January 2015 a senior laboratorian in each of the 19 maternity units in Ireland was telephoned, and a standardized questionnaire was completed based on the NACB laboratory standards on the procedure for OGTTs and the national guidelines for GDM [3, 8]. Clinical staff involved in the care of women with GDM verified all responses. This study complied with the World Medical Association Declaration of Helsinki regarding ethical conduct of research involving human subjects.

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Q1: P value is with three decimal places. It is not acceptable term NS (not significant) or P<0.05. Always specify the exact obtained value. When you have P <0.0001 then write in the form P <0.001 (always with three decimal places)

All units offered selective screening for GDM. The fasting duration varied from six to 12.5 h nationally. Despite the national guidelines recommending the 1-step 75 g OGTT, one unit (5.3%) performed a two-step screening test, 18 (94.7%) performed a one-step test (p<0.0001). For the OGTT, two units (10.6%) used a 100 g load, and 17 (89.4%) used a 75 g load (p<0.0001). Of those using the 75-g OGTT, four units (20.4%) performed a modified OGTT with only two samples: a fasting and the 2-h sample, 13 (68.4%) used the 3-sample OGTT (NS). Of 19 units, the laboratories at 14 (73.7%) received OGTTs that were performed peripherally (in primary care or an outlying antenatal clinic) (p<0.05).

Polycal was the loading challenge source of glucose used in seven units (36.8%), and Lucozade in 12 (NS). Time taken to drink the glucose load varied from 5 min to "in the woman's own time". Eight of 19 (42.1%) units documented the time at which the glucose was finally consumed (NS). Fluoride was the glycolysis inhibitor used in all units (p<0.0001).

Of the 19 units, 17 (89.5%) reported deferring transport of samples to the laboratory until all samples were collected for each woman; only two units (10.5%) reported occasional transport of samples individually to the laboratory (p<0.0001). None of the units placed fluoride samples on an ice-slurry (p<0.0001)- none of the clinical staff were aware of this recommendation [3]. In one unit (5.3%), samples were held overnight before transfer to another hospital for analysis. The phlebotomy-analysis interval, therefore, varied nationally from 2.25–24 h (both minimum and maximum intervals p<0.0001 when compared with recommended 30 min). Two units (10.5%) received samples from primary care that had been refrigerated.

This national survey of all maternity units found that the adherence to national clinical guidelines on GDM and to international laboratory standards for preanalytical management of OGTT glucose samples was suboptimal [3, 8]. A previous Irish study of the implementation of guidelines for gestational diabetes reported threefold differences in GDM between units from 2.2%–7.4%, which raised the strong possibility that GDM is being underdiagnosed [7].

To our knowledge, this is the first national survey of preanalytical handling of OGTTs during pregnancy. Our findings may differ from other countries worldwide. However, informal discussions with colleagues in other English-speaking countries leads us to believe that obstetricians worldwide are, in general, unaware of the importance of preventing glycolysis in maternal glucose samples.

These wide variations in preananalytical standards nationally are potentially serious clinically and legally because if GDM is underdiagnosed, maternal hyperglycaemia may potentially lead to complications such as fetal macrosomia, shoulder dystocia and a brachial plexus injury. Thus, we suggest all countries should develop their own laboratory standards for maternal glucose analysis and preanalytical handling, which are implemented strictly in all settings. Particular care needs to be taken with the fasting plasma glucose for diagnostic purposes whatever threshold is applied. Finally, we recommend that future clinical studies of GDM should state their preanalytical as well as their analytical standards in the methods section of their reports [6].

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