The Diagnosis and Management of Gestational Diabetes Mellitus in the Context of the COVID-19 Pandemic

H. David McIntyre[1] and Robert G. Moses[2]

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The oral glucose tolerance test (OGTT) has, to date, been considered the cornerstone of the diagnosis of gestational diabetes mellitus (GDM). This is despite ongoing national and international disagreement regarding which women require testing, whether "one step" or "two step" testing is optimal, and which glucose thresholds should be used.

However, in the context of the current coronavirus disease 2019 (COVID-19) pandemic, widespread anecdotal evidence suggests that both clinicians and pregnant women are increasingly unwilling to recommend or undergo the OGTT. This is based on valid concerns regarding travel, the possible need for two visits, and the time (up to 3 h) spent in the potentially infectious environment of specimen collection centers. Further, a GDM diagnosis generally involves additional health service visits for diabetes education, glucose monitoring review, and fetal ultrasonography, all of which carry exposure risks during a pandemic.

In response to these concerns, professional societies from the U.K. (1), Canada (2), and Australia (3) have released urgent statements of advice/guidance for modification of GDM diagnostic pathways during the COVID-19 pandemic. Current GDM guidelines differ in each of these jurisdictions, as do the revised recommendations. All seek to reduce the need for OGTTs, both during pregnancy and in postpartum follow-up. All guidelines support use of an early pregnancy HbA_{1c} ≥41 mmol/mol (5.9%) to identify GDM, though some offer other options.

The revised recommendations for standard (24- to 28-week) GDM testing are more divergent. The U.K. currently advocates risk factor–based testing for GDM, and its revised guideline recommends testing of "at risk" women and diagnoses GDM with any of the following: HbA_{1c} ≥39 mmol/mmol (5.7%), fasting venous plasma glucose (VPG) ≥5.6 mmol/L (preferred), or random VPG ≥9.0 mmol/L. Canada's current preferred pathway includes a 50-g glucose screen with formal 75-g OGTT if 1-h glucose is 7.8–11.0 mmol/L. The revised Canadian pathway accepts an HbA_{1c} ≥39 mmol/mol (5.7%) and/or random VPG ≥11.1 mmol/L as GDM. Australia previously recommended a formal 75-g OGTT for all women. The revised Australian pathway does not include HbA_{1c} but recommends a fasting VPG with progression to OGTT only if this result is 4.7–5.0 mmol/L. Fasting VPG <4.7 mmol/L is considered non-GDM, and ≥5.1 mmol/L confirms GDM (based on the World Health Organization [WHO] criteria using the HAPO [Hyperglycemia and Adverse Pregnancy Outcome] odds ratio of 1.75).

Furthermore, in practical terms, the Australian guideline recommends that women with previous GDM should be considered to have GDM in the current pregnancy without further testing. In addition, unless there is a reasonable suspicion of postpartum type 2 diabetes, postpartum follow-up testing, most likely using an OGTT, should be delayed until either the pandemic has been controlled or another pregnancy is contemplated.

It is very likely that by the time of this publication, most countries will have considered and adopted patient-sensitive and safety-motivated revised criteria. To the best of our knowledge, no revised recommendations have been produced specifically for the U.S. health care context. It appears improbable and certainly not practical that any consistent international criteria will be considered or adopted. Therefore, any national or local guidelines should be developed with the primary aim of being protective for pregnant women and workable in the current health crisis.

All published advice notes that the revised recommendations are temporary in response to the unprecedented challenges of the COVID-19 pandemic. The U.K. guidelines have already been amended, suggesting that recommendations will certainly change over time. In general, the revised pathways favor

[1]*Mater Research, The University of Queensland, Brisbane, Queensland, Australia*
[2]*Wollongong Hospital, Illawarra and Shoalhaven Local Health District, Wollongong, New South Wales, Australia*
Corresponding author: H. David McIntyre, david.mcintyre@mater.org.au

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specificity over sensitivity, and it is inevitable that they are likely to "miss" many women currently diagnosed with and treated for GDM, detecting only those with more marked hyperglycemia. Further, the authors appropriately acknowledge that the evidence base for these revised pathways is limited and that each alternative strategy should be evaluated over the course of the current pandemic. It is also possible that the knowledge and experience gained from these changes may influence the reestablishment of national and international recommendations.

We hope that appropriate clinical data collection will allow evaluation of the appropriateness of these strategies over time. Certainly, the OGTT is beloved by very few, and validation of alternative, less cumbersome strategies for diagnosis and classification of GDM are needed. HbA_{1c} has the theoretical advantage of representing mean glycemia over time and the practical advantage of being a nonfasting test. Hence, it forms a key part of the revised U.K. and Canadian guidelines. However, HbA_{1c} is less strongly related to adverse pregnancy outcomes than individual or mean OGTT glucose measures (4). Further, the HbA_{1c} threshold of 39 mmol/mol (5.7%) recommended in the revised U.K. and Canadian guidelines approximates the 99th centile for the HAPO cohort (4). Testing using this HbA_{1c} threshold alone would thus reduce GDM frequency in the HAPO cohort from 17.8% using IADPSG (International Association of the Diabetes and Pregnancy Study Groups) criteria (5) to around 1%. Thus, the vast majority of women currently considered to have GDM would remain undetected and untreated. Validation and regulatory approval of new, nonfasting biomarkers, of which glycated CD59 (6) is currently the most promising, would be welcomed by both clinicians and pregnant women.

Beyond GDM diagnosis, the U.K. (1) and Canadian (2) guidelines also recommend provision of both GDM and general antenatal care via telemedicine rather than face-to-face clinic visits wherever possible. The International Federation of Gynecology and Obstetrics (FIGO) has recently published a global interim guidance on COVID-19 (7). This review notes that, in contrast to the related severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) infections, there is no current evidence that pregnant women are more susceptible to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (the virus that causes COVID-19) or that those infected are more likely to develop severe disease. Further, there is no current evidence of vertical transmission (7).

At the present moment, the WHO has not issued any guidance for alternative testing in order to reduce the risks for pregnant women related to the pandemic. For simplicity and for economic reasons, testing using a fasting VPG alone may be the easiest option. With the WHO 2013 criteria, a fasting VPG of $\geq$5.1 mmol/L (HAPO odds ratio 1.75) would diagnose more than half of GDM cases. With progressively higher fasting glucose diagnostic thresholds, the yield would fall. While unlikely to be acceptable in routine clinical practice, such a strategy would greatly reduce the potential risk of exposure of pregnant women to COVID-19.

In summary, the acute severe risks to life and health posed by the COVID-19 pandemic have necessitated major changes to many aspects of life for millions of people all around the world. In this "new COVID world," GDM should not be ignored but pragmatically merits a lower priority than the avoidance of exposure to the COVID-19 virus. There appears to be no single strategy that is universally applicable to striking a reasonable balance in this context. Pragmatic local measures with careful documentation of outcomes offer the best or, perhaps more accurately, "least worst" solution.

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