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Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14 (2020) 939–942

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Temporary changes in clinical guidelines of gestational diabetes screening and management during COVID-19 outbreak: A narrative review

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ARTICLE INFO

Article history:
Received 25 May 2020
Received in revised form
3 June 2020
Accepted 15 June 2020

Keywords:
Clinical guidelines
Gestational diabetes
COVID-19
Narrative review

ABSTRACT

Background and aims: New clinical approaches are needed to minimize complications of gestational diabetes during the COVID-19 outbreak with timely screening and proper management. The present study aims to highlight changes in the clinical guideline for gestational diabetes during the pandemic.
Methods: In a narrative review, multiple databases were searched. Furthermore, online searches were conducted to identify guidelines or support documents provided by NGOs, local health authorities, and societies and organizations in the field of diabetes and obstetrics.
Results: We included five national guidelines that were published in English from Canada, the United Kingdom, Australia, New Zealand, and Australia health agencies. FBG, A1C, RPG were recommended as alternative tests instead of a 2-h oral glucose tolerance test (OGGT) for GDM screening at 24–28 weeks of gestation. Recommendations also included a deferral of postpartum screening till the end of the pandemic, or postponement of testing to 6–12 months after delivery, use telemedicine and telecare.
Conclusions: Updated temporary changes in clinical guidelines are sensible and accommodates social distancing and minimizes risk of exposure to COVID-19. Despite many unsolved controversies in screening, treatment, and follow-up of gestational diabetes, it seems involvement with novel coronavirus have made a reach to a global agreement simpler.

1. Introduction

Gestational diabetes mellitus (GDM) is defined as hyperglycemia with onset or first recognition during pregnancy, at severity less than those that occur in overt diabetes [1,2]. GDM is a high-risk condition with adverse maternal and neonatal outcomes [3,4]. Identification and treatment of GDM improve pregnancy outcomes, thus requiring earlier therapeutic intervention [5].

Different approaches for the screening of gestational diabetes mellitus have a significant impact on the management of gestational diabetes and its future complications [6]. However, there are still many controversies surrounding GDM diagnosis and management [7].

First prenatal visit is considered the best time to screen for gestational diabetes by the majority of health organizations [1,8]. The aims of early screening are identifying women with overt diabetes and are mainly to diagnose women at low or high risk for gestational diabetes [9]. To obtain such diagnosis, fasting plasma glucose (FPG), random plasma glucose (RPG), and glucose glycosylated hemoglobin A1C (HbA1c) are the most commonly used approaches.

A 75 g 2 h OGTT, at 24–28 weeks of gestation is recommended by IADPSG as the standard test for diagnosis of GDM [10]. Early postpartum follow-up of women with a history of GDM provides an opportunity to assess the health status of both the mothers and their offspring [11]. International guidelines recommend early screening of glucose status for prevention of diabetes at 4–12 weeks postpartum using the 75 g 2 h OGTT and after that [12,13].

Lifestyle changes as an essential component of the management of gestational diabetes mellitus, are recommended in many national clinical practice guidelines. Interventions including advice on healthy eating, increase physical activity, self-monitoring of blood sugar, and training on the use of glucose meter and interpreting

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https://doi.org/10.1016/j.dsx.2020.06.030
1871-4021/

glucose readings, if insulin should be added, may play essential roles in promoting the health of women with gestational diabetes and their children [14].

COVID-19 pandemic impaired routine prenatal care, disrupted traditionally face-to-face communication with patients and reduced access to laboratory testing [15]. Moreover, patient refusal of a long time waiting for the standard test due to the fear of illness shows the necessity of revision in clinical guidelines during the current epidemic. We need to compare the benefits of standard routine care and testing with the risks of exposure to novel coronavirus.

2. Methods

We performed a narrative review using keywords such as COVID-19 and gestational diabetes guideline, novel coronavirus, gestational diabetes clinical, practices, or recommendation.

At first, we searched multiple databases, from inception till May 2020 for the documents related to gestational diabetes screening or management including the Guidelines of the National Institute for Health and Clinical Excellence (NICE) database, the National Guidelines of Clearinghouse (NGC) for evidence-based clinical practice guidelines of the United States, the Medline and Embase database and Guidelines International Network's library. Then gray literature was conducted for all professional societies and organizations in the field of diabetes and obstetrics, which have had a standard guideline before the COVID-19 crisis [16]. If the list of guidelines were not available on their website, we sent an email to request for any updated guideline.

Six national guidelines from Canada, the United Kingdom, Australia, New Zealand, and Australia health agencies were identified. One of the guideline provided by the Australasian Diabetes in Pregnancy Society (ADIPS), the Australian Diabetes Society (ADS), the Australian Diabetes Educators Association (ADEA), and Diabetes Australia (DA) was a duplicate version of the Queensland guideline, so we focused on original recommendation published by Queensland clinical guidelines. Searches were limited to guidelines in the English language.

3. Results

The Summaries of national temporary clinical guidelines for gestational diabetes screening and management during COVID-19 are presented in Table 1.

3.1. Early pregnancy screening in the first trimester

For pregnant women with no pre-existing diabetes, HbA1c and/or FBG or non-fasting random plasma glucose test was recommended. Early testing for GDM should be done solely for women who are at higher risk of overt diabetes with one or more risk factors for GDM. Cutoff thresholds for FBG, HbA1c, Random plasma glucose were different.

During COVID-19, the Canadian guideline recommend no changes to screen for overt diabetes early in pregnancy. The latest guideline from Canada was released in 2018 [17], which indicates early testing should be done only in women who are at risk of overt diabetes. HbA1c or a fasting plasma glucose is recommended if an A1C is unreliable. Women with negative testing should be re-screened at 24–28 weeks gestation.

Australasian Diabetes in Pregnancy Society (ADIPS) and the Australian Diabetes Society (ADS) in the last Updated guideline (April 24, 2020) outlined a three-phase system for GDM testing during the pandemic based on 'contagion risk' of each local and state government. The alternative method for first trimester testing for GDM during the 'Amber & Red status' (risk of contagion is moderate to high) are random blood glucose (RBG) and HbA1c. The advised cutoff point for the diagnosis of GDM were HbA1c $\geq$ 5.9% or random blood glucose (RBG) $\geq$9.0 mmol/L.

Royal Australian and New Zealand College of Obstetricians and Gynecologist (RANZCOG) guideline emphasized on the necessity of early pregnancy screening merely in high-risk pregnant women in the first trimester during antenatal serology testing. HbA1c was the recommended test by this guideline, and a cutoff of 5.9% was considered for GDM diagnosis.

Queensland clinical guideline-recommended HbA1c 41 mmol/mol or more (5.9%) for GDM diagnosis in pregnant women with a risk factor and ignored OGTT testing in the first trimester temporarily.

In the United Kingdon, according to the Royal College of Obstetrics and Gynecology, HbA1c $\geq$ 48 mmol/mol or a random plasma glucose$\geq$11.1 mmol/L are diagnosed as type 2 diabetes. Women with borderline HbA1c (41–47 mmol/mol) and a history of GDM in previous pregnancy should be managed as G.D.M. HbA1c and fasting, or RBG should be repeated for other high-risk pregnant women at 28 weeks of gestation.

3.2. 24–28 weeks screening test

A strong agreement was observed in updated guidelines about 2-h OGTT, as the most important screening test for GDM diagnosis in 24–28 weeks of gestation. All guidelines were in agreement to not perform testing during the pandemic.

FBG, RPG, and A1C have commonly selected alternatives. Based on Canada's Clinical guideline, women with an A1C of $\geq$5.7% or random plasma glucose of $\geq$11.1 mmol/L are identified as having GDM.

RANZCOG guideline considered FBG at 24–28 weeks ($\geq$5.1 mmol/L) as diagnostic of GDM while ADIPS and ADS recommended the performance of an FBG at 24–28 weeks ($\geq$5.1 mmol/L) and further OGTT for women with an FBG between 4.7 and 5.0 mmol/L. Based on this guideline, if the risk of contagion is high, an FBG alone may be enough.

Based on Queensland clinical guidelines at 24–28 weeks gestation, irrespective of COVID-19 status, OGTT is required if FBG is between 4.7 and 5.0 mmol. FBG 5.1 mmol/L or higher does not require OGTT and should be considered as GDM.

Women with HbA1c $\geq$ 39 mmol/mol or FBG $\geq$5.3 mmol/l or random plasma glucose $\geq$ nine mmol/l will be diagnosed as having GDM based on United Kingdom guidelines. Furthermore, glycosuria, suspicion of diabetes due to a clinical symptom, pregnancy with polyhydramnios, or large for gestational age should be screened for GDM regardless of the months of pregnancy.

3.3. Postpartum screening for type 2 diabetes

Deferred or delay of postpartum screening in women with GDM in recent pregnancy was recommended by all of the available national guidelines during the pandemic. Post partum screening is postponed to 3–6 months after delivery by UK (HbA1c only), while the Queensland clinical guideline (Australia) recommended delaying the postpartum OGTT for 6–12 months. Postpartum OGTT should be performed before their child turns 12 months old or before next pregnancy. Continued self-monitoring if mother has greater risk for type 2 diabetes and an HbA1c test at 4–6 months postpartum may also be appropriate based on this guideline.

3.4. Management of gestational diabetes during pregnancy

Virtual management of gestational diabetes using telehealth

Table 1
Summaries of national temporary clinical guidelines for gestational diabetes screening and management during COVID-19.

Agency	Diabetes Canada Clinical Practice Guidelines Steering Committee & SOGC*(Canada) [18]	*ADIPS* &ADS** (Australia)	RANZCOG*** (Australia and New Zealand)	Queensland Health (Australia)	RCOG**** (UK)
Screening in early pregnancy (standard care)	HbA1c or FPG	2 h OGTT OR HbA1c	a75gPOGTT, with venous plasma samples	2 h OGTT OR HbA1c	75 g 2-h OGTT
Screening in early pregnancy (alternative)	HbA1c or FPG at risk of overt diabetes	random blood glucose (RBG) and HbA1c For high risk women	HbA1c For high risk women	HbA1c	HbA1c or a random plasma glucose For high risk women
Screening in 24–28 weeks of gestation (standard care)	all pregnant 50 g glucose challenge followed by a 75 g OGTT	75 g OGTT For all women	2 h OGTT	2 h OGTT	2 h OGTT
Screening in 24–28 weeks of gestation (alternative)	HbA1c & non-fasting RPG	Fasting blood glucose (FBG) OGTT for FBG 4.7–5.0 mmol/L	fasting blood glucose	Fasting blood glucose**	HbA1c and fasting or RPG
Postpartum follow-up	OGTT	OGTT	OGTT	OGTT at 6–12 weeks post-partum	3months after birth
Postpartum follow-up	deferred until after the pandemic	delayed 6 months post-partum HbA1c at 4–6 months post-partum	Postnatal OGTT should be deferred until the resolution of the pandemic	Delay for 6–12 months before baby is 12 months old or woman is pregnant again	HbA1c screening at 3–6 months after birth

*Society of Obstetricians and Gynecologists of Canada.
**Australasian Diabetes in Pregnancy Society (ADIPS), the Australian Diabetes Society (ADS), the Australian Diabetes Educators Association (ADEA).
***Royal Australian and New Zealand College of Obstetricians and Gynaecologists.
****Royal College of Obstetricians & Gynecologists.
*****Random plasma glucose.

advised by published national guidelines during Covid-19 outbreaks.

Canadian guideline suggested that video or phone call reduces face-to-face communication in initial and follow-up visits. Other methods of communication are as follows: Sharing critical clinical data including blood pressure and weight (obtained from in-person visits) between obstetricians and diabetes team; virtual visits by asking individuals to send the result of blood glucose testing via email, use of video conference for virtual classes and teaching insulin injections.

RANZCOG recommends the following: Telehealth and phone consultation with obstetricians and gynecologists; temporary allocation of Medicare Benefits Schedule, a listing of the Medicare services subsidized by the Australian government; self-blood glucose monitoring; self-insulin monitoring; virtual consultation for dietary and exercise plans; delaying of GDM testing for women with positive COVID-19 test, until after isolation; performing an ultrasound screening at 36 weeks for suspected macrosomia or fetal growth restriction cases.

In the United Kingdom, the health authorities' recommendations to patients are inclusive of 1) educational video calls with the diabetes midwife/nurse to ensure safe self-monitoring with a glucose meter and proper dieting. 2) no hospital visits or ultrasound scans. 3) contacting the diabetic health team if blood glucose is higher than the target level.

Moreover, the UK health authorities emphasize on training community midwives to check the mother's blood glucose readings, remotely. Furthermore, women with GDM who are taking metformin and or insulin require an obstetric evaluation at 28–32 weeks' gestation. In such cases, when the in-person visit is necessary, the appointment shall include an opportunity for an ultrasound appointment. Planning for birth is recommended at 36 weeks of gestation, when feasible. Almost all of these guidelines emphasize the importance of making a decision based on contamination risk, the ability of local laboratories to arrange for social distancing and available resources for remote management. They also remind us that temporary alternatives do not replace the standard of care.

4. Discussion

A review of published guidelines up to May 2020 showed a consensus on three important issues in screening and management of gestational diabetes during the COVID-19 crisis. First, replace OGGT with other glucose tests (F.B.G., HbA1c, RPG) for GDM screening at 24–28 weeks of gestation. Second, defer 4–12 weeks postpartum screening test until the end of COVID-19 crisis or delay up to 6–12 months after birth, and Third, use telemedicine and telecare where it is feasible.

The rationales for the suggestion of these temporary measures were: shortening the screening test process to reduce risk of exposure to COVID-19 in laboratories; reducing the burden on pathology centers, diabetes care providers and obstetrics team; minimizing the number of visits and duration of stay in the hospital for pregnant women; and reducing in-person visit by replacing such visits with remote communication with patients.

Although poor specificity of FBG test makes it an inappropriate test for screening in the first trimester [19].Furthermore, There is conflicting evidence about the accuracy of the RPG [20].

The use of 75 g, 2-h OGTT is considered as the golden-standard test for the diagnosis of GDM in 24–28 weeks of gestation, but updated guidelines preferred screening tests (F.B.G., HbA1c, RPG) with more flexibility, and quick turn around that would be feasible and easily available, would not require fasting and would be conducted with minimal laboratory facilities (Table 1).

Poor specificity and high false-positive of FBG restrict its efficiency for GDM screening. However, it can be useful for decision making about the need for the OGGT test and can reduce the

number of required OGTTs about half [21]. Also, HbA1c is not recommended for screening of GDM by international guidelines in 24–28 weeks of pregnancy and is not a useful alternative to an OGTT in pregnant women [22].

Furthermore, there is a conflicting evidence about the accuracy of the RPG. There are limited pieces of evidence on the accuracy of RPG being an excellent predecessor for GDM. Based on a systematic review, a single random glucose measurement is inadequate to screen for GDM [23].

Performance of an OGTT is also a standard test for *postpartum diabetes* screening in women with GDM in recent pregnancy. However, screening for postpartum diabetes in patients with GDM is a challenge worldwide [24–26]. Currently, under Covid-19 epidemic, we require to compare the benefits of the performance of 4–12 weeks postpartum screening tests as a standard routine test versus deferral of this test. .

Interestingly, there were differences between types of tests and cutoff of values for GDM diagnosis. For instance, Canada's guideline recommends that women with an HbA1c of ≥5.7% or RBG of ≥11.1 mmol/L be identified with GDM in 24–28 weeks of gestation. While United Kingdom guideline considers the following thresholds: HbA1c: 5.7%, RBG: 9.o mmol/L; or FPG: 5.3 mmol/L [27]. But the value of these indexes for GDM screening remains uncertain [28].

Challenges faced with new temporary recommendations are: Alternative screening strategies can identify only the women with the highest risk and will miss many women with lower glucose intolerance. This may affect the short- and long-term health status of mothers and their children. Furthermore, new approaches and recommendations during the Covid-19 epidemic are not evidence-based, hence can cause adverse health impacts. Moreover, the implantation of new strategies in the management of GDM may not be suitable for women living in poor-nations with inadequate-resources or roadblocks in the application of telemedicine [15,29]. It should be outlined based on available resources.

One of the limitations of our review was restricted sources as we could not find any guidelines for Asian countries with a high incidence of the Corvid-19 outbreak and developing countries with low-income. Another limitation was limiting our search to the English language. Despite this limitation, it is the first narrative review that collectively provides information, challenges, and limitations of clinical guidelines for screening and management of GDM during this emergency crisis. Appropriate and universal GDM testing and management protocol should be provided base on the risk of exposure to the viral epidemic and available resources. It seems, in spite of many old controversies' in screening, treatment, and follow-up of gestational diabetes, the world is more near to unanimous agreement in this crisis situation.

Author contributions

Idea and study design: NS and JS; Data collection and draft writing: SH and NS; Writing supervision: JS. All authors have read the manuscript and have approved this submission.

Funding

The author(s) received no financial support for the study.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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