Diabetes Ther (2020) 11:1639–1644
https://doi.org/10.1007/s13300-020-00865-3

COMMENTARY

American Diabetes Association "Standards of Medical Care—2020 for Gestational Diabetes Mellitus": A Critical Appraisal

Alpesh Goyal · Yashdeep Gupta · Rajiv Singla · Sanjay Kalra · Nikhil Tandon

Received: May 24, 2020 / Published online: June 20, 2020

ABSTRACT

Introduction: Gestational diabetes mellitus (GDM) is a major public health problem, affecting about one in every six pregnancies globally. The guidelines provided by the American Diabetes Association (ADA) on diagnosis and management of hyperglycemia in pregnancy are widely followed. We aim to provide a critical appraisal of the recently published ADA guidance document, highlighting its strength and limitations with regard to the diagnosis of GDM.

Methods and Results: We reviewed the recent ADA recommendations for the diagnosis and management of hyperglycemia in pregnancy. A periodic update in keeping with the emerging evidence, an inclusive diagnostic approach which increases generalizability, and a clear proposed approach for prenatal testing and postpartum follow-up are strengths of the ADA guidance document. On the other hand, its limitations are a lack of clarity on the applicability of diagnosis of GDM during early pregnancy, use of scientifically inaccurate terms such as "prediabetes" in the context of pregnancy and "overt diabetes prior to gestation" in the definition of GDM, and inconsistent use of terminology between successive publications. Certain issues which merit attention in future publications include a need for uniform global definition of GDM, demarcation of overt diabetes in pregnancy as a distinct entity, clarity on the diagnosis of GDM during early pregnancy, and clear delineation of timelines and appropriate testing strategy for the first prenatal visit.

Conclusions: This article provides a critical appraisal of the recently published ADA guidance document with regard to the diagnosis of GDM. We also share our perspective on issues warranting attention in the future publications. Experts from various professional organizations should aim for a consensus document which can resolve existing controversies in this field, and help clinicians and researchers achieve better health for women in their care.

Keywords: American Diabetes Association; Applicability; Limitations; Diabetes in pregnancy; Diagnosis; Gestational diabetes

Digital Features To view digital features for this article go to https://doi.org/10.6084/m9.figshare.12465734.

A. Goyal · Y. Gupta (✉) · N. Tandon
Department of Endocrinology and Metabolism, All India Institute of Medical Sciences, New Delhi, India
e-mail: yash_deep_gupta@yahoo.co.in

R. Singla
Department of Endocrinology and Metabolism, Kalpavriksh Superspecialty Center, New Delhi, India

S. Kalra
Department of Endocrinology and Metabolism, Bharti Hospital, Karnal, India

mellitus; Hyperglycemia in pregnancy; Standards of medical care 2020

Key Summary Points
The guidelines provided by American Diabetes Association (ADA) on diagnosis and management of hyperglycemia in pregnancy are widely followed
This article provides a critical appraisal of the recent ADA guidance document with regard to the diagnosis of GDM, highlighting its strengths and limitations
The personal perspective of authors on issues warranting attention in the future publications has also been elaborated
The article emphasizes the need for a consensus document to resolve existing controversies in the field of GDM diagnosis

INTRODUCTION

Gestational diabetes mellitus (GDM) is a major public health problem, affecting about one in every six pregnancies globally [1]. The field of GDM diagnosis continues to be marred by controversy, and a need to develop consensus has often been highlighted [2]. While recommendations by major professional organizations provide consensus opinion and better our understanding on a given subject, the existence of nearly 30 different guidelines on the subject of GDM, each with a different perspective, does bring in an element of confusion.

The American Diabetes Association (ADA) "Standards of Medical Care in Diabetes" developed by ADA's multidisciplinary Professional Practice Committee is updated and published annually. The standards provide clinicians and researchers with evidence-based guidelines on a broad range of topics including classification and diagnosis of diabetes, targets for glycemic control, use of technology to improve diabetes care, pharmacological and non-pharmacological treatment of hyperglycemia, management of in-patient hyperglycemia, recognition and management of microvascular and macrovascular complications, and management of diabetes in special groups.

The guidelines provided by American Diabetes Association (ADA) on diagnosis and management of hyperglycemia in pregnancy are widely followed. Herein, we provide a critical appraisal of the recently published document [3], highlighting its strength and limitations with regard to the diagnosis of GDM. Finally, we provide a brief personal perspective on the subject.

STRENGTHS OF ADA STANDARDS OF MEDICAL CARE IN THE CONTEXT OF GDM

1. *Periodic update* Guidelines are formulated on the basis of available evidence that keeps changing with time. This means that guidelines should be updated at periodic intervals. Glyburide (glibenclamide) is a good example of this need. While glyburide was initially preferred over metformin as an alternative to insulin, a 2015 meta-analysis and systematic review suggested that it was associated with a higher rate of neonatal hypoglycemia and macrosomia than insulin or metformin [4]. On the basis of the new data, its role in management of GDM was downplayed in the subsequent ADA guidelines [5]. On the other hand, the Endocrine Society guidelines, which have not been updated since 2013, continue to refer glyburide as the preferred agent [6]. Thus, a regular update of the ADA guidance document in a time-bound manner (released every January as a special supplement) is one of its main strengths.
2. *Flexibility in approach to reflect prevailing practices* In the USA, the National Institutes of Health (NIH) and American College of Obstetrics and Gynecology (ACOG) still recommend the use of a two-step strategy for screening and diagnosis of GDM [7, 8]. This involves an initial screening with 50-g

glucose challenge followed by a 3-h 100-g oral glucose tolerance test (OGTT) interpreted according to Carpenter and Coustan criteria in those who are screen positive. In 2011, ADA modified its recommendation to one-step diagnosis of GDM using International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria instead of the two-step strategy proposed earlier [9]. However, in 2014, ADA amended its viewpoint and recommended the use of either strategy for diagnosis of GDM, while stating that different strategies will identify different degrees of hyperglycemia severity and maternal and fetal risks [10]. In a similar vein, Diabetes Canada Clinical Practice Guidelines identify a preferred (two-step) and an alternate (one-step) screening strategy for GDM [11]. Such an inclusive approach increases generalizability, avoids conflicts, and respects varied viewpoints, especially when the evidence is equivocal.

3. *Clear approach for prenatal testing and postpartum follow-up* ADA guidelines clearly highlight the timing and nature of tests to be performed during pregnancy and in the postpartum period. There is an emphasis on testing for hyperglycemia at the first prenatal visit in high-risk women using standard diagnostic criteria [fasting plasma glucose and/or 2-h plasma glucose post 75-g glucose load and/or hemoglobin A1c (HbA1c)]. This is in response to the increasing burden of undiagnosed diabetes in women of reproductive age worldwide. Screening for GDM at 24–28 weeks is appropriately recommended for women found to have normoglycemia on the initial visit and in those who missed the test in earlier visit. There are data on the increased risk of adverse glycemic outcomes among women with GDM [12–15] and the guidelines aptly bring about the need for testing these high-risk women at 4–12 weeks postpartum using a 75-g OGTT. The preference for OGTT over HbA1c is based upon the increased sensitivity of the former and possibility of misleading results with the latter within 3 months after the delivery. Considering an increase in the lifetime risk for developing diabetes among women with GDM, further testing is recommended in those with normal postpartum OGTT every 1–3 years. The assessment may be performed using annual fasting plasma glucose, annual HbA1c, or three-yearly 75-g OGTT. Finally, there is a clear emphasis on the importance of breastfeeding, contraception, and preconceptional evaluation in women with a history of GDM.

LIMITATIONS OF ADA STANDARDS OF MEDICAL CARE IN THE CONTEXT OF GDM

1. *Time of pregnancy for the diagnosis of GDM* ADA guidelines define GDM as "diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation". ADA clearly states that IADPSG criteria as well as the diagnostic criteria used in the two-step approach were not derived from women enrolled in the first half of pregnancy. In light of this observation, the rationale behind extending the diagnostic criteria to the entire second trimester (13–28 weeks) and selectively excluding the first trimester (< 13 weeks) is not clear. World Health Organization (WHO) 2013 and FIGO (International Federation of Gynecology and Obstetrics) guidelines recommend diagnosis of GDM if the IADPSG criteria are fulfilled anytime during the pregnancy [16, 17]. Clearly, more consensus is needed on the applicability of a diagnosis of GDM during early pregnancy.
2. *Use of term "overt diabetes prior to gestation" in the GDM definition* In 2010, an IADPSG consensus panel introduced a new term, "overt diabetes during pregnancy", which demarcated women with GDM from those with hyperglycemia of greater severity [18]. This term was used to label women who were diagnosed with diabetes (as per standard criteria for diagnosis outside the pregnancy) for the first time during the pregnancy. A similar definition was used

by WHO 2013 guidelines, albeit with a different term "diabetes in pregnancy" [16]. The term "overt diabetes prior to gestation" used in the ADA definition (see above) is not in alignment with our current understanding of GDM and should have been "overt diabetes during gestation".

3. *Use of the term "prediabetes" in the context of pregnancy* One of the recommendations states "test for undiagnosed prediabetes and diabetes at the first prenatal visit in those with risk factors using standard diagnostic criteria". The use of term "prediabetes" in pregnant women is not backed by scientific evidence. This term has never been used previously by any other organizations such as WHO and IADPSG [16, 18]. Further, in the accompanying text, the guidelines recommend that women with "intermediate hyperglycemia" at the first prenatal visit should be diagnosed and treated as GDM. Does this mean that the terms GDM and prediabetes could be used interchangeably?
4. *Inconsistent use of terminology* While the 2019 ADA document used the term "pre-existing pre-gestational diabetes" for values clearly indicative of diabetes, this has been replaced by another term "diabetes complicating pregnancy" in the current version [3, 19]. It is not clear whether this term has been used in the same context or has been intended to include the subgroup of women with hyperglycemia meeting threshold of overt diabetes in pregnancy, but without known pre-existing diabetes.

OUR PERSPECTIVE

As clinicians and researchers, we find the ADA guidance document to be crisp, informative, and clear. A periodic update keeps readers abreast with latest developments, and is praiseworthy. In this section, we briefly discuss certain issues that we feel merit attention in future publications.

1. *Need for a uniform global definition of GDM* Regardless of the criteria used for the diagnosis of GDM, it is imperative that this milder form of hyperglycemia in pregnancy be viewed as a distinct entity. GDM is different from its more severe counterpart "overt diabetes in pregnancy". Both entities have different diagnostic criteria, natural history, therapeutic strategies, and outcomes. We also need to resolve the controversy regarding the time of pregnancy when a diagnosis of GDM should be made. In our opinion, the definition of GDM could be reframed as "hyperglycemia diagnosed during pregnancy that is not overt diabetes".
2. *Definition of intermediate hyperglycemia* The usage of term "prediabetes" for intermediate hyperglycemia detected at the first prenatal visit should be strictly avoided because of lack of scientific evidence. Besides, it is not appropriate to use terms "prediabetes" and "GDM" interchangeably for the following reasons: (a) Diagnostic thresholds for these two conditions on a 75-g OGTT are entirely different—fasting and 2-h plasma glucose of $\geq$ 5.1 mmol/L and $\geq$ 8.5 mmol/L for GDM, and $\geq$ 5.6 mmol/L and $\geq$ 7.8 mmol/L for prediabetes [3, 18]. Moreover, while HbA1c can be used for diagnosis of prediabetes according to ADA criteria, the same is not true for GDM. (b) Prediabetes has only been defined outside the pregnancy and is largely managed with dietary and lifestyle modifications. On the other hand, the implications for even milder forms of hyperglycemia during pregnancy are significant and a sizeable proportion (around 20%) of women with GDM warrant pharmacotherapy [14].
   We, therefore, agree with the WHO classification which avoids the use of such confusing terminology and identifies hyperglycemia during pregnancy into two broad categories—gestational diabetes and diabetes in pregnancy.
3. *Consistent use of terminologies* While we appreciate that ADA recommendations are revised in accordance with the new evidence, the use of terminologies and their meanings should be consistent between successive documents. Wherever possible,

the new term should relate to a term(s) used in the previous editions.

4. *Clear delineation of the first prenatal visit timelines* The guidelines aptly recommend testing for undiagnosed type 2 diabetes at the first prenatal visit. However, since the first prenatal visit may occur well beyond the first trimester in some women, the testing strategy may need to be individualized. For example, HbA1c may still be reliable to diagnose diabetes in the first trimester of pregnancy but is likely to be affected by the physiological changes of pregnancy and provide false results subsequently. Thus, a clear mention of different timelines in the first prenatal visit with appropriate testing strategies for each would be helpful.

CONCLUSIONS

This article provides a critical appraisal of the recently published ADA guidance document, highlighting its strength and limitations with regard to the diagnosis of GDM. We have also shared our perspective on issues warranting attention in the future guidance documents. In our opinion, experts from various professional organizations should aim for a consensus document which can resolve existing controversies in this field, and help clinicians and researchers achieve better health for women in their care.

ACKNOWLEDGEMENTS

Funding. No funding or sponsorship was received for this study or publication of this article.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author contributions. The idea for this paper was conceived by YG. The first draft was prepared by AG and YG which was read and edited by RS, SK, and NT. All authors approved the final version of this manuscript.

Disclosures. Alpesh Goyal, Yashdeep Gupta, Rajiv Singla, Sanjay Kalra, and Nikhil Tandon have nothing to disclose.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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