Attenuating type 2 diabetes with postpartum interventions following gestational diabetes mellitus

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Abstract

Women with a history of gestational diabetes should be screened during and after the postpartum period because of a high risk for developing type 2 diabetes mellitus. Although differences exist between guidelines practiced throughout various parts of the world, all recommend the use of cutoffs for fasting and/or post-load plasma glucose to diagnose diabetes or prediabetes. The use of these glycemic parameters could be optimized when a trend is observed, rather than considering them as isolated values at various time points. As the presence of insulin resistance and beta-cell dysfunction start before glycemic changes are evident, the estimation of insulin sensitivity and beta-cell function by Homeostatic Model Assessment is suggested for women who have additional risk factors for diabetes, such as obesity. Disease-modifying lifestyle intervention should be the first-line strategy to prevent or delay the onset of diabetes in women with a history of gestational diabetes mellitus. Intensive lifestyle interventions are designed to decrease caloric intake and increase physical activity in order to reduce body weight and fat, which will in turn reduce insulin resistance. This article also reviews unique problems of postpartum women, which should be considered when designing and implementing an intervention. Innovative "out of the box" thinking is appreciated, as continued adherence to a program is a challenge to both the women and the health care personnel who deal with them.

Key words: Gestational diabetes mellitus; Glycemic parameters; Lifestyle intervention; Screening; Type 2 diabetes mellitus

Core tip: This article reviews and highlights important areas concerning diabetic risk during and after the postpartum period in women with gestational diabetes mellitus. Optimizing the use of glycemic parameters and assessing beta-cell function, particularly in high-risk women, will facilitate early recognition of those on the path to pre-diabetes and diabetes. Lifestyle interventions designed to attenuate the progression should be carefully planned, taking into consideration the unique set of problems in these women. "Out of the box" thinking is necessary to design lifestyle intervention protocols that will have high acceptance by these women.

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DIABETIC RISK FOR WOMEN WITH GESTATIONAL DIABETES MELLITUS

Gestational diabetes mellitus (GDM), which occurs and is diagnosed during pregnancy[1], is a condition that increases the risk of developing type 2 diabetes mellitus (T2DM)[2,3]. In a large meta-analysis of 20 cohort studies in 2009, Bellamy et al[4] showed that women with GDM have a more than seven-fold increased risk of developing T2DM when compared to women with normoglycemic pregnancies. However, the incidence of diabetes in these women varies, with relative risks ranging from 6[5] to 12[6], possibly due to differences in screening and diagnostic criteria, associated risk factors[7], and inclusion of subjects with overt diabetes uncovered by pregnancy[8]. Feig et al[9] further demonstrated an increase in the probability of developing diabetes from 3.7% at 9 mo to 18.9% at 9 years after delivery, suggesting the need for long-term follow-up and monitoring of women with a history of GDM.

The development of peripheral insulin resistance during pregnancy is facilitated by the increased maternal adiposity and release of insulin-desensitizing hormones from the placenta[10]. The secretion of insulin is increased to compensate, and women with a deficit in this secretion can develop GDM. The effects of pregnancy on glucose homeostasis are alleviated following delivery of the offspring and removal of the placenta, such that the glycemic profile should return to normal within 6-12 wk postpartum.

POSTPARTUM SCREENING OF PATIENTS WITH A HISTORY OF GDM

Despite the lack of a consensus concerning precise recommendations for postpartum screening of women with a history of GDM[11], the importance of optimal screening is universally accepted. The American Diabetes Association recommends using the oral glucose tolerance test (OGTT) to screen these women for persistent diabetes at 6-12 wk postpartum, and lifelong screening for development of diabetes or pre-diabetes at least every three years[11]. However, the Mexico City Diabetes Study demonstrated that the progression from normoglycemia to diabetes ranges over three years with a probable phase of impaired glucose tolerance[12], which suggests that three years between screens is insufficient for high-risk individuals. In the United Kingdom, the National Institute for Health and Clinical Excellence guidelines recommend glucose estimation prior to discharge, at 6 wk postpartum, and annually thereafter using fasting plasma glucose (FPG)[12]. In 2010, however, Kakad et al[13] used retrospective data of 470 women to show that diabetes was missed in 26% of women when only the FPG was used for screening. Furthermore, unlike OGTT, FPG does not allow for detection of impaired glucose tolerance. Hemoglobin A1c, an additional parameter introduced to the diagnostic criteria of pre-diabetes and diabetes in 2009[14], is also considered unsuitable for use in postpartum women due to its low sensitivity on its own[15] or in combination with FPG[14]. Thus, OGTT with 75 g fasting glucose challenge and two-hour glucose measurements is the preferred screening method for women with previous GDM[17]. The interpretations should be based on diagnostic cutoffs for pre-diabetes and diabetes for non-pregnant adults[1].

Tabák et al[18] used serial measurements of yearly glucose levels over 13 years to evaluate glycemic parameters in normoglycemics and diabetics. They found that during the transformation from normoglycemia to diabetes, FPG and post-load glucose gradually increased, followed by an abrupt increase approximately two years before a diagnosis of DM. This indicates that continual glycemic measurements during screening can be even more informative and predictive, despite being within the normal range. Therefore, it is suggested that rather than looking solely at isolated values at any given time, changes in glycemic measures should be observed.

With the global increase in the prevalence of DM[19], the current recommendations for screening women with GDM for the development of T2DM should be revised. The present guidelines detect problems only when they reach the end point (diabetes), or a landmark very close to the end point (pre-diabetes). Can we use knowledge of the underlying pathophysiology to identify these cases earlier, before they reach the end point? The transition from normoglycemia to diabetes is a continuous process[11,18,20]. Although the glycemic profile assessed by FPG or post-load glucose should return to normal after delivery in a woman with a diagnosis of GDM, these parameters are not indicators of the ongoing pathophysiologic process. An analysis of the British Whitehall II study showed a steep decline in insulin sensitivity, along with a marked increase followed by a steep decrease in insulin secretion, approximately 3-5 years before the onset of diabetes[18]. These parameters can be estimated by the Homeostatic Model Assessment[21]. However, this assessment by itself is inappropriate for evaluation of beta-cell function, and serial measurements are required in order to observe the longitudinal changes in insulin secretion[22]. Repetitive monitoring of insulin sensitivity and secretion may be confined to the initial postpartum years due to increased cost, as Kim et al[23] showed that T2DM appears rapidly within the first five years and plateaus after ten years. Furthermore, these measurements can be limited to women with a higher predictive risk of developing diabetes, such
as those who are overweight\cite{23}, have a higher pre-
pregnancy body mass index\cite{24,25}, were diagnosed with
GDM before the 24th week of gestation\cite{25}, and who
needed insulin for glycemic control during pregnancy\cite{23}.
Finally, the recent call for developing standardized
screening protocols for Indian women with GDM\cite{26} is
worth considering for all Asian women, as they show a
greater risk than Caucasian women\cite{23}.

Nonetheless, the risk of developing T2DM can
persist for more than 25 years in women with a history of
GDM\cite{8,18,27} Therefore, continued life-long follow-up
of these women is justified, particularly with recognition
of the fact that ageing is an independent risk factor
for T2DM. In addition, women who are not diagnosed
with GDM but have mild glucose abnormalities\cite{28} or
a single abnormal value in the OGTT\cite{29} should be
screened because of the increased risk for developing
T2DM. However, as revised recommendations stipulate
that only one abnormal value, not two, is sufficient
to for a diagnosis of GDM\cite{1}, more women may be
recommended for T2DM screening.

**LIFESTYLE INTERVENTIONS**

Lifestyle interventions are the most appropriate initial
approach to mitigate the development of diabetes in
high risk individuals, such as those with a history of
GDM\cite{30} and can reduce the incidence of DM by
at least 50%\cite{27,31}. Such interventions may slow down
or arrest the pathophysiologic processes, such as the
beta-cell exhaustion that occurs in response to chronic
insulin resistance\cite{32,33}.

Lifestyle intervention programs designed for
high-risk individuals generally propose a low-calorie,
low-fat diet with moderate intensity physical activity
(e.g., brisk walking) for 150-180 min per week to
achieve a weight reduction of 5%-7% of the initial
body weight\cite{31,34-36}. The recommended calorie limit
varies between 1000-1200 kcal/d\cite{35} and 1200-1800
kcal/d\cite{34}. Although it is advised that no more than
30% of energy should come from fats\cite{36}, a recent
study found adequate glycemic control with a very
low-carbohydrate, high-fat, non-calorie-restricted
diet\cite{37}. Other simple measures include increasing
the amount of fiber in the diet\cite{36}, decreasing the amount
of energy-dense foods, such as fast foods, increasing
the amount of fruit and vegetable intake\cite{38}, and
controlling portion size\cite{31}. Although it is important
to combine physical activity with dietary support to
enhance the efficacy of an intervention program\cite{39},
results of a small study showed that women perceived
diet as more important for the prevention of T2DM
than physical activity\cite{40}, emphasizing the importance
of effective counseling to reinforce the value of both
aspects for weight reduction and maintenance\cite{35}.

Although almost all published protocols are based
on similar principles of intervention, a thorough in-
vestigation of these illustrates minor but important
differences between them, especially when it comes
to the stage of implementation. To augment dietary
and exercise interventions, Gabbe et al\cite{35} suggested
incorporation of behavioral therapy, which includes
stress management, stimulus control, problem solving,
and goal setting. The Mothers After Gestational Dia-
betes in Australia Diabetes Prevention Program offers
an intervention program handbook, six face-to-face
sessions, and two follow-up telephone calls within the
12-mo follow-up period to ensure that participants
achieve the program goals\cite{36}. Substantial decreases in
glycemic and anthropometric parameters after one year
of intervention\cite{41} is strong evidence for implementation
of an effective lifestyle intervention program by
community health workers\cite{34}. A randomized control
study for high-risk Hispanic women initiated inter-
ventions during late pregnancy, and continued for
12 mo postpartum\cite{38}. Further support for prenatal
implementation was provided by greater weight loss
and improved health behaviors in the postpartum
period in mothers who underwent a low glycemic
index dietary intervention during pregnancy\cite{42}. It is
the responsibility of the researchers and health care
personnel planning the interventions to utilize such
reported evidence when designing implementation
strategies for a particular population.

Although almost all programs aimed at preventing
T2DM promote increased physical activity, healthy
eating, and weight loss, “out of the box” thinking is
necessary in order to increase participant acceptance
of, and thus adherence to, a given intervention. A high
level of acceptance was reported in a novel intervention
in England that used group leisure activities for adults
at risk for DM\cite{43}, though the recruitment procedure
may have contributed to these results. Another
interesting study protocol published in 2013 used
motivational interviews to influence lifestyle changes in
individuals with impaired fasting glucose\cite{44}, a method
based on the transtheoretical model of health behavior
change\cite{45}.

Although pharmacologic interventions are also
beneficial in attenuating the onset of T2DM in women
with a history of GDM\cite{27,46}, a discussion of these is
beyond the scope of this review.

**Barriers to effective screening and lifestyle interventions
and strategies to overcome them**

Despite the importance of clear understandings of
the nature of the disease, the risk for developing DM, and
measures to prevent or delay its onset, the knowledge
itself may not be enough. A recent qualitative study
exploring factors that influence postnatal health
behaviors in women with GDM showed that, although
nearly all participants were aware of the increased risk
for diabetes, this knowledge did not motivate them for
action\cite{47}. However, a low level of awareness remains,
even among college-educated affluent women\cite{48},
which justifies the need for intensive awareness
programs to counsel these women.

The health care team has an enormous respon-
sibility to educate these patients about the diabetes risk and the importance of regular screening, to motivate them to adapt to healthy lifestyles, and to support them to adhere to these changes. Although an OGTT is mandatory for women with prior GDM, a population-based cohort study in Canada found that women who chose an obstetrician for follow-up as opposed to a family physician were more likely to undergo a postpartum OGTT, which highlights the importance of educating all levels of health personnel on current recommendations. However, there are conflicting results concerning the efficiency of obstetricians for enforcing postpartum T2DM screening of GDM women. It is the responsibility of the health care personnel to maintain records of these women and routinely remind them, preferably through some form of written information, as postal reminders or laboratory slips greatly increase the screening rates. Text message-reminder systems for screening and internet-based programs for lifestyle intervention are novel approaches worth trying in this era of technological dependence.

Postpartum women are a special group with a unique set of problems. The most common barriers to lifestyle interventions reported by these women were insufficient time, lack of support for child care, and other family commitments. As the amount of available social support is associated with adherence to lifestyle interventions, educational and counseling sessions should be extended to the spouse and the immediate family of these women.

CONCLUSION

This review highlights important aspects concerning the screening of women with GDM, during the prenatal and postpartum periods, and thereafter. Women with GDM are a unique group for whom diabetes prevention strategies can be applied. In addition to being familiar with the general recommendations for screening and managing these patients, health care personnel should be able to appropriately support their patients to ensure greater acceptance of these valuable screening tests and interventional programs. The real challenge is not the planning of a lifestyle intervention, but implementing it effectively within the target population.

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