

Attenuating type 2 diabetes with postpartum interventions following gestational diabetes mellitus

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Author contributions: Wasalathanthri S solely contributed to this paper.

Conflict-of-interest: None.

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Telephone: +94-727-285281

Received: August 28, 2014

Peer-review started: August 28, 2014

First decision: December 17, 2014

Revised: February 4, 2015

Accepted: February 10, 2015

Article in press: February 12, 2015

Published online: May 15, 2015

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 pre-diabetes. 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

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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.

Wasalathanthri S. Attenuating type 2 diabetes with postpartum interventions following gestational diabetes mellitus. *World J Diabetes* 2015; 6(4): 648-653 Available from: URL: <http://www.wjgnet.com>

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*^[6] 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^[9]. 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^[10], 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^[1]. 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^[11], 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^[16]. 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*^[3] 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^[23], have a higher pre-pregnancy body mass index^[24,25], were diagnosed with GDM before the 24th week of gestation^[25], and who needed insulin for glycemic control during pregnancy^[23]. Finally, the recent call for developing standardized screening protocols for Indian women with GDM^[26] is worth considering for all Asian women, as they show a greater risk than Caucasian women^[23].

Nonetheless, the risk of developing T2DM can persist for more than 25 years in women with a history of GDM^[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^[28] or a single abnormal value in the OGTT^[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^[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^[30], and can reduce the incidence of DM by at least 50%^[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^[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^[31,34-36]. The recommended calorie limit varies between 1000-1200 kcal/d^[35] and 1200-1800 kcal/d^[34]. Although it is advised that no more than 30% of energy should come from fats^[36], a recent study found adequate glycemic control with a very low-carbohydrate, high-fat, non-calorie-restricted diet^[37]. Other simple measures include increasing the amount of fiber in the diet^[36], decreasing the amount of energy-dense foods, such as fast foods, increasing the amount of fruit and vegetable intake^[38], and controlling portion size^[35]. Although it is important to combine physical activity with dietary support to enhance the efficacy of an intervention program^[39], results of a small study showed that women perceived diet as more important for the prevention of T2DM than physical activity^[40], emphasizing the importance of effective counseling to reinforce the value of both aspects for weight reduction and maintenance^[35].

Although almost all published protocols are based on similar principles of intervention, a thorough investigation 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*^[35] suggested incorporation of behavioral therapy, which includes stress management, stimulus control, problem solving, and goal setting. The Mothers After Gestational Diabetes 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^[36]. Substantial decreases in glycemic and anthropometric parameters after one year of intervention^[41] is strong evidence for implementation of an effective lifestyle intervention program by community health workers^[34]. A randomized control study for high-risk Hispanic women initiated interventions during late pregnancy, and continued for 12 mo postpartum^[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^[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^[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^[44], a method based on the transtheoretical model of health behavior change^[45].

Although pharmacologic interventions are also beneficial in attenuating the onset of T2DM in women with a history of GDM^[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^[47]. However, a low level of awareness remains, even among college-educated affluent women^[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^[49], 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^[50,51]. It is the responsibility of the health care personnel to maintain records of these women and routinely remind them^[52], preferably through some form of written information^[53], as postal reminders^[54] or laboratory slips^[48] greatly increase the screening rates. Text message-reminder systems for screening^[55] and internet-based programs for lifestyle intervention^[56] 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^[40,57,58], lack of support for child care^[40,47,57], and other family commitments^[40,47]. As the amount of available social support is associated with adherence to lifestyle interventions^[57], 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.

ACKNOWLEDGMENTS

The author would like to thank Ms Thamudi Sundarapperuma for the assistance in identifying the relevant literature.

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P- Reviewer: Tskitishvili E **S- Editor:** Gong XM **L- Editor:** A
E- Editor: Wu HL





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