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REVIEW

Postpartum glucose intolerance: an updated overview

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Abstract The prevalence of type 2 diabetes mellitus has increased worldwide over the past three decades, as a consequence of the more westernized lifestyle, which is responsible for the increasing obesity rate in the modern adult's life. Concomitant with this increase there has been a gradual rise in the overall prevalence of gestational diabetes mellitus, a condition that strongly predisposes to overt diabetes later in life. Many women with previous gestational diabetes mellitus show glucose intolerance in the early postpartum period. Although the best screening strategy for postpartum glucose intolerance is still debated, numerous evidences indicate that identification of these women at this time is of critical importance, as efforts to initiate early intensive lifestyle modification, including hypocaloric diet and physical activity, and to ameliorate the metabolic profile of these high-risk subjects can prevent or delay the onset of type 2 diabetes mellitus. Nevertheless, less than one fifth of women attend the scheduled postpartum screening following gestational diabetes mellitus and they are at increased risk to develop type 2 diabetes mellitus later in their lives. Unsatisfying results have also come from early intervention strategies and tools that have been developed during the last few years to help improving the rate of adherence to postpartum glycemic testing, thereby indicating that more effective strategies are needed to improve women's participation in postpartum screening.

Keywords Type 2 diabetes mellitus · Gestational diabetes mellitus · Glucose intolerance · Prediabetes · Postpartum screening

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Introduction

Postpartum glucose intolerance, either in the form of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or overt type 2 diabetes mellitus (T2DM), is a condition which may appear among women after pregnancy and childbirth. It often represents a late complication of gestational diabetes mellitus (GDM), that, as defined by the American Diabetes Association (ADA), is the type of glucose intolerance that develops during the second and third trimester of pregnancy, leading to hyperglycemia of variable degree [1]. Even though most women with GDM do not develop T2DM later in life, women with a history of GDM carry a high risk for the development of T2DM with respect to the predicted risk in non-pregnant women [2]. Also, as indicated by several observations based on the use of previous diagnostic criteria for GDM (prior to IADPSG criteria) [3], alterations of glucose homeostasis during pregnancy, even if not satisfying the criteria for GDM (i.e., a glycemic value only above the cut-off during oral glucose tolerance test (OGTT), being necessary at least two for diagnosis), are good predictors of postpartum glucose intolerance and T2DM [4–8]. Because of the growing incidence of GDM (over 20% of pregnancies in some ethnic groups) [9, 10], postpartum glucose intolerance has become an emerging health concern worldwide. In the light of these

considerations, more specific and tighter recommendations have been introduced recently, for the diagnosis and management of GDM, and the screening for glucose intolerance in the early post-partum period.

In this review, we provide an update about the prevalence of postpartum glucose intolerance, the pathogenetic mechanisms and predictors, and the revised guidelines for its diagnosis and treatment.

Epidemiological features

T2DM is one of the most common metabolic disorders worldwide and a major source of morbidity and mortality in affected individuals [11, 12]. Its global prevalence is 8.8% in the adult population, whereas current epidemiological estimates say that ~650 million people aged 20–79 years will be affected by T2DM in the world by 2040 [13]. Today, there are nearly 21 million people diagnosed with diabetes in the U.S., and an estimated 8.1 million Americans who have diabetes but are undiasgnosed [14]. In addition to this 29.1 million people with diabetes, another 86 million over age 20 are estimated to have prediabetes, which is a strong precursor toward T2DM [14–17]. Concomitant with this increase has been the rise in the overall prevalence of GDM [18], another condition that strongly predisposes to the occurrence of overt diabetes later in life [19], whereas the cumulative incidence of T2DM 10 years after a GDM pregnancy was 60% [19]. Particularly, the rate of T2DM increases rapidly during the first months after delivery, reaching 3.7% at 9 months, and increases further to 18.9% at 9 years, without signs of a plateau [20]. However, variations in the conversion of GDM to T2DM have been reported, which have been attributed to the different length of follow-up and the selection and diagnostic criteria used, in addition to differences due to ethnic variation [21]. Adjustment for these variables revealed a rapid increase in the cumulative incidence of T2DM in the first 5 years after delivery in different racial groups, with a plateau after 10 years [21]. Although more than 64% of women with previous GDM do not develop T2DM 20 years post-index pregnancy, and the positive predictive value of GDM as a diagnostic test for future T2DM is then limited, it must be considered that women who have had GDM have a seven-fold increased risk of being diagnosed with T2DM later in life [19].

In the recent years, many population-based studies have calculated the rate of postpartum prediabetes and T2DM in women with previous GDM. As shown in Table 1, the prevalence of prediabets ranges from 12.2 to 50% across multiple studies, while the prevalence of overt T2DM ranges from 1.1 to 34.6%. Several different reasons have been proposed that may help to explain these different rates: (1) a higher risk for GDM and T2DM has been correlated with the genetic background of some ethnic groups (native Americans, Hispanics, African-Americans, South Asians, Black Caribbeans, and peoples from Middle Eastern); (2) certain studies have been performed as retrospective and some as prospective studies; (3) different criteria have been employed by various investigators for the diagnosis of GDM and postpartum glucose intolerance; (4) some studies, performed when screening for unknown overt diabetes in early pregnancy was unusual, may included women with preexisting and undiagnosed T2DM; (5) over the last years, the prevalence of postpartum glucose intolerance has grown drastically, because of the increasing trend in body weight and advancing maternal age [20, 22].

Etiological factors

T2DM provides a paradigmatic example of a complex disease in which both precipitating environmental factors and predisposing genetic factors contribute to the development of hyperglycemia, which is the first metabolic abnormality to occur in T2DM [23]. Increasing evidence underlines the role of genetic factors in this context, even if the genetic loci so far identified account for only a modest fraction of the overall heritability of this disease [24–28]. Conversely, environmental factors such as hypernutrition and sedentary lifestyle have been better defined, making it clear that a more Westernized lifestyle, which is responsible for the increasing obesity rate in modern adult's life, has a greater influence on progression to prediabetes and T2DM [23] by decreasing peripheral insulin sensitivity, thereby inducing insulin resistance, which is the first step toward T2DM. The relevance of overweight and obesity in postpartum T2DM has been emphasized by the observation that higher prepregnancy body mass index (BMI) is a risk factor for developing postpartum T2DM in women with previous GDM [29–32]. Also, weight gain has been strongly associated with declining β-cell function in Hispanic women with recent GDM [33]. Among genetically predisposed individuals destined to develop T2DM, pancreatic β-cells initially compensate for peripheral insulin resistance by secreting increased amounts of insulin [23, 34], thus ensuring normal glucose tolerance. When β-cells fail to compensate, the majority of these people will develop T2DM [23, 34] (Fig. 1).

Similar pathogenetic mechanisms are operative during pregnancy in predisposed pregnant women, in which insulin resistance can be triggered by increased maternal adiposity and by the release of insulin-desensitizing hormones (e.g., chorionic somatomammotropin, prolactin, steroid hormones) produced by the placenta [35, 36]. Also in this case, most pregnant women are able to counteract insulin

Table 1 Prevalence of postpartum IFG/IGT and T2DM in different ethnic populations as obtained with OGTT and/or FPG

Authors	Design	Geographic area	Ethnicity	GDM women (N)	Screened women (%)	IFG/ IGT (%)	T2DM (%)
Benhalima et al. [121]	Retrospective	Belgium	Multiethnic	191	70.7	42.2	1.5
Benhalima et al. [122]	Retrospective	Belgium	Multiethnic	231	78.6	39.1	5.3
Bhavadharini et al. [123]	Prospective	India	Indian	212	95.8	16.7	3.4
Buchanan et al. [57]	Prospective	USA	Latin	122	100	50.0	10.0
Capula et al. [60]	Retrospective	Italy	Caucasian	1342	33.8	32.1	4.0
Cho et al. [124]	Retrospective	South Korea	Asian	1686	44.9	44.1	18.4
Feig et al. [20]	Prospective	Canada	Multiethnic	21823	100	–	3.7
Ferrara et al. [72]	Retrospective	USA	Multiethnic	14448	38.2	31.3	2.7
Ghajari et al. [125]	Retrospective	Iran	Middle east	131	45.8	8.5	15.2
Hunt et al. [73]	Retrospective	USA	Multiethnic	707	57	36.1	4.5
Katon et al. [126]	Prospective	USA	Multiethnic	277	100	37.2	5.4
Kerimoglu et al. [85]	Retrospective	Turkey	Caucasian	109	71.6	35.9	34.6
Kim et al. [31]	Prospective	South Korea	Asian	381	100	44.8	5.2
Kitzmiller et al. [61]	Prospective	USA	Multiethnic	527	100	29.6	4.7
Kojima et al. [58]	Prospective	Japan	Asian	72	100	16.7	
Kwak et al. [127]	Prospective	South Korea	Asian	843	100	–	12.5
Kwong et al. [86]	Retrospective	Canada	Multiethnic	909	48.2	17.0	3.2
Jang et al. [59]	Retrospective	South Korea	Asian	392	79.3	23.2	15.1
Lawrence et al. [87]	Retrospective	USA	Multiethnic	11825	50.2	16.3	1.1
Mendez-Figueroa et al. [128]	Retrospective	USA	Multiethnic	414	48.6	34.3	3.0
Nouhjah et al. [129]	Prospective	Iran	Middle east	176	100	17.6	4.5
Noctor et al. [130]	Prospective	Ireland	Multiethnic	270	100	21.7	
Ogonowski and Miazgowski [88]	Retrospective	Poland	Caucasian	855	37.2	12.2	1.3
Russell et al. [131]	Retrospective	USA	Multiethnic	344	45	28.0	8.0
Schaefer-Graf et al. [132]	Prospective	USA	Multiethnic	1636	100	26.0	14.1
Schaefer-Graf et al. [74]	Retrospective	USA	Multiethnic	605	100	16.4	5.5
Stasenko et al. [89]	Retrospective	USA	Multiethnic	745	33.7	28.3	2.0
Weinert et al. [91]	Retrospective	Brazil	Latin	209	51.7	20.4	3.7

Diagnosis of IFG, IGT, and T2DM was made following current ADA criteria

resistance by increasing their pancreatic β-cell insulin secretion. However, when insulin secretion is not sufficiently active to compensate peripheral insulin resistance, then glucose intolerance takes place and the woman develops GDM [37]. Thus, through GDM, pregnancy can unmask abnormalities in β-cell function and increase a woman's potential for T2DM later in life. The pivotal role of β-cells in this scenario has been supported further by the recent findings that most of the genetic variants associated with postpartum T2DM were localized in genes (i.e., *TCF7L2*, *CDKN2A/2B*, and *CDKAL1*) which are involved in β-cell function and insulin secretion [30, 38]. Other factors that may affect the risk of getting postpartum T2DM include the magnitude of hyperglycemia during pregnancy and in the early postpartum period, the number of GDM pregnancies, and the use of progestin-only oral contracptives [39–44] (Fig. 1). In addition, as reported in recent literature, abnormalities in leptin signal transduction and fetuin-A, a pro-inflammatory protein expressed by hepatocytes, which inhibits insulin action, may contribute to T2DM in women with previous GDM [45–47]. All these factors act by reducing tissue insulin sensitivity, thus supporting the notion that peripheral insulin resistance indeed plays a fundamental role in postpartum glucose intolerance. Consistent with this view, dietary and/or pharmacological interventions aimed at ameliorating insulin resistance may also have a positive impact on β-cell function, and this may delay or even prevent the development of T2DM in women who had experienced GDM during pregnancy [2, 48–50].

Indicators and predictors of postpartum glucose intolerance

The identification of predictors of postpartum glucose intolerance represents an important tool in the management

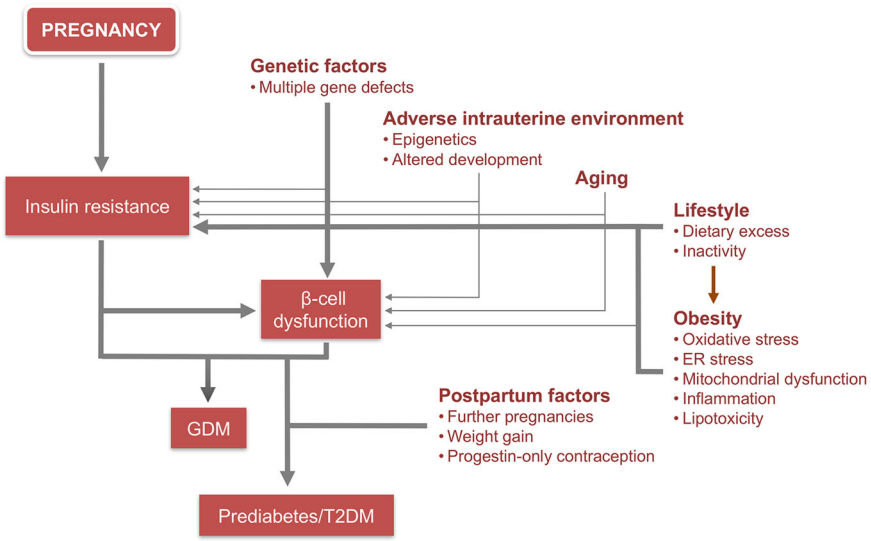

Fig. 1 Schematic representation of the precipitating environmental events and predisposing genetic factors that may contribute to the development of insulin resistance and β-cell dysfunction, leading to the development of GDM and postpartum T2DM

Table 2 Modifiable and unmodifiable predictors of postpartum prediabetes and T2DM

Modifiable predictors	Unmodifiable predictors
Higher pre-pregnancy BMI	Genetic susceptibility
Higher postpartum BMI	Non-white ethnicity
Higher postpartum serum triacylglycerols	Previous GDM
Higher postpartum intake of energy and fat	Previous PCOS
No breastfeeding	Family hystory of T2DM
	Older age at pregnancy
	Earlier GDM diagnosis
	Higher glycemic values at GDM screening
	Insulin treatment during pregnancy
	Lower antepartum insulinogenic index
	Specific antepartum metabolomic profile

PCOS policistic ovary syndrome, *OGTT* oral glucose tolerance test

of women with GDM, either before or after delivery, since it is possible to attenuate or avoid some of them, thereby reducing the adverse outcomes of GDM, generally through intervention aiming at changing lifestyle patterns, particularly diet and exercise. Several antepartum and postpartum predictors have been identified up to date, in women with GDM (Table 2), albeit not all studies show consistent results. Once again, among the reasons for the lack of consistent findings in these studies are the different genetic background of the populations examined; the different diagnostic criteria employed for the diagnosis of GDM and postpartum glucose intolerance; and the influence of the study design (retrospective or prospective) [51]. However, more solid data, in this context, have come from a recent meta-analysis, that included data from 95,750 women with previous GDM [52]. From the analysis of 39 prospective and retrospective cohort studies, higher glucose values during the OGTT and insulin therapy during pregnancy emerged as the stronger predictors of future T2DM [52]. The significance of glycemia during OGTT is consistent with results obtained in a previous systematic review [53]. The other risk factors were overweight or obesity, non-white ethnicity, advanced maternal age, early diagnosis of GDM, increased HbA1c, multiparity, hypertensive disorders in pregnancy, and preterm delivery. Instead, weight gain during pregnancy, macrosomia or breastfeeding were not associated with the risk of future T2DM [52]. Rather, in a more recent meta-analysis, longer and exclusive breastfeeding protected against T2DM in women with previous GDM [54]. Another recent meta-analysis focused on the risk of T2DM in women with hypertensive disorders during pregnancy [55]. By examining 17 studies involving 46,732 T2DM patients with previous GDM, the study demonstrated that overall hypertensive disorders during pregnancy, as well as either preeclampsia or gestational hypertension, were significantly and independently correlated with T2DM risk [55]. Among the factors not considered by these meta-analyses, reduced insulin secretion

and decreased insulin sensitivity resulted as strong predictors of postpartum glucose intolerance in many studies [31, 56–59]. This is consistent with the pathogenetic mechanism whereby β-cell defect is a sine qua non for the development of GDM, and with the increased association of T2DM risk with insulin therapy during pregnancy. Other factors that have been recently associated with higher risk of both postpartum prediabetes and T2DM are prepregnancy diagnosis of policistic ovary syndrome (PCOS) [60] and the intake of high amounts of animal fat during pregnancy [31].

Postpartum screening

There are many evidences that strongly support the importance of the postpartum period for early diagnosis and intervention strategies in order to prevent or delay the development of T2DM and its complications. Among them: the high prevalence, during this period, of glucose intolerance, either in the form of prediabetes or overt T2DM [61]; the close association of glucose intolerance, at this time, with a significantly higher risk to become diabetics later inside life [19]; the effectiveness of diet and exercise, and glucose-lowering in delaying or preventing T2DM in women who experienced postpartum glucose abnormality [2]; the higher risk of cardiovascular disease among women who experienced GDM [62]; the possibility to lower the risk of congenital abnormalities and improve outcome in offspring from women who had postpartum glucose intolerance, but desire additional children [63, 64].

Based on these considerations, guidelines from the main medical societies recommend that women with prior GDM or overt T2DM during pregnancy should undergo a 75-g OGTT for prediabetes or persistent diabetes during the first weeks postpartum, using nonpregnancy criteria, if they do not manifest diabetes immediately postpartum (Table 3). Neverthless, to date there have been no uniform recommendations about this screening test, so that while the Fifth International Workshop-Conference on GDM [65], the Australasian Diabetes in Pregnancy Society [66], and the Endocrine Society [67] recommend the 75-g OGTT at 6–12 weeks postpartum in all women with GDM (Table 3), the Canadian Diabetes Association (CDA) [68] indicates the same test, but for a longer period (6 weeks to 6 months), and the American Congress of Obstetricians and Gynecologists [69] proposes two methods of screening, that is, either the OGTT, or testing for fasting plasma glucose (FPG) at 6–12 weeks postpartum (Table 3). Instead, guidelines from the National Institute of Health and Care Excellence (NICE) suggest the FPG test prior to discharge and at 6–13 weeks after delivery. The NICE recommends to perform the FPG also after this time period, and measurement of HbA1c only if the FPG test is not possible, while it excludes a routine OGTT [70]. More recently, the ADA has modified its indication from 6–12 weeks postpartum to 4–12 weeks postpartum, in order to schedule the test immediately before the standard 6-week postpartum obstetrical checkup, allowing the patient's results to be discussed at the time of the visit [71].

Lacking of uniformity in this context might be a reason for the relatively low rate of postpartum screening observed among women with previous GDM. In fact, if it is true that OGTT is the most sensitive screening tool available at this time in detecting postpartum glucose intolerance [72–74], some limitations of the OGTT, such as test duration, low reproducibility, time of performance (morning only) and a certain patient discomfort during test, have emerged as the most commonly refered reasons for the low rate of women attending postnatal screening [75]. Instead it has been reported [76] that assessment of FPG as screening test, although not sufficiently sensitive to identify all women with IFG or T2DM, increases adherence to screening recommendation, and appears to have greater reproducibility and convenience than OGTT [65]. Other tests, including HbA1c, the homeostatic model assessment for insulin resistance and β-cell function, and the oral disposition index (DIo), although investigated, presented more inconveniences than advantages [31, 77]. More recently, new approaches based on the omics-related technologies (metabolomics, proteomics, and epigenenomics) have been

Table 3 Current recommendations for postpartum screening of glucose intolerance

Year	Society	Time	Test
2017	American Diabetes Association [71]	4–12 weeks postpartum	2 h 75-g OGTT
2015	National Institute for health and Clinical Excellence [70]	6–13 weeks postpartum	FPG
2014	Australasian Diabetes in Pregnancy Society [66]	6–12 weeks postpartum	2 h 75-g OGTT
2013	American Congress of Obstetricians and Gynecologists [69]	6–12 weeks postpartum	2 h 75-g OGTT or FPG
2013	Endocrine Society [67]	6–12 weeks postpartum	2 h 75-g OGTT
2013	Canadian Diabetes Association [68]	6 weeks to 6 months	2 h 75-g OGTT
2007	Fifth International Workshop-Conference on Gestational Diabetes Mellitus [65]	6–12 weeks postpartum	2 h 75-g OGTT

OGTT oral glucose tolerance test, *FPG* fasting plasma glucose

developed, which can help identify novel biomarkers of disease. Although further studies are necessary in this context, many metabolites that are involved in impaired glucose tolerance, or are specific for inflammation and altered redox-balance, have been associated with GDM and postpartum glucose intolerance [78–80]. For example, a metabolic signature that appears to predict the transition from GDM to T2DM has been reported in high-risk women using a quantitative approach called targeted metabolomics. Based on the authors' conclusions, this metabolomics signature holds the potential to replace OGTT, thereby surpassing the issue of lost follow-up and low postpartum screening rate with a single fasting blood sample [81]. Furthermore, evidence has been provided on the identification of metabotypes as potential prognostic biomarkers to predict diabetic complications in women with GDM after delivery [78].

Compliance to postpartum screening

As stated above, despite the vast amount of evidence demonstrating the importance of postpartum screening among individuals with a history of GDM and the increased risk for non-adherent women to develop T2DM later in life [82], the rate of GDM women receiving appropriately timed postnatal glucose testing is inappropriately low, ranging between 18.5 and 61.0% in studies (Table 4), in which the rate and predictors of adherence to postpartum testing were investigated. Higher rates in postpartum screening have been registered in women with GDM in a previous pregnancy [73, 83], as well as in women with earlier diagnosis of GDM [72, 83, 84] probably because of the greater awareness of their risk for developing chronic T2DM and related complications. Likewise, women with older age at pregnancy, higher educational level and income [72, 83, 85–90], as well as those non-obese or with lower parity attended screening test more often [72, 86, 87, 89, 91]. Also, women with a medical history of PCOS were found to be associated with a higher compliance rate for postpartum testing [83]. As an explanation for this, it has been proposed that because of their unpleasant clinical manifestations (i.e., menstrual irregularity, infertility, hirsutism) these women might have more contacts with the healthcare system, thereby be more willing to accept medical recommendations. Similar consideration for women who received antidiabetic medications, especially insulin therapy, during pregnancy. Also in this case, the higher rates of postpartum testing observed [72, 86–90, 92] may reflect the perceived risk of the disease, what may induce women to care more about their own health.

Still in this context, several recent studies have investigated the reasons for non-attendance of women for postpartum screening after GDM [93–99]. Among them the lack of patient understanding and awareness of the risk in relation to T2DM, the lack of interest in patient's personal health, the lack of family support and test discomfort, the inability to travel alone for testing, socioeconomic and ethnic factors, and concerns over current recommendations have been considered the most common barriers that prevent postnatal screening [100]. In addition, there are some concerns regarding the healthcare system, including a poor bridging from antepartum to postpartum care, inadequate communication between obstetrician and primary care physician, the perception among doctors that postpartum follow-up of GDM is not a clinical priority, and the lack of agreed protocols/procedures [101, 102].

Therefore, because of these reasons, many different interventions have been proposed in the recent years, which aim at overcoming barriers to testing, thus improving women adherence to postpartum screening [103]. They include but are not limited to the following: patient and physician reminders [94, 104–109], verbal and written antepartum counseling procedures [84, 89, 98, 109], continuous postpartum follow-up [83], flexible appointment times and dynamic role in decision and planning of medical tests [110] (Table 5). As suggested [110], the best time to remind women about the test would be at the time they go to the hospital for baby's immunizations in their first years of life. The alternative to stay on schedule with postpartum screening, particularly for women who get back to work after postpartum leave [110], is a single medical appointment during which women can also attend for cervical cancer screening [111] or mammography screening [112]. Although the increase observed in postpartum screening rate following these intervention strategies has been recognized, none of them, however, results in anything substantial (Table 5).

Treatment of postpartum glucose intolerance

Once IFG or IGT is established during the postpartum period, lifestyle intervention is recommended as the primary treatment to lower the risk for T2DM among women with a GDM history. In particular, lifestyle measures aimed at lowering prevalence of overweight/obesity through a more healthful dietary intake and physical activity are effective in the disease process and are necessary to improve the lifelong health of these women. Healthful diets include plenty of fruits and vegetables, dried beans, and cereal lean meats and seafood, while reducing the consumption of fast food, saturated fatty acids, red and processed meat and the intake of sugar-sweetened beverages [113]. On the other hand, postpartum physical activity/exercise (30–60 min of aerobic exercise per day for at least 5 days per week) [2] represents

Table 4 Prevalence and predictors of postpartum screening in women with previous GDM

Authors	Geographic area	Women (N)	Type of screening	Women screened (%)	Predictors of postpartum screening
Almario et al. [84]	USA	2617	GCT	33.3	GDM diagnosis < 24 weeks gestation, GCT result > 190 mg/dL, treatment of GDM with insulin or the sulphonylurea glyburide, family history of T2DM
Capula et al. [83]	Italy	1159	OGTT	32.2	PCOS, previous diagnosis of GDM, higher educational status, treatment of GDM with insulin
Chamberlain et al. [93]	Australia	1012	FPG or OGTT	23.2	White ethnicity
Cho et al. [124]	South Korea	1686	OGTT	44.9	Patients in pharmacotherapy for GDM were more likely to be screened. Women with high parity, larger weight gain during pregnancy, and referral from private clinics due to reasons other than GDM treatment were less likely to receive postpartum glucose testing
Ferrara et al. [72]	USA	14448	FPG or OGTT	38.2	Older age, lower parity, not being obese, higher education, GDM diagnosis earlier in pregnancy, use of diabetes medications during pregnancy, more provider contacts after delivery
Hunt and Conway [73]	USA	707	FPG or OGTT	57.0	Less likely to have had GDM, lower prepregnancy BMI, lower point estimates for all glucose levels at GDM diagnosis, non-use of insulin or medications and more control over GDM
Kerimoglu et al. [90]	Turkey	78	FPG or OGTT	47.4	Insulin treatment during pregnancy and higher education (for OGTT screening only)
Korpi-Hyovalti et al. [94]	Finland	266	OGTT	35.7	Normal weight and higher education
Kwong et al. [86]	Canada	909	FPG or OGTT	48.2	Older age, lower parity, and insulin use during pregnancy
Lawrence et al. [87]	USA	11825	FPG or OGTT	50.2	Older age, higher education, higher income, lower parity, foreign-born, vaginal delivery, non-macrosomic infant, having a postpartum visit, having GDM coded diagnosis code, receiving no therapy or insulin (vs oral therapy alone)
Mathieu et al. [133]	USA	373	OGTT	50.0	Patients at a major medical center, high BMI at diagnosis, high fasting glucose, and low education level were less likely to receive postpartum glucose testing
McCloskey et al. [134]	USA	415	FPG, OGTT or HbA1c	23.4	Women aged ≤ 35 years of age and women with a family practice provider were less likely to receive postpartum glucose testing
McGovern et al. [135]	England	788	FPG or OGTT	18.5	Asian ethnicity Current smokers were less likely to return
Ogonowski and Miazgowski [88]	Poland	855	OGTT	37.2	Older age, insulin requirement in pregnancy
Peticca et al. [136]	Canada	556	FPG, OGTT or HbA1c	39.6	Site of care and non-smoking status.
Russell et al. [49]	USA	344	FPG or OGTT	45	Attendance of the postpartum visit
Swan et al. [137]	Australia	84	OGTT	61.0	Women living in small rural areas
Stasenko et al. [52]	USA	745	FPG or OGTT	33.7	Older age, nulliparity, insulin requirement during pregnancy

OGTT oral glucose tolerance test, *FPG* fasting plasma glucose, *GCT* glucose challenge test

Table 5 Adopeted strategies to increment adherence rate

Authors	Country	Adopted strategy	Results
Capula et al. [83]	Italy	Verbal and written counseling	Adherence increases from 32.3 to 62.3%
Carmody et al. [138]	Ireland	Verbal remainders, postal reminders, telephone calls	Adherence increases of 12% on the previous year
Carson et al. [139]	Multicountries	Phone calls, education programs or postal reminders	Adherence increases from 33 to 60%
Clark et al. [106]	Canada	Postal reminders Reminder letters both to physician and patient, to patient only or to physician only vs no reminders sent	Differences rates in the four groups: physician/patient reminder group 60.5% patient-only reminder group 55.3% physician-only reminder group 51.6% no reminder group 14.3%.
Cosson et al. [92]	France	Reminder letter to woman's caregivers	Over 50% increment rate
Halperin et al. [105]	Canada	Improvements in physicians' dictations patient-directed e-mail reminder systems family physician-directed fax reminder systems	Adherence increases of 10% (e-mail reminders improves rates from 33 to 44%)
Khorshidi Roozbahani et al. [140]	Iran	Telephone reminder	Adherence increases from 34.1 to 94.9%
Van Ryswyk et al. [141]	Australia	SMS-reminders	No increase of adherence rate
Shea et al. [142]	Canada	Reminders mails with a laboratory requisition for OGTT, laboratory requisition for OGTT only, laboratory requisition for OGTT and a telephone call, a telephone call only	Adherence increases from 14.0 to 28.0%
Soffer et al. [143]	USA	Advanced order sets for glucose monitoring at the 35-week pregnancy visit, educational modules, and nutritionist phone calls reminding patients to attend postpartum visits fasting	Adherence increases from 17.0 to 36.0%
Vesco et al. [108]	USA	Combined telephone calls/emails and staff education	Adherence increases from 59.5 to 71.5%

an important component among women with recent GDM. Evidence has been provided, in this respect, demonstrating that aerobic physical activity can substantially ameliorate insulin sensitivity and glucose profile, have a positive impact on cardiovascular health, and improve mood and wellbeing, and quality of life [2]. Also, it has been reported that breastfeeding may reduce maternal hyperglycemia [91] and the likelihood of obesity and T2DM later in life [112]. However, recent evidences indicate that adherence to healthy lifestyle for women with a history of GDM is yet suboptimal [114]. If, despite these interventions, postpartum hyperglycemia persists, then drug therapy is initiated [68]. Current guidelines from CDA and NICE recommend treatment with metformin, which improves insulin sensitivity and can prevent or delay the progression from postpartum hyperglycemia to T2DM [2, 115]. Furthermore, no harmful effects of metformin have been found in offspring of mother treated with metformin [116–118], thereby making it a potential ideal drug for women with a history of GDM and abnormal glucose metabolism postpartum. Nevertheless, although there is evidence that interventions based on metformin may improve long-term outcomes of GDM women by preventing T2DM, the effectiveness and side-effects of metformin in this context need further evaluation [119]. The same therapeutic approach can be applied for treating overt T2DM in the early postpartum, taking into account that, if required, insulin can be used during breastfeeding. Non-lactating women with postpartum T2DM can be treated as the general diabetic population [61].

Follow-up

If the postpartum 75-g OGTT is normal, women with GDM during pregnancy should undergo screening for T2DM every 1–3 years, with screening frequency depending on other risk factors, such as family history of diabetes, pre-pregnancy BMI and the need for insulin or oral antidiabetic agents during pregnancy [71]. A FPG every 1–2 years is considered sufficient for women at lower risk [66]. NICE recommends an annual HbA1c to women diagnosed with GDM who have a negative postnatal test for diabetes [71]. Also, future pregnancies should be planned in consultation with healthcare providers [65, 68, 70]. Annual OGTT screening is recommended in women contemplating future pregnancy, in order to identify and correct any degree of glucose intolerance and assure normoglycemia at the time of conception [66]. This is essential to reduce maternal morbidity, and the risk of fetal malformations and obstetric complications [120]. Contraceptives can be an important tool in overcoming poor adherence to interconception care [61] and in help choosing the best time for a new pregnancy. If a hormonal contraceptive is an option, then it can be started 6–8 weeks after delivery if woman is breastfeeding. Progestin-only oral contraceptives should be avoided given that they have been associated with increased risk of T2DM [39–41].

Conclusions

This review provides an update on what is currently known about postpartum glucose intolerance and the revised guidelines that enable practitioners to identify and address a number of issues concerning this topic. As underlined throughout the article, the rate of postpartum glucose intolerance is very high in women with recent GDM, and its precocious identification by early postpartum screening is critically important to establishing an appropriate and effective treatment to reduce the progression toward the chronic form of the disease. Neverthless, despite different strategies have been implemented in the recent years in order to improve the adherence rate of postpartum screening for abnormal glucose tolerance, less than one-half of women with GDM undergo this postnatal screening test. Interventions aimed at increasing adherence of these women to recommended clinical guidelines would definitely enhance their personal quality of life, along with improving health outcomes.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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