Prevalence of diabetes five years after having gestational diabetes during pregnancy – Croatian national study

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[1] Abbreviations used in the article: GD = gestational diabetes

Abstract

Aims. The aim of this study was to determine the prevalence of diabetes among women 5 years after having gestational diabetes during pregnancy. Also, we sought to determine whether women who develop diabetes after GD during pregnancy differ from women who do not develop diabetes after GD during pregnancy.

Methods. This longitudinal study was performed using data from medical birth certificates and CroDiab diabetes registry. Women burdened with gestational diabetes in Croatia in 2011 were followed up until year 2016. Those registered in CroDiab registry were recognised as new patients with diabetes.

Results. Among 40641 deliveries in 2011, gestational diabetes was reported in 1181 (2.9%) women. Among them 853 (72.23%) were followed up in CroDiab diabetes registry and 32 (3.75%) were identified as new patients with diabetes. Median time from childbirth to onset of diabetes was 29.12 months. The diabetes group did not significantly differ to the group without diabetes according to age (p=0.587), level of education (p=0.549) or marital status (p=0.849) except that the diabetes group was significantly more obese than the group without diabetes (p=0.002).

Conclusions. Based on CroDiab diabetes registry data prevalence of diabetes 5 years after pregnancy complicated with gestational diabetes is 3.75% in Croatia. Women with gestational diabetes during pregnancy, and especially those with higher BMIs, are an important risk group for developing diabetes later in life so screening and preventive measures should be oriented toward them in primary care settings.

Keywords: gestational diabetes, pregnancy, diabetes mellitus, epidemiology

Introduction

Gestational diabetes (GD) is a common pregnancy-related condition diagnosed in almost 5% of all pregnancies in Croatia (1). It presents an important risk factor for adverse perinatal outcomes including induction of labour and caesarean section, as well as certain serious short and long-term consequences to both mother and new-born (2). GD is related to a higher risk of neonatal hypoglycemia, hyperbilirubinemia, hypocalcaemia, polycythemia and respiratory distress as well as excessive fetal growth leading to macrosomia (3,4). These risks can be minimized with medical nutritional therapy and good glycemic control (5).

Children born to mothers with GD are more likely to be overweight at an early age and have an increased risk of type 2 diabetes and pre-diabetes in adult childhood compared to children born to mothers without GD (6,7). On the other hand, women burdened with GD during pregnancy are at risk of developing diabetes later in life. Studies have reported that women with GD during pregnancy have a seven to twelve times (8-10) higher risk of developing type 2 diabetes compared with women who are normoglycaemic during pregnancy and, according to a systemic literature review by Kim et al. (11), the occurrence rate is highest in the first 5 years after pregnancy. This systemic review also revealed a wide range of cumulative incidence of diabetes ranging from 2.6% to over 70%, which is presumably due to different follow-up periods among studies expanding from 6 weeks to 28 years postpartum. Specifically, the rate of development of diabetes after GD was almost 14% by 11 years after delivery in Spain (12) and almost 20% by 9 years after delivery in a study performed in Canada (13).

In a recent meta-analysis by Rayanagoudar et al. (14), advanced maternal age, BMI and family history of diabetes were associated with future risk of type 2 diabetes, accentuating the importance of personalised risk of progression to type 2 diabetes in each pregnant woman. A study by Bian et al. (15) came to similar conclusions, where two or more abnormal OGTT values during pregnancy and high BMI of pregnant women were risk factors for developing diabetes later in life. However, similar studies for populations in Southeast Europe are scarce and there is limited data on the long-term maternal consequences of GD. This prevents full comprehension of the relevance and importance of this condition and its possible future effect on diabetes prevalence.

The aim of this study was to reveal the risk of developing diabetes after GD by determining the prevalence of diagnosed diabetes in women 5 years after having GD diagnosed in pregnancy in Croatia. Also, we sought to determine the difference in occurrence of risk factors which might predispose women to develop diabetes after having GD during pregnancy.

Methods

This retrospective longitudinal study was performed using data from medical birth certificates (MBC) collected in Croatia as part of perinatal statistics data collection and data from the CroDiab diabetes registry; a registry gathering data on all patients diagnosed with diabetes in Croatia (16, 17). Both of these registries are reported to the

Croatian Institute of Public Health (CIPH) and are mandatory to complete; data for medical birth certificates are fulfilled by the birth attending doctor while data for the Crodiab diabetes registry is fulfilled by either general practitioners caring for patients with diabetes in primary care or by diabetologists. Data for CroDiab registry is collected from the databases of all primary health care prescriptions and patients diagnosis ensuring complete coverage of diagnosed persons with diabetes in Croatia.

Women burdened with GD in 2011 were identified and followed up until year 2016. Those registered in CroDiab registry were recognised as new patients with diabetes. Also, the registry of deceased was searched in order to identify if any of the followed up women who did not have GD had died. The registry of deceased is part of CroDiab registry, so all women who developed diabetes after GD were included in the follow-up.

In 2011, GD was diagnosed according to national guidelines published by the Croatian Society for Gynaecology and Obstetrics (18, 19) which are still in use today. These guidelines are based on the recommendation of the International Association of the Diabetes in Pregnancy Study Group (IADPSG) (20) and include performing a one-step 75g OGTT test between 24 and 28 weeks for women not previously diagnosed with overt diabetes. GD is diagnosed if plasma glucose values meet or exceed fasting value ≤ 5.1 mmol/L, 1-hour value ≤ 10.0 mmol/L and 2-hour value of ≤ 8.5 mmol/L.

After identifying women who had GD during pregnancy in 2011 through medical birth certificates, several data were collected including age at the end of follow-up period in 2016, body mass index (BMI) before pregnancy, level of education as well as marital status. Level of education was defined as: unfinished primary school and primary school, high school or similar and college, university and postdoc education, while marital status was considered as either married or living in a couple opposed to being single or divorced. Women with GD who were not followed up after childbirth due to lack of identification (ID) number were compared according to age and BMI to women who were followed up just in order to exclude major potential bias caused by loss to follow-up.

Statistical analyses were performed using SAS Enterprise Guide ver. 7.1. Normality of distribution was tested using Shapiro-Wilks test, while homogeneity of variance was tested using Levene test. Differences between groups of independent continuous variables were analysed using t-test and Mann – Whitney U test while differences in the prevalence of individual conditions were compared using the chi $(\chi)^2$ test, with Yates correction when appropriate. Statistical significance was defined as $p<0.05$.

Primary outcome of this study was to find out the prevalence of diabetes 5 years after pregnancy complicated with GD. Secondary outcomes were to determine whether age, level of education, marital status and pre-pregnancy obesity differ between women who develop diabetes after GD during pregnancy and women who do not develop diabetes after GD during pregnancy.

Ethical approval was obtained from CIPH Ethical Committee for Health Researches, grant number 030-02/17-10/1.

Results

Among 40641 deliveries in Croatia in 2011; 1181 (2.9%) women were reported to have GD. Among these women, 853 (72.23%) were identified using ID numbers and followed up in CroDiab diabetes registry. None of them died during the follow up period and 32 (3.75%) were identified as newly diagnosed patients with diabetes five years later. Median (Q_1, Q_3) age at the end of follow-up of women with GD who developed diabetes was 37 (33, 42) years while the comparable age was 36 (33, 40) for women with GD who did not develop diabetes. Median (Q_1, Q_3) BMI before pregnancy in the diabetes group was 26.96 (25.10, 31.56) and in the non-diabetes group 24.55 (21.72, 28.69). Women who developed diabetes and those who did not develop diabetes did not significantly differ according to age (p=0.587), level of education (p=0.549) or marital status (p=0.849) but women who developed diabetes were significantly more obese before pregnancy compared to the women who did not develop diabetes (p=0.002).

Age at the end of follow up, BMI before pregnancy, level of education and marital status of women with GD who developed diabetes and women with GD who did not developed diabetes as well as differences between those two groups are presented in table 1.

Table 1. Differences between women with GD who developed diabetes and women with GD who did not develop diabetes

	Women with GD who developed diabetes	**Women with GD who did not develop diabetes**	**p-value**
Age at the end of follow up (years) *	37 (33, 42)	36 (33, 40)	0.587
BMI before pregnancy (kg/m^2)*	26.96 (25.10, 31.56)	24.55 (21.72, 28.69)	0.002

Level of education			0.549
Up to finished primary school (%)	9.10	5.54	
High school and more (%)	77.27	72.51	
College and more (%)	13.63	21.95	
Marital status			0.849
Un paired (unmarried, divorced, widow) (%)	10.34	9.29	
Paired (married, cohabitation) (%)	89.66	90.71	

* Data are presented as median (first quartile Q_1, third quartile Q_3)

The remaining 328 women who had GD in 2011 but were not followed-up in CroDiab diabetes registry due to lack of ID number were also analyzed. The results showed that these women did not differ significantly compared to followed up GD women concerning age (p=0.185) and BMI (p=0.914).

The Kaplan-Meier estimation of the length of time (in months) until women who have had GD during pregnancy develop diabetes is presented on Figure 1.

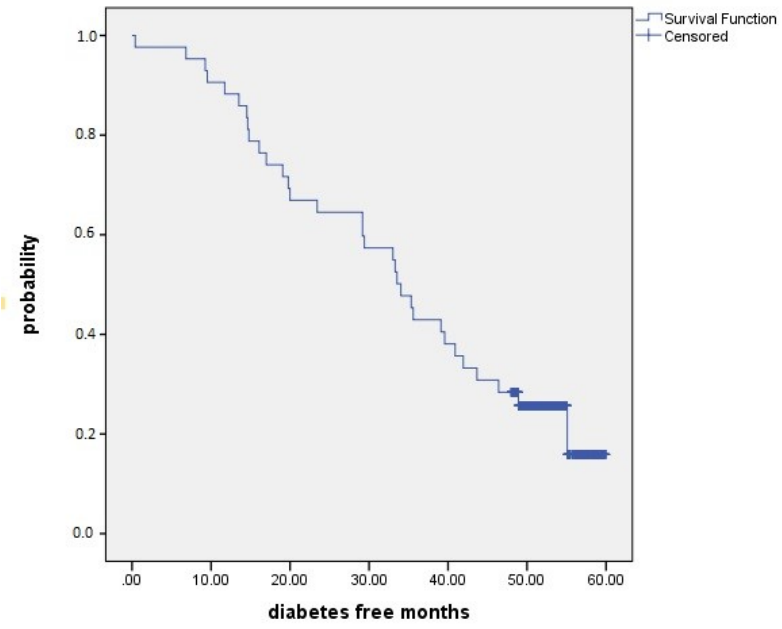

Figure 1. Time to diabetes development in women with gestational diabetes in Croatia who developed diabetes within five years of childbirth

Discussion

Based on available data in CroDiab diabetes registry, prevalence of diabetes 5 years after pregnancy complicated with GD is 3.75%. This result seems to be less compared to previously published studies and similar to only one other study from Sweden where diabetes prevalence was 3.4% among women 3-4 years after childbirth (21). The majority of other studies report higher prevalence rates, ranging from 14% (9) or 20% (13) by 11 or 9 years postpartum and up to 33.3% among women investigated 5-10 years postpartum (15). We believe a longer period of follow up in the latter studies might be the cause of higher diabetes prevalence compared to the one observed in our study. Hence, we find it is difficult to compare our reported prevalence with other studies due to this different follow-up periods involved. Unfortunately, we were unable to perform such a long-term follow-up since good quality data on GD prevalence in Croatia exist from 2011, while earlier data is not representable.

Still, prevalence of gestational diabetes in 2011 reported in this study might be an underestimation as a result of underreporting in the registry of medical birth, mostly due to incomplete or inadequate filling in of data by doctors attending deliveries, which is supported in a report published in 2016 (22). Under diagnosis of the presence of GD in 2011 should also be kept in mind affecting the results in our study. Year 2011 is the year of introduction of new national guidelines for diagnosis and management of GD, so gradual and steady implementation of these guidelines might be a cause of under diagnosis, notably since a better diagnosis and consequently better reporting trend was identified in the following years (22).

Nevertheless, despite this weakness, our study demonstrates that women with GD during pregnancy are at increased risk of developing diabetes even as early as 5 years after delivery. Women with GD represent a high-risk population for development of diabetes later in life and should be followed up and monitored intensely after childbirth in their primary care setting. By performing regular preventive educative measures (i.e. accentuating the importance of a healthy, balanced diet as well as regular physical activity) these women can avoid or postpone developing diabetes later in life. This was confirmed in a randomized controlled trial published in 2008, where both intensive lifestyle and metformin were highly effective in delaying or preventing diabetes in women with a history of GD (23). Also, a recently published systematic review confirmed intervention to be superior to no intervention, but no specific intervention was shown to be superior to others (24).

Additionally, a study by Claesson et al. showed that a third-trimester HbA1c value ≥ 5.4% among women with GD could be used as a mean for selecting women at high risk of developing diabetes later in life (25). Target screening performed after delivery can identify the presence of diabetes in its earliest stage allowing the introduction of appropriate treatment. Health care practitioners in primary care play an essential role in this process since they possess a complete, continuous and long-term insight of women's health condition.

The majority of health authorities worldwide recommend postpartum screening of diabetes between 6 and 12 weeks after delivery (26, 27), but many women with GD during pregnancy do not undergo postpartum glucose testing (28). In most populations, only half of women with a history of GD are screened after childbirth (29). According to a study by Van Ryswyk et al. (30), three most common barriers for women to this include: not having enough time, inadequate childcare and a need to focus on the health of the baby. Health care professotionals also contribute to this, since a study by Shah et al. revealed that despite high rates of postpartum visits to family physicians and obstetricians, few women with GD received the recommended diabetes test (31).

By pointing out the long-term sequels of GD during pregnancy, we believe women might be more motivated to attend early postpartum screening with all benefits it can provide. Likewise, a possible improvement of existing guidelines on postpartum management of gestational diabetes might be including an additional screening scheme one or two years after childbirth- a period when women have more time and focus more on their health but are still at risk of developing diabetes. Also, the importance of postpartum screening among women with GD should be accentuated both to pregnant women diagnosed with GD during pregnancy as well as primary care practitioners who are in charge of future health-related follow up of these women. Primary care practitioners should be more active in motivating and mobilizing their female patients to attend postpartum screening. This is supported by a systematic review by Carson et al. (32), where proactively contacting patients via phone calls, education programs or postal reminders was associated with higher postpartum testing rates.

Finally, additional efforts should be made to raise public awareness of long-term sequels of GD during pregnancy.

Another important observation in this study was that women who develop diabetes after GD in pregnancy had higher pre pregnancy BMI compared with women who did not

develop diabetes after GD in pregnancy. This is in accordance with previously published studies, such as the study by Albadera et al. (9) where prepregnancy BMI was recognized as an important independent predictive factor for diabetes after GD in pregnancy. Considering this, preventive measures and education should be especially oriented toward obese women who develop GD during pregnancy. Median age of women with GD who developed diabetes was higher compared to women with GD who did not develop diabetes, but the result was not statistically significant. This result differs to results of other studies (11), and might be due to a small sample size presented in this study.

Conclusions

Women with a history of gestational diabetes represent a population at high risk for development of diabetes. This was reveled in this study where 3.75% of women with GD during pregnancy developed diabetes within 5 years after delivery. This group of women, and especially the subgroup with higher BMIs, should be recognized, followed up and target screened after delivery in order to identify the presence of diabetes in the earliest stage possible. Primary care practitioners play an essential role in this process with the aim of reducing the number of women developing diabetes early in life.

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Conflict of interest

The authors state that they have no conflict of interest.

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