

# Tight versus less tight 1-hour postprandial glycemic target in women with gestational diabetes mellitus — a single-center cohort study

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## ABSTRACT

**Objectives:** We aimed to assess the impact of the change of 1-hour postprandial glycemic target from < 6.7 mmol/L (120 mg/dL) to < 7.8 mmol/L (140 mg/dL) on gestational diabetes mellitus (GDM) treatment and pregnancy outcomes.

**Material and methods:** In a retrospective analysis of 1021 GDM patients from the Department of Metabolic Diseases, University Hospital in Cracow, Poland, we compared insulin therapy regimens and pregnancy outcomes between women admitted in 2014–2016 (before the change) and in 2018–2019 (after it).

**Results:** A total of 377 patients were admitted between 2014 and 2016 (TIGHT group) and 644 between 2018 and 2019 (LESS TIGHT group). Women from the LESS TIGHT group were older (32 vs 30 years,  $p < 0.001$ ) and gained less weight during pregnancy (7.0 vs 9.0 kg,  $p < 0.001$ ). There was no change in the frequency of any insulin therapy (51.6% vs 56.1%,  $p = 0.168$ ). In the LESS TIGHT group, the basal insulin-only model was used more frequently (32.5% vs 10.2%,  $p < 0.001$ ), while the prandial insulin and basal-bolus model less frequently (23.6% vs 42.6% and 21.4% vs 36.7%,  $p < 0.001$ , respectively) than in the TIGHT group. There were no differences in the frequency of cesarean sections, preterm births, Hbd of delivery, mean birth weight or prevalence of perinatal complications.

**Conclusions:** Less tight glycemic targets in women with GDM, compared to tighter targets, were associated with less frequent use of prandial insulin, with insulin therapy often limited to basal administration. The change in glycemic targets did not affect the prevalence of adverse pregnancy outcomes, providing evidence supporting new recommendations.

**Keywords:** gestational diabetes mellitus; GDM; glycemic targets; pregnancy outcomes; insulin therapy

Ginekologia Polska

## INTRODUCTION

Gestational diabetes mellitus (GDM), defined as any glucose intolerance of variable severity with onset and first recognition during pregnancy, is a common complication of pregnancy. The International Diabetes Federation estimates suggest that globally hyperglycemia in pregnancy affects about 15.8% of live births, with around 84% of these being due to GDM [1].

Numerous studies have shown that even mild hyperglycemia in pregnancy, such as the one during GDM, may adversely affect the perinatal period, and the newborn's and mother's health [2, 3]. These complications include neonatal

macrosomia, hypoglycemia, jaundice, and stillbirth. GDM was also proven to be associated with an increased risk of preeclampsia, delivery at < 37 weeks, primary cesarean delivery, shoulder dystocia, and birth injury [4]. It is also a major risk factor for the emergence of type 2 diabetes, obesity, and cardiovascular disease both in the mother and child in the future [5].

The search for the most successful treatment strategies for GDM has been ongoing for many years. Adequate treatment of hyperglycemia in pregnancy, including lifestyle interventions, such as diet and exercise, and pharmacotherapy — mainly insulin, aims to maintain glycemia throughout

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pregnancy at the level of normoglycemia as in a healthy pregnant woman to reduce the aforementioned risks [6, 7].

Recommendations concerning the target glucose in women with GDM vary internationally. The available recommendations rely to a large degree on expert consensus, as there have been few trials that compared different targets of glucose control in women with GDM in the past [8, 9].

In 2017, Diabetes Poland introduced more liberal glycemic goals for the treatment of diabetes during pregnancy, changing the 1-hour postprandial glycemic target from  $< 6.7$  mmol/L (120 mg/dL) to the new  $< 7.8$  mmol/L (140 mg/dL) [10, 11]. This move, however, requires a close monitoring of real-world mother and child outcomes to be evaluated and compared.

While achieving glycemic goals in GDM was proven to benefit the patients in terms of lower prevalence of adverse outcomes, it may come at a cost of intensified medicalization of pregnant women, with more hospital and clinic visits, and increased risk of hypoglycemia, potentially creating a feeling of overwhelming GDM patients [8].

In this study, we aimed to assess the impact of changing the postprandial glycemic target on administered treatment and pregnancy outcomes of GDM patients treated from 2014 to 2019.

## MATERIAL AND METHODS

### Study population

A retrospective analysis of GDM patients admitted at the Outpatient Clinic of the Department of Metabolic Diseases, University Hospital in Cracow, a tertiary reference center for pregnant women with diabetes in South-Eastern Poland. Medical data of all consecutive patients were collected between 2014 and 2019. The study included all women with GDM whose data was available and complete in the 2014–2016- and 2018–2019-time frames. Women with other types of diabetes (*i.e.* type 1 diabetes, type 2 diabetes, other specific types of diabetes) and those who were referred to the center on initial suspicion of GDM but were not confirmed following additional diagnostic testing were excluded from the analysis.

Gestational diabetes mellitus was diagnosed based on the algorithm described in the Diabetes Poland guidelines adequate for the period investigated [10]. Fasting blood glucose (FPG) was performed as a routine laboratory test for all women in early pregnancy. In the case of FPG below 92 mg/dL (5.1 mmol/L) and no GDM risk factors, the patient was qualified for GDM testing again between the 24<sup>th</sup> and 28<sup>th</sup> week of pregnancy. When the FPG was below 92 mg/dL (5.1 mmol/L) but risk factors for GDM were present or FPG was 92–125 mg/dL (5.1–6.9 mmol/L), an oral glucose tolerance test (OGTT) was performed immediately. When the results were within the normal range, a repeated 75 g OGTT

was performed between the 24<sup>th</sup> and 28<sup>th</sup> week of pregnancy. When the FPG was  $> 125$  mg/dL (6.9 mmol/L) urgent fasting blood glucose retesting was performed. Hyperglycemia first diagnosed during pregnancy was diagnosed according to World Health Organization (WHO) recommendations [12]. In the case of diabetes in pregnancy, it was diagnosed when the general criteria for the diagnosis of diabetes outside of pregnancy were met, *i.e.*, fasting blood glucose  $\geq 126$  mg/dL (7.0 mmol/L); or blood glucose during the second hour of the 75 g OGTT  $\geq 200$  mg/dL (11.1 mmol/L); or random blood glucose  $\geq 200$  mg/dL (11.1 mmol/L), accompanied by clinical signs of hyperglycemia. In the case of GDM, it was diagnosed when fasting plasma glucose was 92–125 mg/dL (5.1–6.9 mmol/L); or blood glucose during the first hour of the 75 g OGTT  $\geq 180$  mg/dL (10 mmol/L); or blood glucose during the second hour of the 75 g OGTT 153–199 mg/dL (8.5–11 mmol/L).

Information regarding each patient's age, week of pregnancy during the first visit, initial weight, age at diagnosis, anthropometric measurements: weight, height, body mass index (BMI) before pregnancy, weight gain during pregnancy, earlier medical history (family diabetes history, history of having child with birthweight  $> 4000$  g, previous delivery of a neonate with a congenital anomaly, history of intrauterine fetal demise, multiparity and polycystic ovary syndrome), comorbidities (including hypertension and hypothyroidism — the diagnosis was based on recorded information concerning the diagnosis and previous or current treatments; hypothyroidism and hypertension were recorded as present when thyroid hormones or antihypertensive treatment were used, respectively), weight change during the pregnancy, OGTT on diagnosis, mode of insulin therapy (basal insulin only, basal-plus or bolus only) and total daily insulin dose were extracted from the electronic hospital database. Additionally, when available (*i.e.*, a woman with GDM had an appointment in the clinic after the delivery or the delivery occurred in the University Hospital Obstetrics and Perinatology Clinic), the mode and week of child's delivery, birthweight, perinatal complications (birth  $< 32$  and  $< 37$  weeks of pregnancy, birthweight  $> 4000$  g and  $< 2500$  g, preeclampsia/eclampsia, risk of premature birth and newborn asphyxia) were also logged.

All women diagnosed with GDM received an intensive diabetes management training program, which involved education on diet and physical activity, glycemic goals and self-monitoring of blood glucose levels (SMBG), insulin therapy, if needed, including modification of insulin doses to achieve glycemic targets as well as frequent outpatient visits. The recommended standard calorie intake was about 30–35 kcal/kg of body weight and depended on the current body weight, height, physical activity and age. The patients were advised to consume 40–50% of

calories from carbohydrates, 20–30% from fats and 30% from proteins. The recommended weight gain depended on baseline body weight (11.3–15.9 kg for women with normal weight, 6.8–11.4 kg for overweight women, 4.5–9.1 kg for women with obesity and up to 18 kg for patients with BMI < 19.8 kg/m<sup>2</sup>). Excess weight gain was managed by reducing food intake. Ketone levels were monitored daily from a morning urine sample [10, 11]. Self-monitoring of blood glucose levels encompassed checking glycemia several times a day, including fasting and 1 hour after each meal, min. 5–6 times/day. According to the guidelines of Diabetes Poland before 2017, self-monitored glucose 3.9–5.0 mmol/L (70–90 mg/dL) at fasting states, < 6.7 mmol/L (< 120 mg/dL) 60 minutes after meals and > 3.3 mmol/L (> 60 mg/dL) between 2 a.m. and 4 a.m. were endorsed [11]. In 2017, these targets were changed for glucose 3.9–5.0 mmol/L (70–90 mg/dL) at fasting states, < 7.8 mmol/L (< 140 mg/dL) 60 minutes after meals and 3.9–5.0 mmol/L (70–90 mg/dL) between 2 a.m. and 4 a.m. [10]. Patients were also instructed on when to adjust insulin doses. If by the 2<sup>nd</sup> day fasting glucose was > 90 mg/dL (5 mmol/L), then an increase of the dose of basal insulin by 1 unit, and if > 100 mg/dL — an increase by 2 units was recommended. If 1-hour postprandial glucose after a given meal was above the target, then the increase of the prandial insulin by 1 unit was recommended.

We compared the frequency of insulin use, mode of insulin therapy and pregnancy outcomes between the women admitted between 2014–2016 (before the change of 1-hour postprandial glycemic target; TIGHT) and between 2018–2019 (after the change; LESS TIGHT).

### Statistical analysis

For normally distributed data, means and standard deviations (SDs) are presented. For non-normally distributed data, medians and interquartile ranges (IQRs) are presented. Paired data clusters were analyzed using the Wilcoxon test, and Friedman test, and unpaired data was analyzed using the Mann–Whitney U-test. Categorical unpaired data was analyzed using the chi-squared test, and paired data were analyzed using the McNemar test. No sample-size calculation was performed. Pairwise deletion (available-case analysis) was used. In the case of missing data, the reported frequencies refer to the number of participants with available data. A *p* value < 0.05 was regarded as statistically significant, and all analyses were performed using Statistical Product and Service Solutions version 29 (SPSS 29)

### Ethics

The study was entirely based on retrospective analysis of patients' medical records, and ethics approval was not required. This retrospective analysis did not impact either

any diagnostic procedures or treatment methods. This type of research is exempt from obtaining informed consent. The authors were granted permission to access and analyze the patients' data by the Hospital Board.

## RESULTS

We collected data from 1021 women treated between 2014 and 2019. A total of 377 patients were admitted between 2014 and 2016 (TIGHT group) and 644 between 2018 and 2019 (LESS TIGHT group). The mean age was 31.3 ± 4.7 years.

Women from the LESS TIGHT group were slightly older [32 (interquartile range; IQR 27–33) vs 30 (IQR 29–35) years, *p* < 0.001], had their 1<sup>st</sup> visit in pregnancy earlier (26 vs 27 Hbd, *p* = 0.003) and gained less weight during pregnancy (7.0 vs 9.0 kg, *p* < 0.001). In the LESS TIGHT more women had GDM risk factors (53.6% vs 30.3%, *p* < 0.001) and hypothyroidism in pregnancy (33.3% vs 20.7%, *p* < 0.001). Maternal clinical characteristics according to study groups are summarized in Table 1.

There was no change in the frequency of prescription of any insulin therapy (51.6% vs 56.1%, *p* = 0.168). Prandial insulin was prescribed more frequently in the TIGHT group (42.6% vs 23.6%, *p* < 0.001). The basal insulin-only model was used more frequently in the LESS TIGHT group (32.5% vs 10.2%, *p* < 0.001), whereas basal insulin with boluses and boluses-only models were prescribed less frequently in the LESS TIGHT group (21.4% vs 36.7% and 1.4% vs 6.1%, *p* < 0.001, respectively). GDM treatment is summarized in Table 2.

There were no differences in the frequency of cesarean sections, preterm births, Hbd. of delivery, mean birth weight and prevalence of all investigated perinatal complications. Clinical characteristics of pregnancy and neonatal outcomes according to the study groups are summarized in Table 3.

## DISCUSSION

In this study, a retrospective analysis was conducted comparing the different 1-hour postprandial glycemic targets — tight versus less tight in women with GDM. We found that the change in this glycemic target did not affect the prevalence of adverse pregnancy outcomes. We also showed it could lead to less burden due to diabetes, with just one injection of basal insulin in more women with GDM than a tighter postprandial target.

There is no universal agreement regarding the target postprandial glucose in women with GDM, mainly due to a lack of high-quality studies [5, 8, 9]. A recent Cochrane review suggested that the risk of the most significant complications, such as large-for-gestational-age, severe infant morbidity, and perinatal mortality were similar between groups of tight and less tight metabolic control [13]. Con-

**Table 1. Maternal clinical characteristics according to study groups**

	<b>Tight control (n = 377)</b>	<b>Less tight control (n = 644)</b>	<b>p value</b>
Age [years]	30 (27–33)	32 (29–35)	< 0.001
Hbd of 1 <sup>st</sup> visit [weeks]	27 (22–30)	26 (15–29)	0.003
Pre-pregnancy body weight [kg]	67.0 (59.0–79.0)	68.0 (59.0–82.0)	0.294
Last recorded pregnancy body weight [kg]	76.0 (68.8–86.5)	76.0 (67.0–88.0)	0.734
Weight gain during pregnancy [kg]	9.0 (5.5–12.0)	7.0 (3.0–11.0)	< 0.001
GDM risk factors*, n (%)	98 (30.3%)	336 (53.6%)	< 0.001
Hypothyroidism in pregnancy, n (%)	71 (20.7%)	214 (33.3%)	< 0.001
Hypertension in pregnancy, n (%)	21 (6.1%)	42 (6.5%)	0.802
FPG in OGTT [mmol/L]	4.9 (4.4–5.3)	5.1 (4.6–5.5)	< 0.001
1-h OGTT [mmol/L]	9.8 (8.5–10.6)	10.0 (8.6–11.0)	0.114
2-h OGTT [mmol/L]	8.7 (7.7–9.4)	8.6 (7.1–9.3)	0.048
HbA1c [%]	5.1 (4.8–5.4)	5.1 (4.9–5.6)	0.243

\*pregnancy beyond 35 years of age, history of having a child with birthweight > 4000 g, previous delivery of a neonate with a congenital anomaly, history of intrauterine fetal demise, hypertension, overweight or obesity, family history of diabetes type 2, gestational diabetes during previous pregnancies, multiparity, polycystic ovary syndrome; Hbd — weeks of gestation; GDM — gestational diabetes mellitus; FPG — fasting plasma glucose, OGTT — oral glucose tolerance test, HbA1c — glycosylated hemoglobin; Results are presented as mean ± standard deviation (SD) or median and interquartile range (IQR) for continuous variables or n (%) for categorical variables

**Table 2. Treatment during pregnancy**

	<b>Tight control (n = 377)</b>	<b>Less tight control (n = 644)</b>	<b>p value</b>
Insulin use, n (%)	194 (51.6%)	361 (56.1%)	0.168
Prandial insulin, n (%)	146 (42.6%)	152 (23.6%)	< 0.001
Insulin therapy mode			< 0.001
Basal only, n (%)	35 (10.2%)	209 (32.5%)	
Basal-plus, n (%)	126 (36.7%)	138 (21.4%)	
Bolus only, n (%)	21 (6.1%)	9 (1.4%)	
Daily total insulin dose [units]	25.0 (9.0–51.0)	15.0 (7.0–33.8)	0.001

Results are presented as N (%) for categorical variables

**Table 3. Clinical characteristics of pregnancy and neonatal outcomes**

	<b>Tight control (n = 377)</b>	<b>Less tight control (n = 644)</b>	<b>p value</b>
Hbd of delivery [weeks]	39 (38–40)	39 (38–39)	0.046
Cesarean section, n (%)	84 (52.8%)	58 (57.4%)	0.468
Birthweight [g]	3300.0 (3022.5–3687.5)	3290.0 (3040.0–3570.0)	0.629
Birthweight > 4000 g, n (%)	7 (4.4%)	7 (7.6%)	0.286
Birthweight < 2500 g, n (%)	8 (5.3%)	5 (5.4%)	1.000
Preeclampsia, eclampsia, n (%)	2 (1.6%)	3 (3.0%)	0.449
Risk of premature birth, n (%)	3 (2.3%)	2 (2.0%)	0.876
Newborn asphyxia, n (%)	7 (5.4%)	3 (3.0%)	0.381
Birth < 32 weeks of pregnancy, n (%)	1 (0.01%)	0	1.000
Birth < 37 weeks of pregnancy, n (%)	13 (8.6%)	12 (12.8%)	0.296

Hbd — weeks of gestation; Results are presented as mean ± standard deviation (SD) or median and interquartile range (IQR) for continuous variables or n (%) for categorical variables. In the case of missing data, the reported frequencies refer to the number of participants with available data

versely, tighter glycemic control can be associated with an increased risk of hypertensive disorders during pregnancy, small for gestational age and both maternal and newborn hypoglycemia [5, 13]. One must also consider potential risks associated with hypoglycemic events [8]. Asymptomatic episodes of hypoglycemia and mean glucose levels  $< 87$  mg/dL (4.8 mmol/L) were reported to be associated with an increased risk of small-for-gestational-age infants [14]. In clinical practice, the 1-hour postprandial glucose is used to titrate insulin doses, as it was reported in a study that proved it improved glycemic control in GDM women and reduced the risk of neonatal complications [15].

Currently, glycemic treatment targets recommended in the most prominent international guidelines in women with GDM are fasting plasma glucose  $\leq 5.3$  mmol/L, 1-hour postprandial plasma glucose  $\leq 7.2$ – $7.8$  mmol/L, and two-hour postprandial plasma glucose  $\leq 6.7$  mmol/L [12, 16, 17]. American Diabetes Association recommends fasting glucose  $< 95$  mg/dL (5.3 mmol/L) and either one-hour postprandial glucose  $< 140$  mg/dL (7.8 mmol/L) or two-hour postprandial glucose  $< 120$  mg/dL (6.7 mmol/L) [12] according to the Fifth International Workshop-Conference on Gestational Diabetes Mellitus [18].

Until 2017, Diabetes Poland recommended a fasting glycemic goal of 70–90 mg/dL (3.9–5.0 mmol/L), and more tight postprandial glycemic goals with the 1-hour postprandial glycemic target of  $< 120$  mg/dL (6.7 mmol/L) and  $> 60$  mg/dL (3.3 mmol/L) between 2 a.m. and 4 a.m. [11]. In 2017, Diabetes Poland liberalized the 1-hour postprandial glycemic target to  $< 7.8$  mmol/L (140 mg/dL) and  $> 70$  mg/dL (3.9 mmol/L) between 2 a.m. and 4 a.m. [10].

In our study population, applying lower glycemic goals did not result in a higher prevalence of adverse neonatal outcomes. Although this was an observational study, not a randomized trial, only, it may be assumed that the shift towards less strict glycemic control is safe regarding fetal growth and optimal infant body size. Nevertheless, it should be considered that due to partially missing data regarding the pregnancy outcomes, this result might have been biased. It is possible that women with GDM who lived in the vicinity of the clinic were more likely to attend an appointment in the clinic after the delivery than those living outside Cracow. Moreover, it can also be assumed that women with the highest risk of pregnancy complications tended to deliver children in the University Hospital Obstetrics and Perinatology Clinic, a tertiary reference center for pregnancy and neonatal care, with the remaining women, for whom data was unavailable, delivering in less specialized units. This finding is in line with a recent report which proved similar results between tighter ( $< 7.4$  mmol/L,  $< 133$  mg/dL) and less tight ( $< 8.0$  mmol/L,  $< 144$  mg/dL) glycemic control groups of GDM patients [19] regarding birthweight, SGA and

macrosomia. Nevertheless, the mentioned study reported a higher risk of serious infant morbidity in the less tight glycemic control group, but also a higher risk of serious maternal health outcomes [19]. Still, due to this surprising discrepancy and study limitations, the authors refrained from formulating clinically relevant conclusions [19].

Recently, another retrospective study from Poland was published, reporting that applying a lower threshold for 1-hour postprandial glycemia of  $< 120$  mg/dL, as compared to  $< 140$  mg/dL in GDM patients, led to the reduction of the incidence of LGA and macrosomia in their offspring, without increasing the risk of SGA. Moreover, in the multivariable model using a less tight 1-hour postprandial target was an independent predictor for both LGA and macrosomia [20]. There were no differences between groups regarding the need for any type of insulin therapy, the frequency of cesarean section, or preterm delivery [20].

These discrepancies between our and the mentioned results are intriguing as basic demographic characteristics were comparable. First, in our study a larger number of women was investigated, possibly increasing the power of statistical analyses. Another possible explanation for these differences may be the numerically higher use of insulin in our cohort, potentially affecting the frequency of adverse neonatal outcomes.

Another important finding in our study concerns the pharmacological therapies and insulin use in GDM patients. While there were no differences in the frequency of any insulin use between the groups, prandial insulins were more commonly used in the tight control group. In the less tight control group, patients were more commonly prescribed one injection of basal insulin. As previously reported, applying tighter glycemic targets, subsequently requires patients to use more complex models of insulin therapy, and can lead to an increase in healthcare costs and a higher disease burden in patients [8]. Finally, too strict glucose control can not only lead to normalizing birth weight but also to a higher proportion of SGA infants [21]. We did not report on maternal hypoglycemia, however previous studies of patients across different types of diabetes showed a significantly higher risk of hypoglycemia in patients under intensive insulin treatment with tight glycemic control [22, 23].

There is no risk threshold in the association of fetal macrosomia and maternal glycemia, as reported by the investigators of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study [3]. Early diagnosis of GDM and its subsequent effective treatment is crucial to reduce the risk of perinatal complications [5]. Still, due to the lack of high-quality evidence, a recent Cochrane overview of systematic reviews on the effectiveness of different treatment strategies for GDM was largely inconclusive [24]. One must

also consider potential risks associated with it, such as hypoglycemic events [8]. Asymptomatic episodes of hypoglycemia and mean glucose levels  $< 87$  mg/dL (4.8 mmol/L) were reported to be associated with an increased risk of SGA infants [14].

Despite a proper diet and physical activity during pregnancy, insulin therapy may be necessary in about half of women with GDM [5].

According to Diabetes Poland Guidelines [25], and summaries of product characteristics of available drugs, metformin and insulin are approved for the treatment of hyperglycemia during pregnancy. Insulin therapy regimen in GDM may consist of a single evening injection of basal insulin if fasting glucose levels are elevated, sometimes with an additional daytime injection to control hyperglycemia before meals during the first half of the day, with mealtime rapid-acting insulin when postprandial hyperglycemia occurs. Recently, several risk factors were reported for a requirement to introduce insulin in GDM, including maternal age over 30 years, family history of diabetes, pre-pregnancy obesity, a history of prior GDM, diagnosis of GDM before the third trimester, fasting hyperglycemia  $\geq 5.3$  mmol/L and HbA1c at GDM diagnosis  $\geq 5.5\%$  ( $\geq 37$  mmol/mol) [26].

It has been suggested that women with GDM should be divided based on specific diabetes phenotypes. By recognizing hyperglycemia on diagnosis, its severity and glycemic profile during the pregnancy, and genetic and physiologic features, it may be possible to define subtypes of GDM [5]. Then, it would be possible to more easily identify women who are more likely to require and benefit from insulin therapy, and further, which mode of insulin therapy would fit them the best [27]. This can be done by assessing selected maternal features, such as maternal age  $> 30$  years, family history of diabetes, pre-pregnancy obesity, GDM in previous pregnancies and early diagnosis of GDM, and performing additional tests, such as OGTT or HbA1c% [26, 27]. It is possible that one set of global recommendations will not fit all women with GDM, requiring rather a precision medicine approach to tackle current diagnostic and treatment strategies and goal controversies.

Finally, the variety of technologies available for people with diabetes, including women with hyperglycemia in pregnancy, has been constantly and rapidly increasing throughout recent years. Continuous glucose monitoring systems (CGMS), insulin pumps with automatic insulin delivery and health apps for smartphones significantly improve diabetes monitoring and treatment. This ever-evolving technological progress has been investigated in the perinatal care of GDM women as well. We suspect that by wider use of CGMS, new data will emerge, providing information that will allow the further improvement of current guidelines [28]. Evidence suggests that CGMSs are superior to SMBG in

GDM in terms of detecting a wider glycemic variability, and hypo- and hyperglycemic episodes [29]. Preliminary data suggests that CGMSs improve glycemic control, particularly HbA1c% and FPG, but not postprandial glycemia, insulin dose or maternal weight gain. There was also no significant impact on the incidence of adverse perinatal outcomes [30]. An interesting issue regards GDM diagnosis based on CGMS readings, with promising results from early reports [31].

Hypothyroidism was substantially more prevalent in the group with less tight as compared to the more tight glycemic targets. Considering the magnitude of this difference, the most likely possible explanation seems to be an increased awareness among the medical team regarding the screening and treatment of thyroid diseases in pregnancy, reflected in a significant increase in levothyroxine use during the last 20 years [32]. We also observed a major increase in the prevalence of GDM risk factors, which may be attributed to an increasing age of GDM patients. Moreover, similar observations were previously reported, attributing this trend also to an increasing multiparity and a higher incidence of obesity [33]. It should also be noted that there was a shift in recommendations regarding the diagnosis and initiation of treatment for hypothyroidism in pregnancy between the two study periods, as reflected in the local and international guidelines [34, 35]. Still, we think that in our cohort, its source may also be attributed to better quality data recorded in the medical records for women in the most recent period.

The major strength of this study is the inclusion of homogenous and non-selected cohorts of GDM patients from a tertiary reference center. Moreover, women attending the clinic received standardized care, including education, dieting, physical activity, SMBG and insulin therapy.

The main limitation of the study is that it was a retrospective analysis of patients' data, which is prone to multiple biases. As there could have been multiple confounding factors, such as the impact of insulin use in pregnancy and newborn complications, our results should be considered with caution. We also were not able to collect glycemic data as this information was not included in the electronic medical records. Finally, the data on obstetric and newborn complications were not available for all participants.

## CONCLUSIONS

In our study population, the less tight postprandial glycemic target in women with GDM, compared to the tighter target, led to reduced prandial insulin use and did not affect the prevalence of adverse pregnancy outcomes. This may suggest that liberalization of postprandial glycemic targets in GDM was safe for women and their children and could lead to lesser diabetes burden. These findings can be used to aid decisions on the glycemic targets women with GDM should use in the future.



## Article information and declarations

### Data availability statement

The data analyzed in the paper is available from the corresponding author upon reasonable request.

### Ethics statement

The study was based on a retrospective analysis of patients' medical records, and ethics approval was not required. Obtaining the informed consent of the patients analyzed was not required. Neither any diagnostic procedures nor treatment methods were affected by this study. The authors were granted permission to access and analyze the patients' data by the Hospital Board.

### Author contributions

MiK conceived and designed the analysis, collected and analyzed the data, wrote the initial draft and prepared the final version of the manuscript; MW collected and analyzed the data and reviewed the final version of the manuscript; IG collected the data and reviewed the final version of the manuscript; MaK contributed and collected the data and reviewed the final version of the manuscript; KC conceived and designed the analysis, contributed the data, helped write the initial draft and reviewed the final version of the manuscript; MTM supervised the study and reviewed the final version of the manuscript; MS conceived and designed the analysis, supervised the study, collected the data, helped write the initial draft and reviewed the final version of the manuscript

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### Conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

### Supplementary material

None.

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