

# Maternal-fetal Complications in Pregnancy: A Retrospective Comparison Between Type 1 and Type 2 Diabetes Mellitus

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## Research article

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# Abstract

**Background:** The aim of the study was a retrospective comparison of the differences in maternal-foetal outcomes between women with T1DM and T2DM

**Methods:** A cohort of 135 patients with pre-gestational diabetes, 73 with T1DM (mean age  $29 \pm 5$  years) and 62 with T2DM (mean age  $33 \pm 6$  years), in intensive insulin treatment throughout pregnancy were evaluated. Clinical and metabolic parameters and the prevalence of maternal and foetal complications were assessed.

**Results:** Women with T1DM showed lower pregestational BMI ( $p < 0.001$ ), pregestational weight ( $p < 0.001$ ), weight at delivery ( $p < 0.001$ ),  $\Delta$ \_total insulin requirement at the first, second and third trimesters (all  $p < 0.001$ ) and higher weight gain during pregnancy ( $p < 0.001$ ) pregestational HbA1c ( $p = 0.040$ ), HbA1c in the first ( $p = 0.004$ ), second ( $p = 0.020$ ) and third ( $p = 0.010$ ) trimesters than T2DM. Women with T1DM had a higher risk of large for gestational age (LGA) ( $p = 0.005$ ) than T2DM, while women with T2DM showed higher prevalence of abortion ( $p = 0.037$ ) than T1DM. At multivariate analysis, pregestational BMI and  $\Delta$ \_total insulin requirement of the first trimester were independently associated with abortion in T2DM, while weight gain during pregnancy was independently associated with LGA in T1DM.

**Conclusion:** Women with T1DM have a higher risk of LGA than T2DM due to the weight gain throughout pregnancy. By contrast, women with T2DM have a higher risk of spontaneous abortion than T1DM, due to pregestational BMI and  $\Delta$ \_total insulin requirement in the first trimester.

## Background

The prevalence of pregestational diabetes among women in the reproductive age is increasing. From 5–16% of pregnant population have gestational diabetes and about 1% have pregestational type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) [1].

Pregnancies complicated by diabetes mellitus are currently still characterized by a high incidence of unfavourable maternal and foetal outcomes, despite great advances in therapeutic intervention, probably related to poor glycaemic control, particularly in the periconceptional period and in the first trimester of pregnancy [2]. Generally, the perinatal/neonatal specific risks of diabetes in pregnancy include spontaneous abortion (before the 24th week), foetal abnormalities, preeclampsia, perinatal death, macrosomia (> 97th percentile), neonatal hypoglycaemia, hyperbilirubinemia and neonatal respiratory distress syndrome. In addition, women with pregestational diabetes may have an aggravation of diabetes complications such as retinopathy, nephropathy or chronic hypertension and an increased risk of obesity [3–5].

Pregnancy is physiologically characterized by an increase in insulin resistance and a reduced sensitivity to insulin action, due to the effects caused by placental hormones, such as human placental lactogen,

progesterone, prolactin, placental growth hormone, and cortisol. This change in maternal metabolism is directed towards providing adequate nutrition for the foetus [5, 6].

Although it is known that diabetes mellitus transforms pregnancy into high risk pregnancy [5–7], various factors are associated with adverse perinatal outcomes in women with T1DM and T2DM. However, which factors are more or less involved in the maternal and perinatal complications in women with pregestational T1DM and T2DM remains controversial.

The aim of this study was to evaluate maternal demographic characteristics and glycaemic control at early gestation and during pregnancy in a cohort of women with pregestational T1DM and T2DM in order to identify a possible correlation with maternal-foetal outcomes.

## Methods

We conducted a retrospective real-life based study on 135 pregnant women with pregestational diabetes (73 with T1DM, and 62 with T2DM on basal bolus insulin regimen), followed at the Unit of Endocrinology, University of Palermo (Italy) from June 2012 to June 2017. All procedures of the study were in accordance with the ethical standards of the local committee on human experimentation (institutional and national) and with the Declaration of Helsinki (1964), as revised in 2013. Approval was obtained from the Ethics Committee of the Policlinico Paolo Giaccone Hospital, University of Palermo. At the time of the first visit in our Out-Patients' Clinic, informed consent for the scientific use of the data was obtained from all patients recruited in the study. Inclusion criteria were unscheduled pregnancies, no previous pregnancies, duration of diabetes mellitus of at least 1 year before pregnancy and basal bolus insulin treatment for T1DM and oral hypoglycaemic drugs for T2DM. Exclusion criteria were twin pregnancies, T1DM

on insulin therapy by continuous subcutaneous insulin infusion and T2DM on diet treatment.

Conventional basal bolus insulin therapy consisted of a minimum of 4 daily subcutaneous insulin doses, 3 of a short-acting analogue before the main meals and 1 of a long-acting analogue after dinner.

During the first visit between the 5th and 8th weeks of amenorrhea, a detailed medical history was extracted for each patient, with particular attention to the previous obstetric history, diabetic disease and related chronic complications (retinopathy, nephropathy and arterial hypertension), history of poliabortivity, duration of diabetes and age at pregnancy. Body mass index and weight were extracted from charts. All patients had been trained in self-monitoring of blood glucose by the use of a glucose meter, with the instruction to perform a minimum of 6 daily measurements (before and 2 hours after meals), in order to modify and optimize insulin therapy, if necessary. The following target glucose levels were recommended: fasting glucose levels between 3.9 and 5 mmol/L and glucose levels 2 hours after the meal of less than 6.7 mmol/L. Patients also received a diet plan based on their pregestational BMI and weight. Patients with pregestational BMI  $\geq 30$  kg/m<sup>2</sup> were considered obese. Hypoglycaemia was

defined as glucose levels < 3.9 mmol/L. At early gestation and after 4 weeks, HbA1c was assessed and repeated every three months.

The outpatient visits were at intervals of two or three weeks until delivery, after which a re-evaluation was carried out after 30 days and 3–4 months after delivery. Acute complications were recorded during follow-up: episodes of ketosis, ketoacidosis and hypoglycaemic events. Mean fasting plasma glucose (FPG), postprandial breakfast glucose (PBG), postprandial lunch glucose (PLG) and postprandial dinner glucose (PDG) at first, second and third trimesters of pregnancy were recorded for each patient.

Maternal outcomes were also assessed. Nephropathy was defined as absent for microalbuminuria < 30 mg/24 h; incipient with urinary albumin excretion between 30 and 300 mg/24 h; macroalbuminuria with albumin excretion > 300 mg/24 h found on at least two consecutive measurements or with creatinine clearance < 50 mg/dl/24 h. With regard to the progression of renal damage, a significant increase in urinary albumin excretion or worsening of renal function indices was monitored. The pre-gestational arterial hypertension was defined with the detection of systolic blood pressure values > 140 mmHg; diastolic > 90 mmHg and/or taking antihypertensive drugs before pregnancy, while pregnancy-induced hypertension was diagnosed for detection of systolic blood pressure values > 140 mmHg and diastolic > 90 mmHg after the 20th week of gestation, and of pre-eclampsia if associated with proteinuria > 300 mg/24 h.

As obstetrical outcomes we assessed the loss of pregnancy before the 24th week of gestation, defined as spontaneous abortion, gestational hypertension, pre-eclampsia, caesarean section and preterm delivery. Preterm birth was defined as completion of birth before the 37th week. Perinatal/neonatal outcomes such as birth weight (grams and percentiles), birth length (cm and percentiles), foetal macrosomia or large for gestational age (LGA), defined as birth weight  $\geq$  90th percentile, hypoglycaemia, hypocalcaemia, jaundice and respiratory stress syndrome were extracted from the medical charts.

Total insulin requirement for each trimester and the change from the end to the start of the trimester ( $\Delta$ \_total insulin requirement) were calculated.

## Assays

Glycaemia was measured by standard methods (Modular P800, Roche, Milan). HbA1c levels were determined by HPLC with an ion-exchange resin (Bio-Rad Laboratories, Milan, Italy).

## Statistical analysis

SPSS version 17 and MedCalc version 11.3 were used for data analysis. Baseline characteristics were presented as mean  $\pm$  SD for continuous variables; rates and proportions were calculated for categorical data. Normality of distribution for quantitative data was assessed by the Shapiro-Wilk test. The differences between the two groups (T1DM and T2DM) were detected by the unpaired Student's t test for continuous variables (after testing for equality of variance: Levene test) and by the  $\chi^2$  test and Fisher's exact test (when appropriate) for categorical variables.

ANOVA was used for comparison of the pregestational variables HbA1c, HbA1c at the first, second and third trimesters, pregestational BMI, maternal weight at early gestation and at delivery, total insulin requirement at early gestation and at delivery,  $\Delta$ \_total insulin requirement in the first, second and third trimesters in the two groups of patients (T1DM and T2DM) after testing for equality of variance. The Fisher least significant difference post-hoc correction was applied if the variables had equal variances and the Dunnett post-hoc correction was applied if the variables did not have equal variances.

An univariate analysis in order to identify the dependent and independent variables to be included in the multivariate analysis was done.

Therefore, two different Generalized Linear Models (GLM) were performed on the variables "Abortion" and "LGA". The two different logistic regression models were as follows:

1. (Abortion) = Type of diabetes + Maternal age + Pregestational BMI + Pregestational HbA1c + HbA1c first trimester +  $\Delta$ \_total insulin requirement first trimester
2. (LGA) = Type of diabetes + Pregestational BMI + Pregestational HbA1c + HbA1c first trimester + HbA1c second trimester + HbA1c third trimester +  $\Delta$ \_ weight.

The differences between the two groups with p-value less than 0.05 were considered statistically significant.

## Results

The clinical characteristics of pregnant women with pregestational T1DM and T2DM are shown in Table 1. Age at pregnancy was significantly lower ( $p < 0.001$ ) and duration of diabetes was significantly longer in women with T1DM than in those with T2DM ( $p < 0.001$ ). Pregestational body weight ( $p < 0.001$ ), BMI ( $p < 0.001$ ), and weight at delivery ( $p < 0.001$ ) were significantly lower in women with T1DM than in those with T2DM (Table 1). However, the weight gain ( $\Delta$ \_weight) was higher in women with T1DM than T2DM ( $p < 0.001$ ).

Table 1  
Maternal characteristics of women with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM)

|   | <b>T1DM</b>   | <b>T2DM</b>   | <b><i>p</i></b> |
|---|---------------|---------------|-----------------|
|   | <b>No.=73</b> | <b>No.=62</b> |                 |
|   | Mean ± SD     | Mean ± SD     |                 |
| Duration of diabetes (years)            | 14.1 ± 8.05   | 4.11 ± 3.1    | < 0.001         |
| Age at pregnancy (years)                | 29.5 ± 5.42   | 33.7 ± 6.1    | < 0.001         |
| Pregestational BMI (Kg/m <sup>2</sup> ) | 21.8 ± 2.9    | 31.4 ± 6.7    | < 0.001         |
| Pregestational weight (Kg)              | 59.1 ± 8.8    | 82.2 ± 19.2   | < 0.001         |
| Weight at delivery (Kg)                 | 72.5 ± 10.7   | 90.8 ± 20.1   | < 0.001         |
| Δ_weight                                | 13.5 ± 4.4    | 8.61 ± 6.8    | < 0.001         |
|   | Subjects (%)  | Subjects (%)  |                 |
| Recurrent ketonuria                     | 3 (4.2%)      | 4 (6.5%)      | 0.552           |
| Pregestational diabetic retinopathy     | 16 (22.2%)    | 2 (3.2%)      | 0.016           |
| Diabetic retinopathy progression        | 6 (8.3%)      | 1 (1.6%)      | 0.082           |
| Pregestational diabetic nephropathy     | 10 (13.7%)    | 1 (1.6%)      | 0.018           |
| Nephropathy progression                 | 6 (8.3%)      | 5 (8.1%)      | 0.966           |
| Pregestational arterial hypertension    | 3 (4.2%)      | 9 (14.5%)     | 0.037           |
| History of poliabortivity               | 7 (9.6%)      | 3 (4.8%)      | 0.290           |

Women with T1DM showed a higher prevalence of pregestational diabetic retinopathy ( $p = 0.016$ ), nephropathy ( $p = 0.018$ ) (Table 1). By contrast, women with T2DM showed a higher prevalence of pregestational arterial hypertension ( $p = 0.037$ ) than those with T1DM (Table 1).

Patients with T1DM had significantly lower  $\Delta_{total}$  insulin requirement at the first ( $p < 0.001$ ), second ( $p < 0.001$ ) and third ( $p < 0.001$ ) trimesters than T2DM (Fig. 1).

In addition, patients with T1DM showed higher pregestational HbA1c ( $p = 0.040$ ), HbA1c of first ( $p = 0.004$ ), second ( $p = 0.020$ ) and third ( $p = 0.010$ ) pregnancy trimesters than those with T2DM (Fig. 2A). Women with T1DM showed a higher prevalence of hypoglycaemic events in the first trimester ( $p = 0.015$ ) (Fig. 2B) than T2DM, while women with T2DM showed a higher prevalence of hypoglycaemic events in the third trimester than those with T1DM ( $p < 0.001$ ) (Fig. 2B).

No differences in average fasting and postprandial glycaemia obtained from SMBG were observed between the groups except for a higher post-dinner glycaemia level for women with T2DM than with T1DM ( $p = 0.022$ ) (Fig. 3).

With regard to obstetrical complications, women with T2DM had higher prevalence of spontaneous abortion ( $p = 0.037$ ) than those with T1DM. By contrast, women with T1DM showed higher birth weight percentiles ( $p = 0.044$ ) and a higher prevalence of LGA ( $p = 0.005$ ) than those with T2DM (Table 2).

Table 2  
Neonatal and perinatal outcomes for women with type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM)

|                                 | <b>T1DM</b><br><b>No.=73</b> | <b>T2DM</b><br><b>No.=62</b> | <b><i>p</i></b> |
|---------------------------------|------------------------------|------------------------------|-----------------|
|                                 | Subjects (%)                 | Subjects (%)                 |                 |
| Obstetrical complications       |                              |                              |                 |
| Gestational hypertension        | 15 (20.8%)                   | 13 (21.0%)                   | 0.977           |
| Preeclampsia                    | 9 (12.5%)                    | 5 (8.2%)                     | 0.418           |
| Preterm delivery                | 23 (31.5%)                   | 12 (19.1%)                   | 0.102           |
| Caesarean section               | 68 (93%)                     | 50 (81.2%)                   | 0.093           |
| Abortion                        | 3 (4.2%)                     | 9 (14.5%)                    | 0.037           |
| Neonatal and perinatal outcomes |                              |                              |                 |
| Large for gestational age (LGA) | 36 (49.2%)                   | 16 (25.8%)                   | 0.005           |
| Hypoglycaemia                   | 24 (32.8%)                   | 16 (25.8%)                   | 0.376           |
| Hypocalcemia                    | 10 (13.6%)                   | 4 (6.4%)                     | 0.171           |
| Jaundice                        | 20 (27.4%)                   | 13 (20.9%)                   | 0.382           |
| Respiratory distress syndrome   | 20 (27.4%)                   | 12 (19.3%)                   | 0.277           |
|                                 | Mean $\pm$ SD                | Mean $\pm$ SD                |                 |
| Birth weight (g)                | 3314 $\pm$ 650               | 3285 $\pm$ 700               | 0.803           |
| Birth weight percentiles        | 72.6 $\pm$ 27.6              | 62.4 $\pm$ 30.7              | 0.044           |
| Birth length (cm)               | 48.6 $\pm$ 3.3               | 48.6 $\pm$ 2.1               | 0.997           |
| Birth length percentiles        | 60 $\pm$ 32.6                | 51.2 $\pm$ 28.6              | 0.100           |

At multivariate analysis, after stepwise selection in model 1 the significant variables that influenced the probability of having an abortion were the type of diabetes, with a higher risk in women with T2DM than

T1DM (OR 3.03;  $p = 0.011$ ), pregestational BMI (OR 2.06;  $p = 0.047$ ) and the  $\Delta_{\text{total}}$  insulin requirement of the first trimester (OR 2.02;  $p < 0.001$ ) (Table 3).

Table 3

Logistic regression of the generalized linear models abortion and large for gestational age (LGA)

| <b>Outcome variable: ABORTION</b>   |                       |       |                  |         |
|---|-----------------------|-------|------------------|---------|
|   | $\beta$ (coefficient) | SE    | OR (IC)          | $p$     |
| Constant  | -2.880                |       |                  |         |
| DM type   | 1.109                 | 0.434 | 3.03 (1.29–7.10) | 0.011   |
| Pregestational BMI  | 0.726                 | 0.365 | 2.06 (1.01–4.22) | 0.047   |
| $\Delta_{\text{total}}$ insulin requirement of first trimester  | 0.752                 | 0.328 | 2.02 (0.98–4.02) | < 0.001 |
| General model: $p = 0.007$  |                       |       |                  |         |
| <b>Outcome variable: LGA</b>  |                       |       |                  |         |
|   | $\beta$ (coefficient) | SE    | OR (IC)          | $p$     |
| Constant  | -0.430                |       |                  |         |
| $\Delta_{\text{weight}}$  | 0.861                 | 0.252 | 2.36 (1.44–3.87) | < 0.001 |
| General model: $p < 0.001$  |                       |       |                  |         |
| $\beta$ = coefficient of determination; SE: standard error; OR = odds ratio; IC = confidence interval |                       |       |                  |         |

In model 2 the neonatal outcomes of the two groups were compared, with evidence of a higher incidence of LGA in children of women with T1DM. After stepwise selection we observed that LGA variable was influenced by the maternal weight gain with a risk of 2.36 for each kilogram of weight increase between early gestation and delivery (adjusted for type of diabetes) (OR 2.36;  $p < 0.001$ ) (Table 3).

## Discussion

Our data show that pregnant women with pregestational T2DM have a higher incidence of spontaneous abortion (within the 24th week of gestation) than women with pregestational T1DM and that it is correlated with the pregestational BMI and the  $\Delta_{\text{total}}$  insulin requirement of the first trimester. In addition, we found that women with pregestational T1DM have a higher incidence of perinatal complications, such as LGA, than T2DM and it is correlated with the higher weight gain during pregnancy.

The differences in patient backgrounds, such as longer duration of diabetes, higher insulin requirement at early gestation, higher incidence of retinopathy and nephropathy in women with T1DM, and higher pregestational BMI and weight in women with T2DM are in line with those reported in other studies [8, 9].

In the current study women with T2DM had a higher incidence of spontaneous abortion and it was correlated with pregestational BMI and  $\Delta$ \_total insulin requirement of the first trimester. These findings suggest that obesity and consequent decrease of insulin sensitivity during the first trimester of pregnancy increase the risk of obstetrical complications. As known, women with T1DM need a net reduction in insulin dose in early and late gestation and about a 20% increase in the second and third trimesters [10]. By contrast, women with T2DM require a much greater increase in insulin dose from the start to the end of each trimester with a progressive increase. Although the increase in insulin requirement is presumably due to the effects of the placental hormones, some factors may have an influence in determining insulin requirement during pregnancy, such as pregestational BMI. An increase in adiposity is associated with higher production of pro-inflammatory cytokines and adipokines, which are responsible for the changes in insulin sensitivity [10].

Previous studies have shown that T2DM is associated with higher incidence of early and late spontaneous abortion and in turn spontaneous abortion is associated with a high risk of developing T2DM [11]. T2DM, like other cardiovascular risk factors, is associated with endothelial dysfunction and therefore with placenta abnormalities [12, 13]. The pregnancies of women with T2DM are known to be more prone to a higher risk of perinatal death, as well as congenital malformations, than those of women with T1DM [14]. In a study conducted by Clausen and colleagues, 61 women with T2DM were compared with 240 women with T1DM, demonstrating a 4 to 9 times higher incidence of foetal perinatal death in women of the first group compared to the second, although the latter had worse metabolic compensation [15]. These data were also confirmed by a recent meta-analysis of 33 observational studies published in the last 20 years, where women with T2DM have a higher incidence of perinatal death despite having a lower duration of diabetes, lower HbA1c values and lower rates of diabetic complications at the time of pregnancy than T1DM [14]. By contrast, McGrogan and colleagues found a similar frequency of spontaneous abortion in women with T2DM and women with T1DM, despite being greater than 20% compared to the general population [16]. In the current study, pregestational HbA1c was not associated with perinatal complications in women with T2DM and T1DM, even though pregestational maternal glycaemic control is known to reduce perinatal complications in pregnant women with diabetes, and current guidelines recommend a similar treatment strategy for both women with T1DM and T2DM [17]. A recent meta-analysis has shown that despite less severe glycaemic disturbance, women with T2DM did not have better perinatal outcomes than those with T1DM, suggesting that factors other than glycaemic control also affect perinatal complications in women with T2DM [14]. Indeed, pregnancy-induced insulin resistance adds to the pre-existing insulin resistance, typical of T2DM, and the pre-existing pancreatic  $\beta$ -cell defect compromises the ability to enhance insulin secretion during pregnancy, leading to marked hyperglycaemia [12]. Pregnancy-induced metabolic changes in women with T2DM require more intensive monitoring and closer titration of treatment. Unlike normal pregnancies, which in the first trimester tend to have lower glucose values, in pregnant women with T2DM higher glucose spikes are generally observed and strict insulin therapy adjustment is required [12].

Taken together, the above findings regarding pregnancy in T2DM on a background of metabolic syndrome suggest that obesity and insulin resistance before and during the first trimester of pregnancy

may greatly influence the risk of perinatal complications, more than glycaemic control [13, 16, 18].

With regard to women with T1DM, in the present study about 50% of them had perinatal/neonatal complications such as LGA and consequently higher birth weight percentiles and this percentage was higher than in women with T2DM, in line with other studies [19]. We found LGA was correlated with maternal weight gain during pregnancy, rather than pregestational HbA1c. Similar results were obtained in a Danish observational study, carried out on a group of 115 women with T1DM, which demonstrated that weight gain was an independent risk factor for foetal overgrowth [20]. In addition, a retrospective analysis of pregnant women with T1DM showed that excess weight gain was correlated with high risk of LGA [21]. Other studies showed that, in addition to weight increase, HbA1c values also correlated with the risk of LGA. In a study conducted by Morrens and colleagues, out of 180 pregnant women with T1DM, there was an increased frequency of LGA equal to about 42.5% of cases, certainly a higher incidence than that of the general population, correlating this finding with both weight gain and HbA1c values in early gestation and at delivery [22]. This result can be explained by longer duration of diabetes, greater glycaemic instability [22] and, according to other studies, greater weight of the placenta [23] in women with T1DM compared to women with T2DM. Also worthy of note is the need for greater surveillance for hypoglycaemias in LGA infants of women with T1DM given the 2.5-fold greater risk for these infants of hypoglycaemia. This factor can be considered a better predictor of neonatal hypoglycaemia, compared to maternal glycaemic control [24]. It has been suggested that glycaemic fluctuations and hypoglycaemia may influence the course of pregnancy in women with long-standing T1DM, but the effectiveness of different insulin treatments for glycaemic control and variability and hypoglycaemic episodes in pregnant women with T1DM has not been elucidated [25, 26]. In the current study no differences were found in the prevalence of hypoglycaemia between women with T1DM and T2DM.

The present study has limitations. First, our study had a retrospective cross-sectional design. Second, the sample size was small. Because of these limitations, the results of the present study should be carefully interpreted. Nonetheless, we believe that our findings have an important implication for clinical management and treatment of pregnant women with diabetes. To confirm our findings, future studies with a prospective design and larger sample size including women with and without perinatal complications are warranted.

In conclusion, women with T1DM have a higher risk of LGA than T2DM due to the weight gain throughout pregnancy. By contrast, women with T2DM have a higher risk of spontaneous abortion than T1DM, due to pregestational BMI and  $\Delta_{\text{total}}$  insulin requirement in the first trimester. Management of pregnancy complicated by diabetes mellitus is challenging for both the health care provider and the patient. Despite the efforts and results obtained over the past decades, maternal foetal outcomes still continue to be worse than those not complicated by diabetes mellitus.

## Declarations

**Ethical approval:** It was waived by the local Ethics Committee of University of Palermo in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

**Consent to participate:** Informed consent was obtained from all individual participants included in the study

**Availability of data and material:** All data generated or analysed during this study are included in this published article

**Competing interests:** The authors declare that they have no competing interests.

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**Authors' contributions:** V. Guarnotta and MI Mineo: manuscript writing, data analysis, editing; E. Giacchetto and MP Imbergamo: data collection; C. Giordano: protocol development, editing

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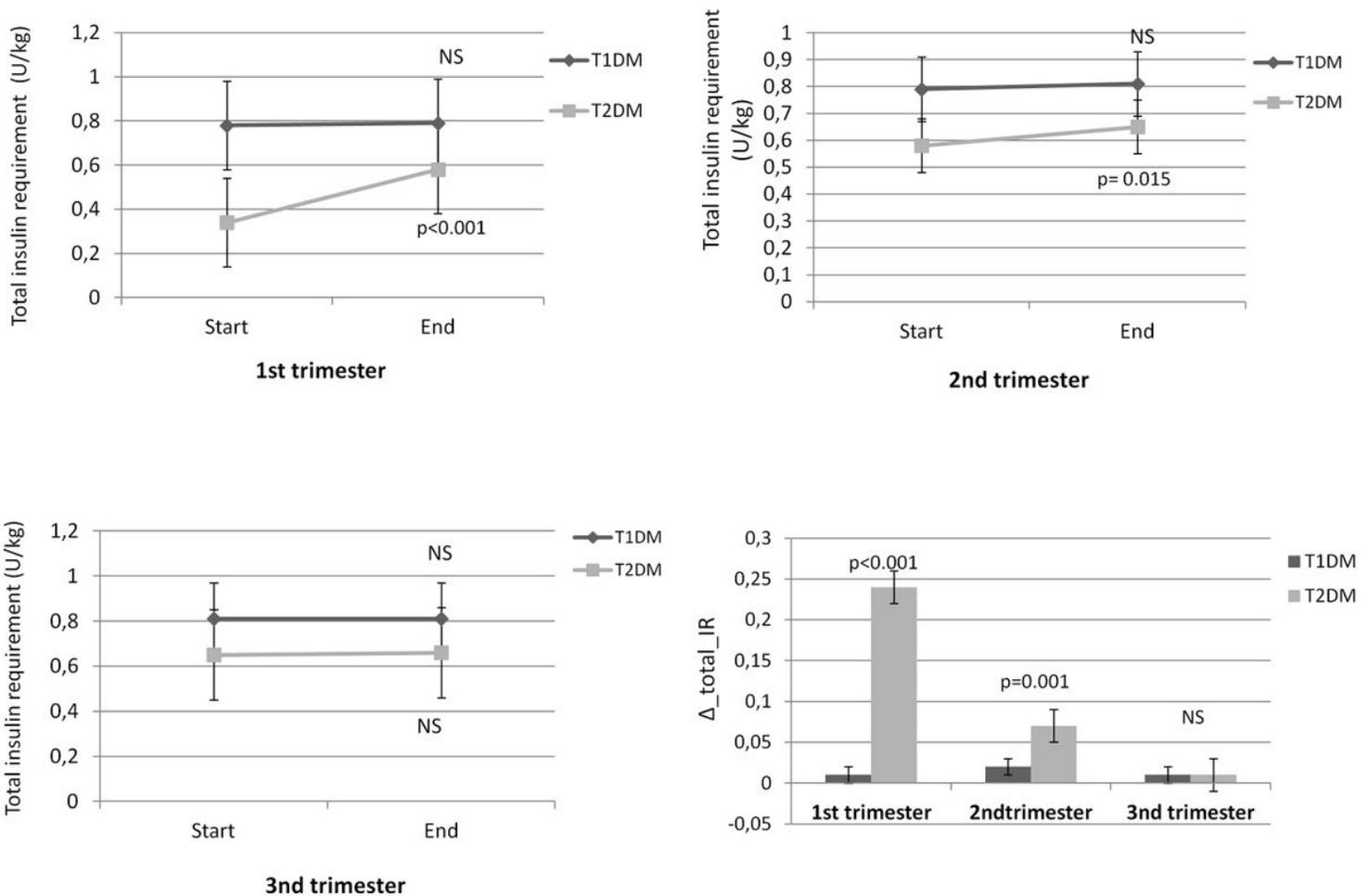
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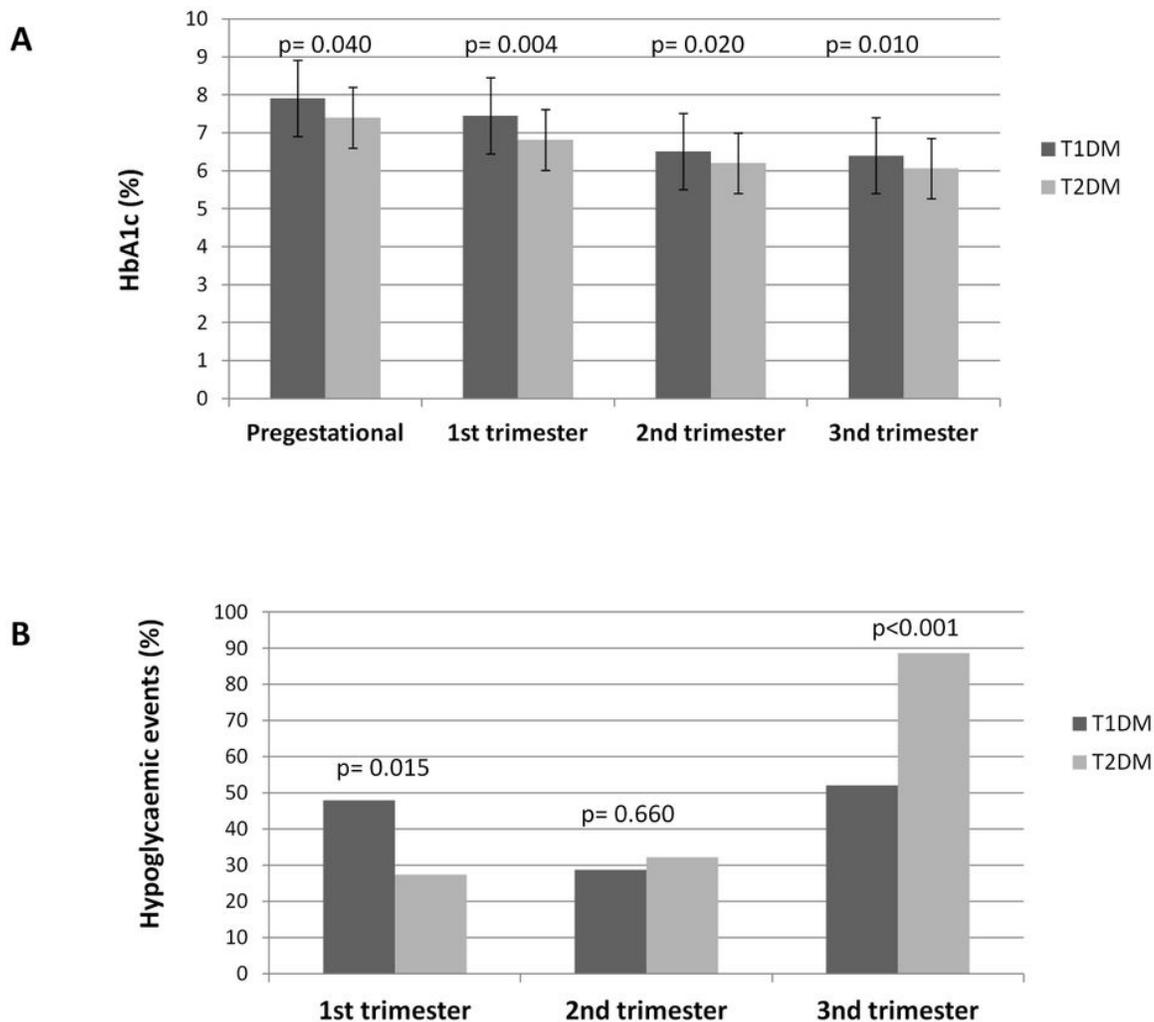
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## Figures



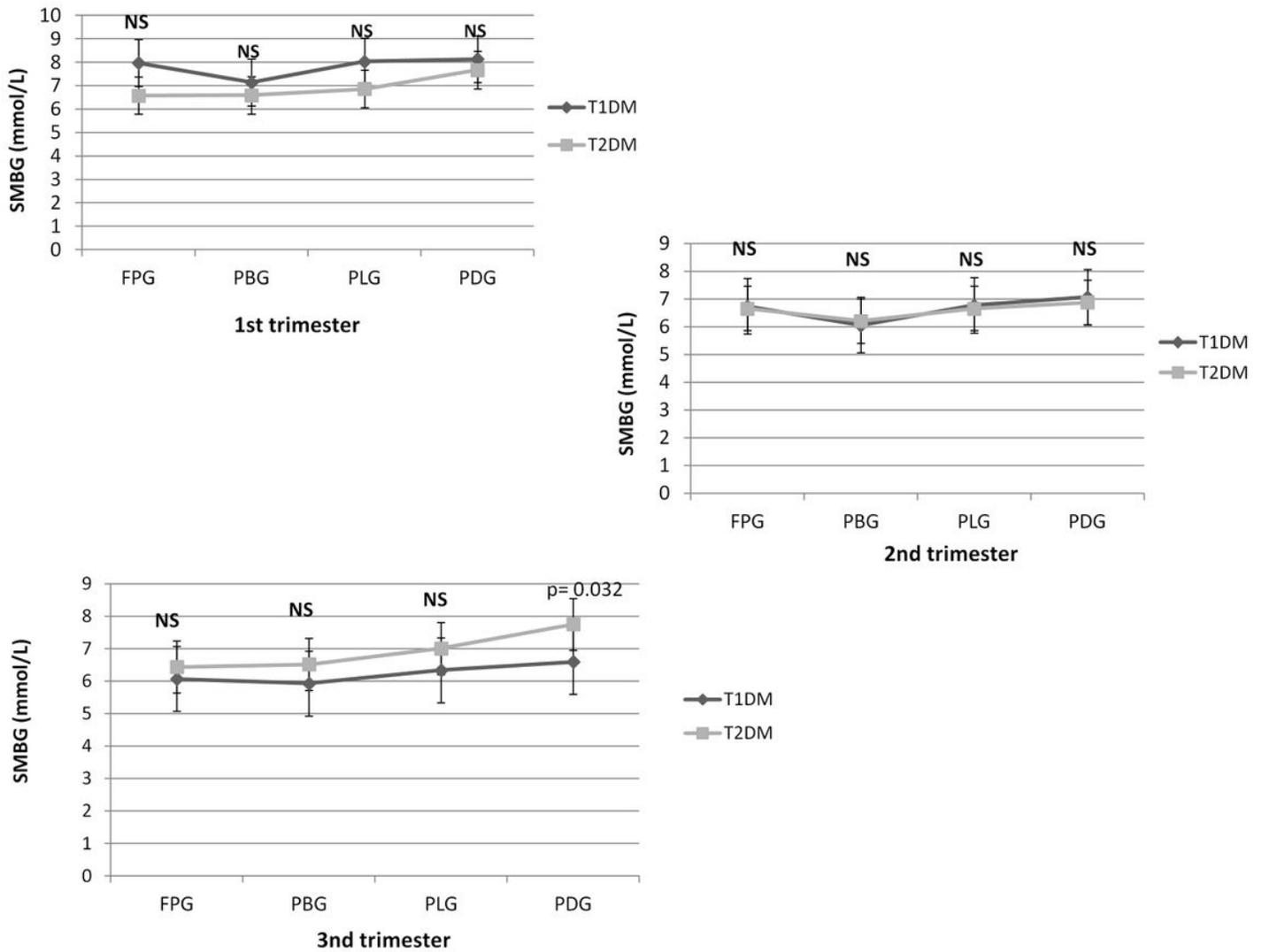
**Figure 1**

Total daily insulin requirements measured in units/kg during pregnancy (first, second and third trimester) in type 1 and type 2 diabetes mellitus (T1DM and T2DM). Change ( $\Delta$ ) from end to start of each trimester for insulin requirement (IR) in women with T1DM and T2DM.



**Figure 2**

A. HbA1c in preconception and during trimesters in pregnant women with T1DM (dark grey) vs. T2DM (light grey). Values are mean  $\pm$  SD. Student's test was used to evaluate the differences between groups. B. Number of pregnant women with T1DM and T2DM who experienced hypoglycaemic events during first, second and third trimester



**Figure 3**

Average fasting and postprandial glycaemia obtained from SMBG in pregnant women with T1DM and T2DM. Data are presented as mean  $\pm$  SD values. Student's test was used to evaluate the differences between the groups. FPG: fasting plasma glucose. PBG: postprandial breakfast glucose. PLG: postprandial lunch glucose. PDG: postprandial dinner glucose. NS: not significant.