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Gestational diabetes mellitus: Impact of adherence on patient management and maternal-neonatal complications

Federico Pigato [a,*], Riccardo Candido [b], Giorgio Zanette [c], Giulia Zamagni [d], Marta Paulina Trojniak [a], Barbara Brunato [e], Giulia Fornasier [a], Erika Specogna [f], Michela Zenarola [f], Sandra Agus [g], Paola Rossi [h], Anna Arbo [a]

[a] Pharmacy and Clinical Pharmacology Unit, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy
[b] Diabetes Centre, Azienda Sanitaria Universitaria Giuliano Isontina (ASUGI), 34100 Trieste, Italy
[c] Diabetes Centre, Azienda Sanitaria Friuli Occidentale (ASFO), 33170 Pordenone, Italy
[d] Clinical Epidemiology and Health Services Research, Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy
[e] Diabetes Centre, Azienda Sanitaria Universitaria Giuliano Isontina (ASUGI), 34074 Monfalcone (Gorizia), Italy
[f] Pharmaceutical Service, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), 33100 Udine, Italy
[g] Diabetes Centre, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), 33100 Udine, Italy
[h] Central Direction for Health, Social Policy, and Disability - Service for Planning, Control, Health Economics and Pharmaceutical Care of Friuli-Venezia Giulia, 34121 Trieste, Italy

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ABSTRACT

Background: Gestational diabetes mellitus is a form of diabetes whose prevalence is constantly increasing, thus leading to a growth in the necessary resources and organization of diabetes and obstetric facilities. The literature suggests that adherence to diet and therapy in patients with GDM might be highly variable and only sometimes optimal, and that this suboptimal compliance might be associated with more complicated treatment management or some adverse perinatal outcomes. This study evaluates this adherence and the benefits of constant blood glucose monitoring regarding maternalneonatal complications.

Methods: We conducted a multicentre prospective observational study, including all patients diagnosed with gestational diabetes mellitus and aged $\geq$ 18 years, between January 2019 and November 2021. We measured patients' adherence by clinical diary monitoring (medical evaluation) and observation of data obtained from glycaemic control (glucometer analysis). Patients were divided into three groups the adherent patient group, the non-adherent patient group and the partially adherent patient group; then, we compared the groups to assess the impact of non-adherence on patients' health.

Results: 122 (46.9 %) were classified in the adherent group (AG), 91 (35.0 %) in the partially adherent group (PG), and 47 (18.1 %) in the non-adherent group (NG) out of a population of 260 patients. The AG and PG groups were associated with a RRR of 74 % (95 % CI:0.13–1.03, p = 0.057) and 32 % (95 % CI:0.25–1.84, p = 0449) in operative delivery, respectively. Finally, this study proved that full or partial adherence is associated with decreased insulin administration during labour in 67 % (OR=0.33 p = 0.038).

Conclusion: The study showed that patients' adherence to diet and/or therapy proposed by the diabetologist could significantly influence optimal glycaemic control during pregnancy Better compliance may lead to a lower incidence of operative deliveries and insulin utilization during pregnancy and labour.

1. Introduction

Gestational Diabetes Mellitus (GDM) is a form of diabetes diagnosed in the second or third trimester of pregnancy that does not appear before. GDM generally regresses after delivery but often recurs with the characteristics of type 2 diabetes some time later [1].

In recent years, the worldwide increasing prevalence of GDM has highlighted the importance of proper management of this clinical condition in terms of prevention, diagnosis, and treatment. The scientific literature indicates a heterogeneous prevalence in Europe for areas

* Corresponding author.
E-mail address: federico.pigato@burlo.trieste.it (F. Pigato).

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ranging from 10.0 % to 11.8 % [2]. Targeted studies confirmed the expected significant increase of GDM in Italy, with an estimated prevalence of about 11–13 %, leading to an increase in the necessary resources and organization of diabetes and obstetrics facilities [1,3–5].

Because of this prevalence, GDM ranks first among the most common complications during pregnancy and, if untreated, can lead to significant risks both for the mother (such as hypertension and more frequent caesarean delivery) and for the foetus and newborn (such as higher incidence of macrosomia, hyperbilirubinemia, hypocalcaemia, polycythaemia, hypoglycaemia) [5,6]. Therefore, patients diagnosed with GDM should be instructed on a personalized diet and proper lifestyle to achieve optimal blood glucose levels and to prevent these complications. However, insulin therapy should be started promptly if this goal is not obtained after 2 weeks of dietary-only treatment. [1].

The literature suggests that adherence to antidiabetic therapy in patients with GDM might be highly variable and not always optimal and that this suboptimal compliance might be associated with more complicated treatment management and some adverse perinatal outcomes [7–9].

In addition, the follow-up of glucose tolerance after delivery is a critical issue, because the percentage of women who undergo screening after delivery is very low, less than 30–40 % [10,11]. Failure to screen for glucose tolerance after a pregnancy complicated by GDM represents a missed opportunity to prevent type 2 diabetes and cardiovascular disease [12].

The aim of this study is to assess the effective adherence to diet and/or therapy suggested by the diabetologist, and to evaluate the benefit of constant blood glucose monitoring for the reduction of maternal-neonatal complications.

2. Methods

2.1. Study population and recruitment

The study was approved by the FVG Regional Ethics Committee (project no. 0003915).

This is a multicentre, prospective, observational study conducted in the Friuli Venezia Giulia Region (FVG), involving all diabetes centers, obstetrics and gynecology departments, and pediatric departments of the region between January 2019 and November 2021. The diabetologist enrolled eligible women in the presence of the pharmacist after adequate information and signing the informed consent and personal data authorization module.

We included all patients diagnosed with gestational diabetes mellitus and aged ≥18 years, excluding patients with cognitive difficulties and those with type I or type II diabetes mellitus.

A positive oral glucose tolerance test (OGTT) was required for diagnosis, as prescribed by regional and national authorities according to guidelines published in 2011 by the Istituto Superiore di Sanità (ISS). [13].

On their first appointment and during the follow-up after GDM diagnosis, all pregnant women received a multidisciplinary visit to the Diabetes Centre from a diabetologist, a certified dietician, a nurse, and a pharmacist. We instructed patients on the maternal and fetal risks related to untreated GDM. We prescribed them a diet according to BMI range before pregnancy, basal metabolic rate, and adjusted for trimester relating to protein amount. Glucose self-monitoring education was performed by fasting and one hour after breakfast, lunch, and dinner.

2.2. Data collection

Several pharmacists were tasked with collecting patient data from computerized medical records in the *Smart Digital Clinic* software and inputting them into *REDCap*, a secure web application for creating and managing online databases. Pharmacists were also responsible for monitoring patients' treatment adherence at all centres involved in the study.

An average of three follow-ups were collected for each patient during pregnancy, in addition to delivery and newborn data (Table 1).

We measured patients' adherence by clinical diary monitoring (medical evaluation) and observation of data obtained from glycaemic control (glucometer analysis). Adherence was identified by analysing whether patients followed the directions given by diabetologists regarding diet, drug therapy, and glycaemic self-monitoring.

Subsequently, further analysis was conducted to assess the concordance between the two classifications.

Therefore, patients were divided into three groups:

- adherent patient group, if adherent for both assessments;
- non-adherent patient group, if non-adherent for both assessments;
- partially adherent group, if adherent for only one of the two assessments.

After establishing that, it was possible to compare the three groups to assess the impact of non-adherence on patients' health.

2.3. Statistical analysis

Categorical variables were reported as counts and percentages, while continuous variables were presented as mean and standard deviation or as median and interquartile range, based on the results of the Shapiro-Wilk normality test. Differences between groups were evaluated with a Chi-square test (or Fisher, when appropriate) for categorical variables and with one-way ANOVA or Kruskal-Wallis test for continuous variables. In the latter case, when we found significance in the overall analysis, we performed post hoc comparisons using Student's t-test or Wilcoxon-Mann-Whitney test to determine where the differences came from. Concordance between the results of the medical evaluation and those of the glucometer analysis was assessed with Gwet's agreement coefficient. Values less than 0.2 indicate none to a poor agreement; 0.21–0.4 fair; 0.41–0.6 moderate; 0.61–0.8 substantial and > 0.8 almost perfect agreement. A multinomial logistic regression model with non-adherence as a reference category was estimated to identify factors predicting total or partial adherence. Moreover, the role of adherence in predicting perinatal outcomes was investigated using multinomial or binary logistic regression based on the type of response variable. Statistical significance was set at 0.05. All the presented analyses were conducted with StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.

3. Results and discussion

3.1. Enrolment data

In this multicentre prospective observational study, 287 patients were enrolled (Table 2a).

The mean age of these was 34 years (IQR: 31–38 years), and the

Table 1
Main data collected during the study phases.

Enrolling	Follow-ups	Delivery data	Newborn data
• biographical data, • family history of diabetes, • date of GDM diagnosis, • BMI, • current diseases/ therapies.	• glucometer values, • current therapies, • adherence and appropriateness to self-monitoring and treatment.	• Week of delivery, • mode of delivery (caesarean/ operative/ spontaneous delivery), • complications,	• APGAR (Appearance, Pulse, Grimace, Activity and Respiration), • weight/height (centiles), • hypoglycaemias, • hypocalcaemia, • type of nutrition.

Table 2a
Data at enrolment of patients.

Enrolment	N = 287
Age	34 (31–38)
Week of gestation	27 (24–29)
Previous pregnancies	1 (0–2)
Familiarity with diabetes	
No	147 (51.2)
Yes	140 (48.8)
Previous GDM	
No	243 (84.7)
Yes	44 (15.3)
Other diseases	
No	210 (73.2)
Yes	77 (26.8)
BMI	25.5 (22.5–29.8)
BMI classes	
Underweight	1 (1.0)
Normal weight	128 (44.9)
Overweight	79 (27.7)
Obesity I	49 (17.2)
Obesity II	15 (5.3)
Obesity III	11 (3.9)
Only diet therapy	
No	29 (10.1)
Yes	257 (89.6)
Unknown	1 (0.3)
Insulin administration	
No	258 (89.9)
Yes	29 (10.1)
Type of insulin	
Only Lispro	1 (3.4)
Only Detemir	23 (79.4)
Only Glargine	2 (7.0)
Aspart+Detemir	1 (3.4)
Lispro+Detemir	1 (3.4)
Lispro+Glargine	1 (3.4)
Other antidiabetics	
No	29 (100.0)
Yes	0
Drugs for other diseases	
No	212 (73.9)
Yes	75 (26.1)
Contraindicated drugs	
No	42 (56.0)
Yes	32 (47.7)
Unknown	1 (1.3)

diagnosis of GDM was generally made at a gestational age of 27 weeks (IQR: 24–29 weeks).

Patients with a familial history of type 2 diabetes were 140 (48.8 %); 77 women (26.8 %) had at least one other comorbidity, and 75 used at least one medication for their condition. Table 2b shows in detail the other 96 concurrent diseases found in the study; these were classified through the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).

Table 2b
Other diseases were compared first with the 77 patients who had at least one concurrent disease, and then compared with total of patients.

Other diseases	N = 77	N = 287
Endocrine, nutritional and metabolic diseases, and immunity disorders	38 (49,4)	38 (13,2)
Diseases of blood and blood-forming organs	15 (19,5)	15 (5,2)
Diseases of the nervous system and sense organs	10 (13,0)	10 (3,5)
Complications of pregnancy, childbirth, and the puerperium	7 (9,1)	7 (2,4)
Diseases of the circulatory system	7 (9,1)	7 (2,4)
Diseases of the digestive system	7 (9,1)	7 (2,4)
Diseases of the respiratory system	3 (3,9)	3 (1,0)
Diseases of the musculoskeletal system and connective tissue	2 (2,6)	2 (0,7)
Diseases of the skin and subcutaneous tissue	2 (2,6)	2 (0,7)
Mental disorders	2 (2,6)	2 (0,7)
Congenital anomalies	1 (1,3)	1 (0,3)
Diseases of the genitourinary system	1 (1,3)	1 (0,3)
Symptoms, signs, and ill-defined conditions	1 (1,3)	1 (0,3)

At the time of enrolment, 257 patients (89.6 %) were on diet therapy only, data of 1 patient were missing, and the remaining 29 were taking insulin, mainly basal insulin (n = 25).

In addition, 75 women were taking medications for other conditions.

We evaluated the adherence of 260 patients excluding all the subjects who had only one follow-up (16); the other 11 cases were not included due to missing data or failing to show up regularly for visits scheduled by their diabetologists.

As can be seen in Table 3, 260 patients were divided into three groups:

- non-adherent patient group (NG), 47 (18.1 %);
- adherent patient group (AG), 122 (46.9 %);
- partially adherent group (PG), 91 (35.0 %).

These two classifications (medical evaluation and glucometer analysis) coincided in 65.0 % of cases; statistical Gwet's coefficient indicated

Table3
Data at enrolment of patients divided by the three groups.

Enrolment	NG N = 47	AG N = 122	PG N = 91	p-value
Age	35.8 (5.1)	33.9 (4.7)	33.5 (4.9)	**0.028**
Week of gestation	27 (22–29)	27 (25–29)	26 (22–28)	0292
Previous pregnancies	1 (0–2)	1 (0–1)	1 (0–2)	0057
Familiarity with diabetes				0684
No	25 (53.2)	57 (46.7)	47 (51.7)	
Yes	22 (46.8)	65 (53.3)	44 (48.3)	
Previous GDM				0143
No	38 (80.9)	108 (88.5)	72 (79.1)	
Yes	9 (19.19	14 (11.5)	19 (20.9)	
Other diseases				0459
No	36 (76.6)	89 (73.0)	61 (67.0)	
Yes	11 (23.4)	33 (27.0)	30 (33.0)	
BMI	25.7 (22.1–29.1)	24.6 (22.1–29.1)	26.1 (22.5–29.8)	0539
BMI classes				0457
Underweight	1 (2.1)	3 (2.5)	0	
Normal weight	20 (42.6)	60 (49.2)	39 (42.9)	
Overweight	15 (31.9)	30 (24.6)	28 (30.8)	
Obesity I	8 (17.0)	21 (17.2)	15 (16.5)	
Obesity II	0	6 (4.9)	6 (6.6)	
Obesity III	3 (6.4)	1 (1.6)	3 (3.3)	
Insulin administration				0385
No	40 (85.1)	112 (91.8)	80 (87.9)	
Yes	7 (14.9)	10 (8.2)	11 (12.1)	
Type of insulin				
Fast	0	1 (10.0)	0	0125
Delayed	7 (100.0)	9 (90.0)	8 (72.7)	
Both	0	0	3 (27.3)	
Type of insulin (drugs)				1000
Only Lispro	0	1 (10.0)	0	
Only Detemir	7 (100.0)	8 (80.0)	8 (72.7)	
Only Glargine	0	1 (10.0)	0	
Aspart+Detemir	0	0	1 (9.1)	
Lispro+Detemir	0	0	1 (9.1)	
Lispro+Glargine	0	0	1 (9.1)	
Drugs for other diseases				0347
No	38 (80.9)	89 (72.9)	63 (69.2)	
Yes	9 (19.1)	33 (27.1)	28 (30.8)	
Contraindicated drugs				0299
No	3 (33.3)	18 (54.6)	18 (64.3)	
Yes	6 (66.7)	15 (45.5)	10 (35.7)	

a modest concordance because suboptimal blood glucose values do not necessarily mean patient non-adherence. This result highlighted how vital a careful evaluation by an experienced professional figure is to interpret the glucometer data correctly.

3.2. First follow-up data

Follow-up results are presented in Table 4. At the first follow-up, correct fasting (AG:95.9 %, PG:93.4 %, NG:68.1; p = 0.001) and postprandial blood glucose (AG:96.7 %, PG:91.2 %, NG:63.8 %; p < 0.001) measurements were more frequently reported for patients' adherent to treatment.

A statistically significant difference emerged concerning the patients classified as adherents through analysing glycaemic values. Indeed, a higher frequency in both preprandial glycaemic values ≤ 90 mg/dl (AG:79.9 %, PG:50.0 %, NG:34.8 %; p < 0.001) and postprandial values ≤ 130 mg/dl (AG:89.6 %, PG:87.3 %, NG:79.0 %; p = 0.001) was found.

In addition, the non-adherent group showed a higher frequency of hyperglycaemic peaks (AG:66.4 %, PG:74.7 %, NG:95.7 %; p < 0.001), while there was no statistically significant difference in hypoglycaemic peaks (AG:30.3 %, PG:28.6 %, NG:38.3 %; p = 0351).

Finally, the percentage of patients taking only diet therapy was significantly higher in the adherent group (AG:59.8 %, PG:41.8 %, NG:23.4 %; p < 0.001). Thus, in the group of non-adherent patients, it was more frequently necessary to include drug therapy to achieve an optimal glycaemic target.

3.3. Last follow-up data

The results of the first follow-up were also confirmed by the last one. Indeed, correct fasting (AG:98.4 %, PG:93.4 %, NG: 55.3; p < 0.001) and postprandial blood glucose (AG:96.7 %, PG:87.9 %, NG:53.2 %; p < 0.001) measurements were more frequently reported for patients' adherent to treatment.

The analysis of the glycaemic values revealed a statistically significant difference in the group of patients classified as adherents. A higher frequency in both preprandial glycaemic values ≤ 90 mg/dl (AG:86.0 %, PG:52.6 %, NG:46.1 %; p < 0.001) and postprandial values ≤ 130 mg/dl (AG:94.1 %, PG:76.3 %, NG:77.2 %; p < 0.001) was found.

In addition, the non-adherent group revealed a higher frequency of hyperglycaemic peaks (AG: 54.9 %, PG:73.6 %, NG:91.5 %; p < 0.001), while there was no significant difference in hypoglycaemic peaks (AG: 36.9 %, PG: 35.5 %, NG: 34.1 %; p = 0342).

Finally, the percentage of patients taking only diet therapy was remarkably higher in the adherent group (AG:59.8 %, PG: 31.9 %, NG: 19.2 %; p < 0.001).

3.4. Factors predicting adherence

Table 5 shows the results of the logistic regression analyses to identify factors associated with partial and total adherence. As maternal age at enrolment increased, the risk of being partially or entirely adherent was reduced by 10 % and 8 %, respectively, compared to non-adherent patients (p = 0.010 and p = 0.025, respectively). Moreover, an association was found between the presence of hyperglycaemic peaks and adherence. For patients with hyperglycaemic peaks, the probability of being totally adherent was strongly reduced, regardless of whether they occurred at the first follow-up (RRR=0.08, p = 0.001) or at the last (RRR=0.09, p < 0.001).

On the other hand, the risk of partial adherence compared to non-adherence had a smaller decrease but was still noteworthy, with an 86 % and an 80 % reduction at the first and last follow-up, respectively (p = 0.011 and p = 0.013). Furthermore, insulin use was a risk factor for non-adherence, regardless of follow-up. The risk of being always adherent, in the case of insulin prescription, was reduced by 79 % at the first follow-up (p < 0.001) and by 84 % at the last (p < 0.001). The need for insulin

Table4
Data at all patients' first and last follow-ups divided into three groups.

	First follow-up				Last follow-up			
	AG N = 122	PG N = 91	NG N = 47	p-value	AG N = 122	PG N = 91	NG N = 47	p-value
Correct preprandial glycaemic measurement				**0001**				**<0.001**
No	4 (3.3)	6 (6.6)	15 (31.9)		1 (0.8)	6 (6.6)	21 (44.7)	
Yes	117 (95.9)	85 (93.4)	32 (68.1)		120 (98.4)	85 (93.4)	26 (55.3)	
Not specified	1 (0.8)	0	0		1 (0.8)	0	0	
Correct postprandial glycaemic measurement				**<0.001**				**<0.001**
No	4 (3.3)	8 (8.8)	17 (36.2)		4 (3.3)	11 (12.1)	22 (46.8)	
Yes	118 (96.7)	83 (91.2)	30 (63.8)		118 (96.7)	80 (87.9)	25 (53.2)	
Fasting blood glucose ≤90 mg	79.9 (56.7–92.0)	50.0 (26.3–78.0)	34.8 (12.5–67.3)	**<0.001**	86.0 (69.2–100.0)	52.6 (43.7–72.2)	46.1 (18.0–59.0)	**<0.001**
Postprandial blood glucose ≤130 mg	89.6 (77.6–98.0)	87.3 (75.0–93.0)	79.0 (65.3–90.7)	**0001**	94.1 (88.6–100.0)	76.3 (88.1–94.4)	77.2 (57.1–90.3)	**<0.001**
Hyperglycaemic peaks				**<0.001**				**<0.001**
No	41 (33.6)	21 (23.1)	2 (4.4)		48 (39.3)	23 (25.3)	3 (6.4)	
Yes	81 (66.4)	68 (74.7)	45 (95.7)		67 (54.9)	67 (73.6)	43 (91.5)	
Unknown	0	2 (2.2)	0		7 (5.7)	1 (1.1)	1 (2.1)	
Hypoglycaemic peaks				0351				0342
No	85 (69.7)	63 (69.2)	29 (61.7)		69 (56.6)	55 (60.4)	30 (63.8)	
Yes	37 (30.3)	26 (28.6)	18 (38.3)		45 (36.9)	35 (35.5)	16 (34.1)	
Unknown	0	2 (2.2)	0		8 (6.6)	1 (1.1)	1 (2.1)	
Insulin administration				**<0.001**				**<0.001**
No	73 (59.8)	38 (41.8)	11 (23.4)		73 (59.8)	29 (31.9)	9 (19.2)	
Yes	49 (40.2)	53 (58.2)	36 (76.6)		49 (40.2)	62 (68.1)	38 (80.8)	
Type of insulin				0433				0081
Fast	5 (10.2)	3 (5.8)	4 (11.1)		4 (8.2)	6 (9.7)	2 (5.3)	
Delayed	35 (71.4)	44 (84.6)	25 (69.4)		33 (67.4)	46 (74.2)	20 (52.6)	
Both	9 (18.4)	5 (9.6)	7 (19.4)		12 (24.5)	10 (16.3)	16 (42.1)	
Fast insulin units	5 (2–9)	8 (5–11)	8 (5–10)	0297	7.5 (5–17.5)	10.0 (4–12)	11.5 (5–12)	0943
Delayed insulin units	6 (4–12)	6 (4–10)	8 (5.5–12.5)	0231	12.0 (7–18)	12.0 (8–16)	13.5 (8–21)	0315

Table5
Univariate multinomial regression models for partial and total adherence (reference: non-adherence).

Variables	RRR	95 % CI	p-value
Age at enrolment			
AG	0.92	[0.85, 0.99]	**0.025**
PG	0.90	[0.84, 0.98]	**0.010**
BMI at enrolment			
AG	0.99	[0.93; 1.07]	0.955
PG	1.01	[0.95; 1.09]	0.604
GA at enrolment			
AG	1.01	[0.94; 1.09]	0.712
PG	0.97	[0.90; 1.05]	0.413
Number of pregnancies			
AG	0.75	[0.56; 1.02]	0.064
PG	1.07	[0.81; 1.42]	0.631
Familiarity of GDM			
AG	1.29	[0.66; 2.54]	0.451
PG	1.06	[0.53; 2.15]	0.863
Previous GDM			
AG	0.54	[0.22; 1.37]	0.197
PG	1.11	[0.46; 2.70]	0.811
Other pathologies			
AG	1.21	[0.55; 2.66]	0.629
PG	1.61	[0.72; 3.60]	0.246
Hyperglycaemic peaks at 1st follow-up			
AG	0.08	[0.02; 0.38]	**0.001**
PG	0.14	[0.03; 0.64]	**0.011**
Hyperglycaemic peaks at the last follow-up			
AG	0.09	[0.03, 0.33]	**<0.001**
PG	0.20	[0.06; 0.72]	**0.013**
Hypoglycaemic episodes at 1st follow-up			
AG	0.70	[0.35, 1.42]	0.323
PG	0.66	[0.32; 1.40]	0.283
Hypoglycaemic episodes at the last follow-up			
AG	1.22	[0.60; 2.50]	0.581
PG	1.19	[0.57, 2.50]	0.640
Insulin at enrolment			
AG	0.51	[0.18, 1.43]	0.201
PG	0.79	[0.28; 2.18]	0.643
Insulin at 1st follow-up			
AG	0.21	[0.09; 0.44]	**<0.001**
PG	0.41	[0.18; 0.90]	**0.026**
Insulin at the last follow-up			
AG	0.16	[0.07; 0.36]	**<0.001**
PG	0.51	[4.05; 16.21]	**<0.001**
Units of rapid-acting insulin at 1st follow-up			
AG	0.91	[0.71; 1.17]	0.459
PG	1.01	[0.76; 1.33]	0.943
Units of rapid-acting insulin at the last follow-up			
AG	1.02	[0.91; 1.14]	0.719
PG	1.01	[0.89; 1.13]	0.913
Units of basal insulin at 1st follow-up			
AG	0.98	[0.92; 1.04]	0.504
PG	0.97	[0.91; 1.04]	0.379
Units of basal insulin at the last follow-up			
AG	0.97	[0.94; 1.00]	0.087
PG	0.99	[0.96, 1.01]	0.313

was also associated with a decreased risk of being partially adherent, both at first (RRR=0.21; p = 0.026) and at the last follow-up (RRR=0.51; p < 0.001).

3.5. Delivery data

The analysis (Table 6) showed no differences in the distribution of the delivery mode between the three groups (p = 0.226). In particular, the most frequent type was always spontaneous delivery (AG:69.8 %, PG:68.1 %, NG:56 %), followed by caesarean section (AG:22.4 %, PG:17.6 %, NG:26.1 %) and operative delivery (AG:7.8 %, PG:14.3 %, NG:17.4 %).

Furthermore, labour induction was necessary for most patients without significant differences between groups (p = 0.196). However, the percentage of induced labour seemed lower for AG patients (AG:50.9 %, PG:62.6 %, NG:60.9 %; p = 0196).

Table6
Delivery data.

	AG N = 116	PG N = 91	NG N = 46	p-value
Type of delivery				0226
Caesarean section	26 (22.4)	16 (17.6)	12 (26.1)	
Spontaneous	81 (69.8)	62 (14.3)	26 (56.5)	
Operative	9 (7.8)	13 (14.3)	8 (17.4)	
Induction of labour				0196
No	55 (47.4)	32 (35.2)	18 (39.1)	
Yes	59 (50.9)	57 (62.6)	28 (60.9)	
Unknown	2 (1.7)	2 (2.2)	0	
Complications				0421
No	95 (81.9)	69 (75.8)	34 (73.9)	
Yes	21 (18.1)	22 (24.2)	12 (26.1)	

Finally, no differences were found regarding maternal complications in the different groups (p = 0.421).

3.6. Newborn data

The results of the analyses of newborn data are reported in Table 7. The median APGAR scores in the first minute of life and after 5 min were not significantly different in the three groups (p = 0.954 and p = 0.809, respectively).

No statistically substantial difference was found for weight at birth (p = 0566), while a trend toward statistical significance was found for length at birth (p = 0061).

No significant differences also emerged about hypoglycaemia in the fourth and sixth hour of life (respectively p = 0254 and p = 0192).

3.7. Outcome analysis

As can be observed in Table 8, the AG and PG groups were associated with a decrease in the Relative Risk Ratio (RRR) of 30 % (95 % CI:0.31–1.57, p = 0382) and 46 % (95 % CI:0.23–1.34, p = 0194) in caesarean delivery, respectively compared to NG patients.

Furthermore, AG and PG were linked to a reduced RRR of 74 % (95 % CI:0.13–1.03, p = 0057) and 32 % (95 % CI:0.25–1.84, p = 0449) in operative delivery, respectively. Although the latter result was not statistically meaningful, probably due to the small sample size, the trend toward significance has to be considered. The result may become statistically noteworthy, parallel to the increased number of subjects enrolled. Focusing on the second part of Table 8, all data presented are not statistically significant. However, the number of patients taking insulin during labour was low: 4 NG, 3 AG and 1 PG. This percentage might explain why the statistical significance was not reached despite the importance of the results (AG: OR, 0.29, p = 0111; PG: OR, 0,12, p = 0061). Furthermore, the results became significant if AG and PG were compared to NG (OR=0.33, p = 0.038).

4. Discussion

Data from the entire pregnancy of patients with GDM were analysed. In agreement with the literature [7,8], the study highlights that there is not always good adherence in these patients. In particular, only 46.9 % of patients were classified as fully adherent, 35.0 % as partially adherent, and non-adherence was about 18.1 %. The glucometer data clearly showed that as adherence decreased, glycaemic control worsened. In fact, the analysis of glycaemic values showed a statistically significant difference in favour of AG in both preprandial glycaemic values ≤ 90 mg/dl, postprandial glycaemic values ≤ 130 mg/dl, and frequency of hyperglycaemic peaks, while there was no statistically significant difference in hypoglycaemic peaks. This difference between the three groups remained significant throughout pregnancy, and in the

Table 7
Newborn data.

	AG N = 118	PG N = 91	NG N = 46	p-value
APGAR 1'	9 (8–9)	9 (8–9)	9 (8–9)	0954
APGAR 5'	10 (9–10)	10 (9–10)	10 (9–10)	0809
Weight at birth				0566
<10th	7 (5.9)	6 (6.6)	2 (4.3)	
10th-24th	22 (18.6)	10 (11.0)	6 (13.0)	
25th-49th	37 (31.4)	20 (22.0)	13 (28.3)	
50th-74th	20 (17.0)	25 (27.5)	13 (28.3)	
75th-89th	14 (11.9)	16 (17.6)	7 (15.2)	
≥90th	15 (12.7)	13 (14.3)	5 (10.9)	
Unknown	3 (2.5)	1 (1.1)	0	
Length at birth				0061
<10th	3 (2.5)	7 (7.7)	2 (4.3)	
10th-24th	17 (14.4)	6 (6.6)	2 (4.3)	
25th-49th	34 (28.8)	13 (14.3)	11 (23.9)	
50th-74th	28 (23.7)	29 (31.9)	15 (32.6)	
75th-89th	11 (9.3)	15 (16.5)	9 (19.6)	
≥90th	13 (11.0)	9 (9.9)	4 (8.7)	
Unknown	12 (10.2)	12 (13.2)	3 (6.5)	
Hypoglycaemia in 4th hour				0254
No	99 (83.9)	83 (91.2)	39 (84.8)	
Yes	19 (16.1)	8 (8.8)	7 (15.2)	
Hypoglycaemia in 6th hour				0192
No	107 (90.7)	88 (96.7)	42 (91.3)	
Yes	11 (9.3)	3 (3.3)	4 (8.7)	

Table 8
Outcome analysis.

Outcome: Type of delivery (ref. vs Spontaneous)	RRR	95 % CI	p-value
Caesarean section (vs NG)			
AG	0,70	[0.31, 1.57]	0382
PG	0,56	[0.23; 1.34]	0194
Operative (vs NG)			
AG	0,36	[0.13; 1.03]	0057
PG	0,68	[0.25; 1.84]	0449
Outcome	**OR**	**95 % CI**	**p-value**
Induction (vs NG)			
AG	0,69	[0.34; 1.38]	0296
PG	1,15	[0.55; 2.38]	0717
Complications to the mother (vs NG)			
AG	0,62	[0.27; 1.40]	0251
PG	0,89	[0.39; 2.01]	0779
Insulin during labour (vs NG)			
AG	0,29	[0.06; 1.34]	0111
PG	0,12	[0.01; 1.10]	0061
Complications to the newborn (vs NG)			
AG	0,84	[0.30; 2.38]	0741
PG	1,11	[0.39; 3.18]	0840
Hypoglycaemia (vs NG)			
AG	2,13	[0.24, 18.99]	0497
PG	1,63	[0.16; 16.29]	0679
Resuscitation (vs NG)			
AG	0,69	[0.28; 1.72]	0437
PG	0,82	[0.33; 2.08]	0679

case of postprandial glycaemic values ≤ 130 mg/dl it increased further in favour of the AG.

This worsening resulted in more complex patient management, as also shown by the increased use of pharmacological support in less adherent patients. At the time of enrolment, 257 patients were following diet therapy alone, 112 of AG (91.8 %), 80 of PG (87.9 %) and 40 of NG (85.1 %).

This frequency decreased during pregnancy: at the first follow-up 73 of AG (59.8 %), 38 of PG (41.8 %) and 11 of NG (23.4 %), and at the last follow-up 73 of AG (59.8 %), 29 of PG (31.9 %) and 9 of NG (19.2 %). Therefore, as can be seen, in general it was more often necessary to include drug therapy to achieve an optimal glycaemic goal in PG and NG, and this difference between the three groups increased throughout pregnancy.

Finally, it was analysed how suboptimal glycaemic control may affect delivery. In this regard, most of the results did not demonstrate statistical significance. This can be explained by considering increased attention by diabetes centres to more complicated cases and would confirm the good performance of the health care team involved in the management of these patients. However, the study shows that AG and PG were associated with a reduced RRR in operative delivery of 74 % and 32 %, respectively. It also suggests that full or partial adherence is associated with lower insulin administration during labour in 67 % of cases.

5. Conclusions

The study highlights how patients' adherence to diet and therapy suggested by the diabetologist can significantly influence optimal glycaemic control throughout pregnancy.

Furthermore, this study underscored the importance of diabetes centres in caring for patients with GDM. Frequent monitoring and constant education of patients were the only way to prevent the complications due to suboptimal glycaemic control, which could be detrimental to the health of pregnant women and children.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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