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Prepregnancy Body Mass Index and Serum C-Peptide as Complementary Predictors of Insulin Requirement in Gestational Diabetes Mellitus: A Retrospective Cohort Study

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ABSTRACT

Purpose: To identify routinely available factors associated with insulin requirement in women with gestational diabetes mellitus (GDM), focusing on prepregnancy body mass index (BMI) and serum C-peptide as clinical proxies of insulin resistance and β-cell secretory capacity.

Methods: Retrospective cohort of 110 women with GDM meeting standard 75-g glucose tolerance test criteria, followed at a tertiary internal medicine clinic in Istanbul, Türkiye (2020–2023). Insulin was started when glycaemic targets were not met with medical nutrition therapy. Associations were examined by multivariable logistic regression with bootstrap validation.

Results: Insulin was required in 45 women (40.9%), rising from 13.6% to 52.8% across prepregnancy BMI categories (*P* for trend = 0.003). After adjustment for age, glucose tolerance test values, HbA1c and referral timing, higher prepregnancy BMI (adjusted odds ratio [aOR] 1.18 per kg/m^2; 95% confidence interval [CI] 1.06–1.31) and lower C-peptide (aOR 3.42 per halving; 95% CI 1.67–6.97) were independently associated with insulin requirement. Insulin need was 71.4% in women with both obesity and below-median C-peptide versus 8.7% in those with neither (aOR 24.5; 95% CI 4.3–139.7). Adding C-peptide increased the area under the curve from 0.76 to 0.82 (optimism-corrected 0.78). Insulin-treated women had more preterm births (aOR 6.01; 95% CI 1.01–35.65) and accounted for all cases of macrosomia.

Conclusion: Prepregnancy BMI and C-peptide appear to capture complementary insulin-resistance and insulin-secretory pathways to insulin requirement in GDM. Combining these inexpensive measures at diagnosis may help identify women likely to need insulin; prospective validation is warranted.

Keywords: β-cell function; maternal obesity; glycaemic control; precision medicine; caesarean section

What does this study adds to the clinical work

In women with gestational diabetes, higher prepregnancy BMI and lower fasting C-peptide independently identified those who would need insulin, with insulin required in 71% of women with both features versus 9% with neither. These two inexpensive measures may support early risk stratification and closer glucose surveillance.

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common medical complications of pregnancy and its prevalence continues to rise in parallel with maternal obesity and advancing maternal age [1,2]. Maternal hyperglycaemia is continuously associated with fetal overgrowth, caesarean delivery and neonatal morbidity [3,4], and treatment that achieves maternal normoglycaemia reduces these complications [5]. Medical nutrition therapy and physical activity are first-line treatment; however, a substantial proportion of women—between roughly 15% and more than 50% depending on population, diagnostic criteria and treatment targets—fail to reach glycaemic targets and require pharmacological therapy, for which insulin remains the preferred agent [6–8].

Early identification of women who will need insulin could allow closer monitoring and timelier treatment escalation. A recent systematic review by the American Diabetes Association/European Association for the Study of Diabetes Precision Medicine in Diabetes Initiative concluded that routinely measured characteristics, including body mass index (BMI), previous GDM and glucose concentrations at diagnosis, may help predict treatment escalation, but that the available evidence is heterogeneous and largely derived from small retrospective studies [8]. Findings on the role of maternal adiposity are inconsistent: some cohorts identified prepregnancy BMI as a strong determinant of pharmacological treatment [9,10], whereas others found that fasting and post-load glucose and HbA1c, rather than BMI, predicted insulin requirement [11–13].

One explanation for these discrepancies is that GDM is physiologically heterogeneous. Physiological studies have shown that GDM arises from a predominant defect in insulin sensitivity, a predominant defect in insulin secretion, or a combination of both, and that these subtypes differ in their clinical characteristics and perinatal risk [14–16]. BMI is a readily available proxy of insulin resistance, whereas serum C-peptide, which is secreted in equimolar

amounts with endogenous insulin and is not subject to first-pass hepatic extraction, reflects endogenous insulin secretory capacity [17]. Whether these two simple measures, considered together, improve identification of women who will need insulin has not been well established. The aim of this study was therefore to evaluate demographic, anthropometric and metabolic factors associated with insulin requirement in women with GDM, with particular emphasis on prepregnancy BMI and serum C-peptide as complementary markers of insulin resistance and insulin secretion, and to describe maternal and neonatal outcomes according to treatment modality.

METHODS

Study design and setting

This retrospective cohort study was conducted at the internal medicine outpatient clinic of the University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, a tertiary referral centre in Istanbul, Türkiye. Women with GDM referred from the obstetrics department and followed between January 2024 and December 2025 were identified from the hospital electronic records. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [18].

Participants

Women aged ≥18 years with a singleton pregnancy who had been diagnosed with GDM using a 75-g oral glucose tolerance test (OGTT) and who were followed in our clinic until delivery were eligible. GDM was diagnosed by the referring obstetric service according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria (fasting plasma glucose ≥92 mg/dL, 1-h glucose ≥180 mg/dL or 2-h glucose ≥153 mg/dL) [19]. Exclusion criteria were pre-existing type 1 or type 2 diabetes; recorded diagnostic OGTT values not meeting IADPSG thresholds; and missing data on prepregnancy BMI, mode of

delivery or treatment modality. Of 131 women with GDM followed during the study period, 21 were excluded because their recorded OGTT values did not meet IADPSG thresholds, leaving 110 women for analysis. Some women were referred to internal medicine after 28 weeks of gestation even though the diagnosis had been established earlier; gestational age at the first internal medicine visit was therefore recorded and analysed as a potential confounder.

Data collection and definitions

Age, family history of diabetes in first-degree relatives, gravidity, parity, height, self-reported prepregnancy weight, and weight, blood pressure and gestational age at the first internal medicine visit were extracted from medical records. Prepregnancy BMI was calculated from self-reported prepregnancy weight and measured height and categorised according to World Health Organization cut-offs (<25, 25–29.9 and ≥30 kg/m^2). Weight gain until the first visit was calculated as measured weight minus prepregnancy weight. Parity was defined as the number of previous births.

OGTT glucose values (fasting, 1-h and 2-h) were retrieved from the diagnostic test. At the first internal medicine visit, before any pharmacological treatment, fasting venous blood was drawn for HbA1c, serum C-peptide, lipids, blood count, and renal and liver function. HbA1c is reported in % and mmol/mol (NGSP converter). HbA1c levels were measured with a COBAS 311 analyzer using the particle-supported immunoturbidometric method (Roche Diagnostics GmbH, Mannheim, Germany). HbA1c results are stated as percentage of total Hb in accordance with the Diabetes Control and Complication Trial/ National Glycohemoglobin Standardization Program (DCCT/NGSP). C-peptide levels were determined by electrochemiluminescence (ECLA) assay in a random-access analyzer (Cobas E411, Roche Diagnostics, Les PennesMirabeau, Bouches-du-Rhône, France).

Treatment protocol and outcome

All women received individualised medical nutrition therapy and physical activity advice and performed self-monitoring of blood glucose. In line with the American College of Obstetricians and Gynecologists recommendations, glycaemic targets were fasting glucose <95 mg/dL and either 1-h postprandial glucose <140 mg/dL or 2-h postprandial glucose <120 mg/dL [20]. Insulin was initiated when these targets were not consistently achieved despite lifestyle measures over 1–2 weeks; please specify the usual time frame and insulin regimens used (basal, prandial, basal–bolus). Oral glucose-lowering agents were not used. The primary outcome was insulin requirement at any time during pregnancy.

Secondary outcomes were mode of delivery (vaginal or caesarean), preterm birth (delivery before 37 completed weeks) and macrosomia (birth weight ≥4000 g), obtained from delivery records.

Statistical analysis

Continuous variables were assessed for normality with the Shapiro–Wilk test and are presented as mean ± standard deviation or median (interquartile range), and were compared using Student's *t* test or the Mann–Whitney *U* test, as appropriate. Categorical variables are presented as number (percentage) and were compared using the χ^2 test or Fisher's exact test. Trends across BMI categories were tested by logistic regression with the category entered as an ordinal term. Correlations were assessed with Spearman's coefficient.

Associations with insulin requirement were estimated by logistic regression and expressed as crude or adjusted odds ratios (ORs, aORs) with 95% confidence intervals (CIs). Covariates for the multivariable model were selected *a priori* on the basis of clinical relevance and prior literature rather than by stepwise selection [8]. Model 1 included age, prepregnancy BMI, fasting and 1-h OGTT glucose, HbA1c and referral after 28 weeks of gestation. Model 2 additionally included serum C-peptide, which was $\log_2$-transformed because of its right-skewed distribution; its OR is expressed per halving of C-peptide concentration. The 2-h OGTT

value was not included because it was unrelated to insulin requirement in univariable analysis. With 45 events, Model 2 had approximately 6.4 events per variable; because this is below the conventional threshold of ten [21–23], CIs for the main estimates were additionally derived from 2,000 bootstrap resamples, and a parsimonious model including only prepregnancy BMI and C-peptide was fitted. Multicollinearity was assessed with variance inflation factors and calibration with the Hosmer–Lemeshow test. The contribution of C-peptide was evaluated with the likelihood-ratio test. Discrimination was quantified with the area under the receiver operating characteristic curve (AUC); the change in AUC and model optimism were estimated by bootstrap internal validation [24].

To illustrate the joint contribution of adiposity and insulin secretion, women were classified into four groups by prepregnancy obesity (BMI ≥30 kg/m^2) and C-peptide below or above the cohort median. Predefined sensitivity analyses repeated the models (i) after exclusion of women with fasting OGTT glucose ≥126 mg/dL or HbA1c ≥6.5% (48 mmol/mol), values compatible with overt diabetes in pregnancy; (ii) stratified by gestational age at referral (≤28 vs. >28 weeks); and (iii) with additional adjustment for weight gain, family history of diabetes and parity. Associations between insulin treatment and delivery outcomes were adjusted for age, prepregnancy BMI and parity. There were no missing data for the analysed variables. A two-sided P <0.05 was considered statistically significant. Analyses were performed with IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA) and Python 3 (statsmodels and scikit-learn). A large language model (Claude, Anthropic) was used to assist with writing the statistical analysis code and with drafting and language editing of the manuscript; the authors verified all analyses and text and take full responsibility for the content.

The study was approved by the Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital (2023/514/244/15) and conducted in accordance with the Declaration of Helsinki.

RESULTS

Characteristics of the study population

Of 131 women with GDM, 21 whose recorded OGTT values did not meet IADPSG thresholds were excluded, and 110 were included in the analysis. Mean age was 32.7 ± 5.1 years, mean prepregnancy BMI was 29.0 ± 4.9 kg/m^2, and 53 women (48.2%) were obese before pregnancy. Eighty-two women (74.5%) reported a family history of diabetes and 33 (30.0%) were nulliparous. Sixty women (54.5%) were first seen in internal medicine after 28 weeks of gestation. Overall, 45 women (40.9%) required insulin, and 65 (59.1%) achieved glycaemic targets with lifestyle measures alone (Table 1).

Comparison according to insulin requirement

Women who required insulin had higher prepregnancy BMI (30.6 ± 4.6 vs. 27.8 ± 4.8 kg/m^2; $P = 0.003$) and BMI at the first visit (34.3 ± 5.4 vs. 31.1 ± 5.1 kg/m^2; $P = 0.002$) than those treated with lifestyle measures alone, whereas age ($P = 0.201$) and weight gain until the first visit ($P = 0.119$) did not differ significantly. Fasting OGTT glucose ($P = 0.023$), 1-h OGTT glucose ($P < 0.001$) and HbA1c ($P < 0.001$) were higher in the insulin group, whereas 2-h OGTT glucose did not differ ($P = 0.465$). Serum C-peptide was significantly lower in women who required insulin (median 2.48 [1.00–3.49] vs. 3.16 [2.40–3.80] ng/mL; $P = 0.004$). Family history of diabetes, parity, blood pressure, lipid profile and gestational age at referral did not differ between groups (Table 1).

The proportion of women requiring insulin increased from 13.6% (3/22) in women with normal prepregnancy BMI to 40.0% (14/35) in those with overweight and 52.8% (28/53) in those with obesity (P for trend = 0.003; Fig. 1a). C-peptide correlated weakly and positively with prepregnancy BMI ($\rho = 0.19$; $P = 0.042$) but not with fasting, 1-h or 2-h OGTT glucose or HbA1c (all $P > 0.3$).

Factors independently associated with insulin requirement

In univariable analysis, prepregnancy BMI, fasting and 1-h OGTT glucose, HbA1c and $\log_2$ C-peptide were associated with insulin requirement (Table 2). In Model 1, prepregnancy BMI was the only factor independently associated with insulin requirement (aOR 1.12 per kg/m^2; 95% CI 1.02–1.23; P = 0.016; bootstrap 95% CI 1.02–1.28), corresponding to an aOR of 1.78 (95% CI 1.11–2.86) per 5 kg/m^2. When obesity was entered instead of continuous BMI, the aOR was 2.26 (95% CI 0.95–5.36; P = 0.064).

Adding C-peptide (Model 2) significantly improved model fit (likelihood-ratio test P <0.001; Nagelkerke R^2 0.43 vs. 0.27). In this model, both higher prepregnancy BMI (aOR 1.18 per kg/m^2; 95% CI 1.06–1.31; P = 0.002; per 5 kg/m^2: 2.28, 1.35–3.83; bootstrap 95% CI 1.06–1.39) and lower C-peptide (aOR 3.42 per halving; 95% CI 1.67–6.97; P <0.001; bootstrap 95% CI 2.00–11.01) were independently associated with insulin requirement (Table 2). Calibration was adequate (Hosmer–Lemeshow P = 0.76). The AUC was 0.67 (95% CI 0.57–0.77) for prepregnancy BMI alone, 0.76 (0.67–0.84) for Model 1 and 0.82 (0.74–0.89) for Model 2, with an optimism-corrected AUC of 0.78 for Model 2 (Fig. 1c). Adding C-peptide increased the AUC by 0.062 (bootstrap 95% CI 0.009–0.131).

When adiposity and C-peptide were considered jointly, insulin requirement was 8.7% (2/23) in women with neither obesity nor below-median C-peptide, 44.1% (15/34) in non-obese women with low C-peptide, 40.6% (13/32) in obese women with high C-peptide, and 71.4% (15/21) in obese women with low C-peptide (P for trend <0.001; Fig. 1b). Compared with women with neither feature, the age-adjusted OR was 7.88 (95% CI 1.70–36.51) for women with one feature and 24.46 (95% CI 4.28–139.71) for women with both.

Sensitivity analyses

Results were materially unchanged after excluding ten women with values in the overt-diabetes range (prepregnancy BMI aOR 1.18, 95% CI 1.07–1.32; C-peptide aOR 3.28 per halving, 95% CI 1.61–6.67), after further adjustment for weight gain, family history of diabetes and parity,

and in a parsimonious model including only prepregnancy BMI and C-peptide (aOR 1.18, 95% CI 1.07–1.30, and 2.91, 95% CI 1.63–5.19, respectively). Both associations persisted regardless of referral timing (Online Resource 1).

Pregnancy outcomes

Caesarean delivery was more frequent in insulin-treated women (88.9% vs. 69.2%; $P = 0.016$), although the association was attenuated after adjustment for age, prepregnancy BMI and parity (aOR 2.86; 95% CI 0.95–8.68; $P = 0.063$). Preterm birth occurred in 15.6% of insulin-treated women and 3.1% of women treated with lifestyle measures alone ($P = 0.030$; aOR 6.01; 95% CI 1.01–35.65), although the number of events was small. All 13 cases of macrosomia occurred in the insulin-treated group (28.9% vs. 0%; $P < 0.001$), whereas macrosomia was not associated with prepregnancy BMI (OR 1.01 per kg/m^2; 95% CI 0.89–1.13) (Table 3).

DISCUSSION

In this cohort of women with GDM, two in five required insulin. Higher prepregnancy BMI and lower serum C-peptide were independently associated with insulin requirement, after accounting for OGTT glucose values and HbA1c. The two measures were only weakly correlated and their effects were additive: insulin need increased about eight-fold from women with neither feature to those with both. These findings suggest that adiposity-related insulin resistance and inadequate insulin secretory capacity represent distinct, complementary routes to treatment failure with lifestyle measures alone.

Our findings on adiposity are consistent with studies in which prepregnancy overweight and obesity were associated with a greater need for glucose-lowering medication [9,10] and with the Precision Medicine in Diabetes Initiative review, which identified BMI, together with previous GDM and glucose concentrations at diagnosis, as a routinely available predictor of treatment escalation [8]. Other cohorts, however, found that glucose concentrations at diagnosis and HbA1c, rather than BMI, independently predicted insulin requirement [11–13].

In our univariable analyses, fasting and 1-h OGTT glucose and HbA1c were all associated with insulin need, but they did not retain independent associations once BMI was considered, possibly because adiposity partly underlies these glycaemic measures, as suggested by the correlation between BMI and HbA1c in our cohort. Differences in diagnostic criteria, glycaemic targets and populations probably also contribute.

The novel finding of this study is the independent inverse association between C-peptide and insulin requirement. Normal pregnancy requires a compensatory 2- to 3-fold increase in insulin secretion to overcome progressive insulin resistance, and GDM develops when β-cell compensation is insufficient [1]. Using detailed physiological measurements, Powe et al. showed that about half of women with GDM have a predominant insulin secretion defect, a smaller fraction a predominant sensitivity defect, and the remainder a mixed defect [14]. In the prospective Belgian Diabetes in Pregnancy (BEDIP-N) cohort, the need for insulin did not differ significantly between subtypes defined by insulin resistance [15]; however, those subtypes were defined by measures of insulin sensitivity, not insulin secretion. Our data, using a simple and widely available marker, suggest that relatively low endogenous insulin secretion identifies women who are less able to compensate for the insulin resistance of late pregnancy—especially when superimposed on obesity—and therefore more likely to require exogenous insulin. Previous studies of C-peptide in pregnancy have mainly addressed the risk of developing GDM [25]; to our knowledge, few have examined C-peptide as a determinant of treatment requirement once GDM is diagnosed.

The phenotype-based approach illustrated in Fig. 1b may have practical value. Both measures are inexpensive and widely available. Women with obesity and low C-peptide, among whom more than two-thirds required insulin, might benefit from closer glucose monitoring and a lower threshold for early treatment escalation, whereas women with neither feature were rarely treated with insulin. Such an approach is in line with the move towards precision medicine in

GDM [8]. Adding C-peptide improved discrimination beyond conventional predictors; however, the confidence intervals around the phenotype estimates were wide and the groups were derived from cohort medians, so they should be considered hypothesis-generating until validated in independent, prospective cohorts with standardised fasting C-peptide measurement.

Insulin-treated women had higher rates of caesarean delivery and preterm birth, and all cases of macrosomia occurred in this group; however, the excess caesarean risk was attenuated after adjustment for BMI, age and parity, and the preterm estimate was imprecise because of few events. These observations are consistent with the known continuous relationship between maternal glycaemia and fetal overgrowth [3,4], but they should not be interpreted as effects of insulin therapy itself. Insulin requirement is a marker of more severe maternal hyperglycaemia, and confounding by indication cannot be excluded in an observational design [26]. Maternal obesity also has well-established short- and long-term consequences for mother and offspring [27,28], supporting preconception weight management as a strategy that may reduce both GDM severity and the need for insulin.

Gestational age at referral was not associated with insulin requirement, although later referral shortens the window for lifestyle intervention, and dietary adherence, which we could not assess, influences glycaemic control [29].

Strengths and limitations

Strengths include the evaluation of an insulin-secretion marker alongside conventional predictors, pre-specified modelling with bootstrap validation, and consistent sensitivity analyses. First, the retrospective single-centre design and modest sample size limit precision and generalisability, and the events-per-variable ratio of the full model was below ten; however, bootstrap CIs and a parsimonious two-variable model gave consistent results. Second, prepregnancy weight was self-reported. Third, C-peptide was measured once, at

referral rather than at a standardised gestational age, and without simultaneous insulin or glucose-based indices of insulin secretion and sensitivity. Fourth, self-monitoring glucose data, previous GDM, total gestational weight gain, birth weight and neonatal hypoglycaemia were unavailable, and the few macrosomia and preterm events precluded robust multivariable analysis.

Conclusion

In women with GDM, higher prepregnancy BMI and lower serum C-peptide were independently and additively associated with the need for insulin therapy. These findings support the concept that insulin resistance and insufficient insulin secretion contribute separately to treatment requirement in GDM. Combining these two simple measures at diagnosis may help identify women who will require insulin and warrants prospective validation.

Author Contribution

Bozkurt OF: Data collection or management, Data analysis; Böyük B: Protocol/project development, Manuscript writing/editing; Erman H: Data analysis, Manuscript writing/editing; Akın S: Data collection or management.

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Consent to participate: The requirement for informed consent was waived by the Ethics Committee because of the retrospective design and the use of anonymised routine clinical data. — please confirm, or replace with: Informed consent was obtained from all individual participants included in the study.

Consent to publish: Not applicable; the manuscript contains no individually identifiable data.

Data availability: The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Table 1. Characteristics of women with gestational diabetes mellitus according to insulin requirement

Characteristic	All (n = 110)	Insulin (n = 45)	Lifestyle only (n = 65)	*P*
Demographic and clinical				
Age, years	32.7 ± 5.1	33.5 ± 5.4	32.2 ± 4.8	0.201
Gravidity	2 (1–3)	3 (1–3)	2 (1–3)	0.412
Parity, n (%)				0.788
0	33 (30.0)	12 (26.7)	21 (32.3)	
1	29 (26.4)	13 (28.9)	16 (24.6)	
≥2	48 (43.6)	20 (44.4)	28 (43.1)	
Family history of diabetes, n (%)	82 (74.5)	36 (80.0)	46 (70.8)	0.275
Prepregnancy BMI, kg/m^2	29.0 ± 4.9	30.6 ± 4.6	27.8 ± 4.8	0.003
Prepregnancy BMI category, n (%)				0.007
<25 kg/m^2	22 (20.0)	3 (6.7)	19 (29.2)	
25–29.9 kg/m^2	35 (31.8)	14 (31.1)	21 (32.3)	
≥30 kg/m^2	53 (48.2)	28 (62.2)	25 (38.5)	
BMI at first visit, kg/m^2	32.4 ± 5.4	34.3 ± 5.4	31.1 ± 5.1	0.002
Weight gain until first visit, kg	8.9 ± 4.3	9.6 ± 4.7	8.3 ± 4.0	0.119
Gestational age at first visit, weeks	29 (26–32)	29 (26–32)	29 (27–32)	0.381
First visit >28 weeks, n (%)	60 (54.5)	23 (51.1)	37 (56.9)	0.547
Systolic blood pressure, mmHg	120 (110–120)	120 (110–120)	120 (110–120)	0.997
Diastolic blood pressure, mmHg	75 (70–80)	75 (70–80)	80 (70–80)	0.829
Glycaemic and laboratory				
OGTT fasting glucose, mg/dL	90 (80–99)	92 (85–101)	86 (79–95)	0.023
OGTT 1-h glucose, mg/dL	104 (91–120)	115 (102–130)	98 (90–115)	<0.001
OGTT 2-h glucose, mg/dL	180 (165–195)	175 (165–195)	180 (165–195)	0.465
HbA1c, %	5.50 (5.20–5.78)	5.60 (5.50–6.00)	5.50 (5.10–5.60)	<0.001
HbA1c, mmol/mol	37 (33–40)	38 (37–42)	37 (32–38)	<0.001
C-peptide, ng/mL	3.00 (2.01–3.68)	2.48 (1.00–3.49)	3.16 (2.40–3.80)	0.004
Total cholesterol, mg/dL	208 (176–245)	201 (174–240)	208 (180–248)	0.527
Triglycerides, mg/dL	180 (120–245)	159 (103–235)	184 (129–250)	0.343
LDL cholesterol, mg/dL	116.2 ± 38.9	121.6 ± 43.0	112.4 ± 35.7	0.228
HDL cholesterol, mg/dL	60 (50–74)	59 (50–70)	60 (50–76)	0.429
Haemoglobin, g/dL	11.7 (11.0–12.4)	12.0 (11.0–12.5)	11.6 (10.8–12.1)	0.207
Creatinine, mg/dL	0.47 (0.39–0.54)	0.48 (0.40–0.57)	0.46 (0.39–0.52)	0.246
ALT, U/L	12 (8–15)	12 (9–14)	12 (8–15)	0.836

Values are mean ± SD, median (interquartile range) or n (%). *P* values from Student's *t* test, Mann–Whitney *U* test or χ^2 test, as appropriate. ALT, alanine aminotransferase; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; OGTT, 75-g oral glucose tolerance test.

Table 2. Factors associated with insulin requirement in women with gestational diabetes mellitus: univariable and multivariable logistic regression

Variable	Univariable OR (95% CI)	*P*	Model 1 aOR (95% CI)	*P*	Model 2 aOR (95% CI)	*P*
Age, per year	1.05 (0.97–1.13)	0.200	1.04 (0.95–1.13)	0.428	1.01 (0.92–1.10)	0.916
Prepregnancy BMI, per kg/m^2	1.13 (1.04–1.24)	0.005	1.12 (1.02–1.23)	0.016	1.18 (1.06–1.31)	0.002
OGTT fasting glucose, per mg/dL	1.03 (1.00–1.05)	0.021	1.00 (0.97–1.03)	0.934	1.01 (0.98–1.05)	0.560
OGTT 1-h glucose, per mg/dL	1.03 (1.01–1.05)	0.003	1.02 (1.00–1.04)	0.091	1.02 (1.00–1.04)	0.077
OGTT 2-h glucose, per mg/dL	1.00 (0.98–1.01)	0.592	–		–	
HbA1c, per 1% (10.9 mmol/mol)	4.64 (1.81–11.90)	0.001	2.48 (0.81–7.62)	0.114	1.82 (0.53–6.24)	0.341
First visit >28 weeks	0.79 (0.37–1.70)	0.547	0.79 (0.33–1.88)	0.586	0.58 (0.21–1.54)	0.272
C-peptide, per halving[a]	2.38 (1.43–3.97)	<0.001	–		3.42 (1.67–6.97)	<0.001
Family history of diabetes	1.65 (0.67–4.08)	0.277	–		–	
Parity, per birth	1.07 (0.76–1.51)	0.713	–		–	
Weight gain until first visit, per kg	1.08 (0.98–1.18)	0.124	–		–	
Model performance						
Nagelkerke R^2			0.27		0.43	
Hosmer–Lemeshow *P*			0.72		0.76	
AUC (95% CI)			0.76 (0.67–0.84)		0.82 (0.74–0.89)	
Optimism-corrected AUC			–		0.78	

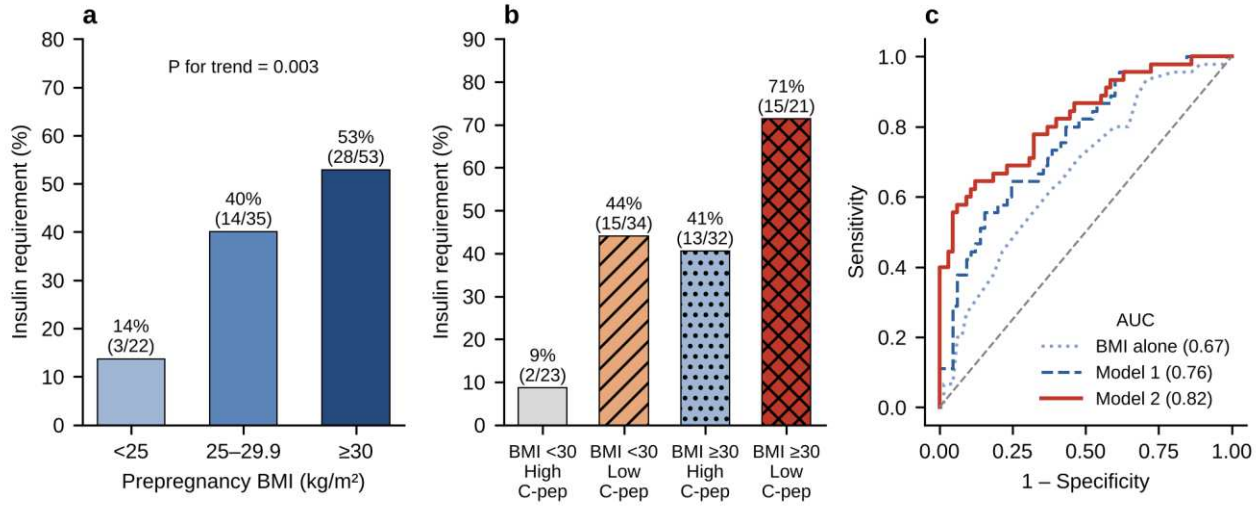
Model 1 (n = 110, 45 events) included age, prepregnancy BMI, fasting and 1-h OGTT glucose, HbA1c and first visit >28 weeks. Model 2 (n = 110, 45 events) additionally included $\log_2$-transformed C-peptide; likelihood-ratio test for adding C-peptide *P* <0.001. Bootstrap (2,000 resamples) 95% CIs: prepregnancy BMI 1.02–1.28 (Model 1) and 1.06–1.39 (Model 2); C-peptide per halving 2.00–11.01. [a] OR for a 50% lower C-peptide concentration. aOR, adjusted odds ratio; AUC, area under the receiver operating characteristic curve; BMI, body mass index; CI, confidence interval; OGTT, oral glucose tolerance test; OR, odds ratio.

Table 3. Delivery and neonatal outcomes according to insulin requirement

Outcome	Insulin (n = 45)	Lifestyle only (n = 65)	*P*	aOR (95% CI)[a]
Caesarean delivery, n (%)	40 (88.9)	45 (69.2)	0.016	2.86 (0.95–8.68)
Preterm birth (<37 weeks), n (%)	7 (15.6)	2 (3.1)	0.030[b]	6.01 (1.01–35.65)
Macrosomia, n (%)	13 (28.9)	0 (0.0)	<0.001[b]	Not estimable[c]

[a] Adjusted for age, prepregnancy BMI and parity. [b] Fisher's exact test. [c] No events in the lifestyle-only group. aOR, adjusted odds ratio; CI, confidence interval.

Fig. 1 Insulin requirement according to prepregnancy BMI and serum C-peptide. (a) Proportion of women requiring insulin by prepregnancy BMI category. (b) Proportion requiring insulin according to combined prepregnancy obesity (BMI ≥30 kg/m^2) and C-peptide below ("low") or at/above ("high") the cohort median of 3.0 ng/mL. (c) Receiver operating characteristic curves for prepregnancy BMI alone, Model 1 (age, prepregnancy BMI, fasting and 1-h OGTT glucose, HbA1c, first visit >28 weeks) and Model 2 (Model 1 plus $\log_2$ C-peptide); n = 110; values in the panel c legend are AUCs. AUC, area under the curve; BMI, body mass index



Supplementary Files

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- Tables.docx
- ESM1.pdf