



# Predictive factors for postpartum glucose intolerance in women with gestational diabetes mellitus

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1 ORIGINAL ARTICLE

2 **Predictive factors for postpartum glucose intolerance in women with gestational**  
3 **diabetes mellitus**

4

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23

24 Running title: Postpartum glucose intolerance in GDM

25

26 **Abstract**

27 **Aim:**

28 The aim of this prospective cohort study was to evaluate the risk factors for postpartum  
29 glucose intolerance (GI) in women with gestational diabetes mellitus (GDM).

30 **Method:**

31 A total of 140 women with GDM were enrolled. Of these, 115 underwent a 75-g oral  
32 glucose tolerance test (OGTT) at 12 weeks after delivery. Clinical factors and  
33 parameters in the antepartum 75-g OGTT associated with postpartum GI were evaluated  
34 by logistic regression analyses.

35 **Results:**

36 Twenty-two (19.1%) of the 115 women with GDM developed postpartum GI. The  
37 univariate and multivariable logistic regression analyses revealed that low oral  
38 disposition index (DI) was a risk factor for postpartum GI (OR, 0.2; 95% CI, 0.04–0.7;  
39  $p<0.05$ ), and that no clinical factors were associated with postpartum GI.

40 **Conclusions:**

41 Lower oral DI on the antepartum 75-g OGTT may be a useful marker for identifying

42 GDM women who are at high risk for postpartum GI.

43

44 **Key Words:**

45 Gestational diabetes mellitus, glucose intolerance, oral disposition index, postpartum,

46 75-g oral glucose tolerance test

47

## 48 **Introduction**

49 Pregnant women with gestational diabetes mellitus (GDM) have an increased risk of  
50 glucose intolerance (GI). A systematic review and meta-analysis has demonstrated that  
51 women with GDM have a 7.4-fold increased risk of developing type 2 diabetes mellitus  
52 (DM) after delivery compared with those without GDM <sup>1</sup>. Prenatal prediction of  
53 postpartum GI may allow clinicians to identify pregnant women who required long-term  
54 follow-up to assess the development of type 2 DM. The American Diabetes Association  
55 (ADA) recommend screening for GI, including type 2 DM, in women with GDM at  
56 4–12 weeks after delivery, using 75-g oral glucose tolerance test (OGTT) <sup>2</sup>.

57         We have reported that, in women with GDM, the low insulinogenic index (II)  
58 levels on the antepartum 75-g OGTT is a risk factor for developing GI during the early  
59 postpartum period <sup>3</sup>. However, the previous study evaluated only parameters of the  
60 antepartum 75-g OGTT, and did not evaluate any clinical factors, such as body mass  
61 index (BMI) prior to pregnancy, weight gain during pregnancy, and family history of  
62 DM, etc.

63         This prospective cohort study aimed to assess predictive clinical factors and  
64 laboratory parameters in the antepartum 75-g OGTT for GI during the early postpartum

65 period among women with GDM.

66

## 67 **Material and Methods**

### 68 *Study design and participants*

69 This prospective cohort study enrolled women with singleton pregnancies who were  
70 diagnosed with GDM by the 75-g OGTT during pregnancy and delivered at the Kobe  
71 University Hospital from January 2011 to December 2018. The study followed the  
72 principles of the Declaration of Helsinki, and it was approved by the Institutional  
73 Review Board of the Kobe University Hospital (reference number B200228). Written  
74 informed consent was obtained from all participants.

### 75 *Procedures*

76 All pregnant women who visited or were referred to the Kobe University Hospital  
77 underwent screening for GDM both at 10–14 and 24–28 gestational weeks (GW).  
78 Pregnant women who had casual blood glucose (BG) levels of  $\geq 100$  mg/dL  
79 (5.5 mmol/L) at 10–14 or 24–28 GW, or those who had 1-hr BG levels of  $\geq 140$  mg/dL  
80 (7.8 mmol/L) on 50-g glucose challenge tests (GCT) at 24–28 GW, or those with risk

81 factors for GDM, including obesity, family history of DM, past history of macrosomia,  
82 presence of persistent glycosuria, polyhydramnios, and suspected heavy for date (HFD)  
83 underwent the 75-g OGTT. According to the International Association of Diabetes and  
84 Pregnancy Study Groups (IADPSG) criteria <sup>4</sup>, the diagnosis of GDM is made when any  
85 of the following are met: fasting BG (FBG)  $\geq 92$  mg/dL (5.1 mmol/L), 1-hr BG  
86  $\geq 180$  mg/dL (10.0 mmol/L), or 2-hr BG  $\geq 153$  mg/dL (8.5 mmol/L). BG and  
87 immunoreactive insulin (IRI) levels at fasting, 0.5, 1, 1.5, and 2 hr after the oral  
88 ingestion of 75-g glucose were also measured, and the total area under the curve (AUC)  
89 of glucose and insulin were calculated by the trapezoid method <sup>5</sup>.

90 As an insulin resistance parameter, the homeostasis model assessment-insulin  
91 resistance (HOMA-IR) ( $=\text{FBG (mg/dL)} \times \text{fasting IRI (FIRI)} (\mu\text{U/mL}) / 405$ ) was used.  
92 HOMA- $\beta$  ( $=360 \times \text{FIRI} (\mu\text{U/mL}) / [\text{FBG (mg/dL)} - 63]$ ) and insulinogenic index (II) ( $=$   
93  $[\text{0.5-hr IRI} (\mu\text{U/mL}) - \text{FIRI} (\mu\text{U/mL})] / [\text{0.5-hr BG (mg/dL)} - \text{FBG (mg/dL)}]$ ) were  
94 calculated for evaluating the insulin secretory capacity of pancreatic  $\beta$  cells. The oral  
95 disposition index (DI), which represents the compensation of pancreatic  $\beta$  cells for  
96 insulin resistance, was calculated as the product of the Matsuda index of insulin  
97 sensitivity and the ratio of the AUC of insulin to the AUC of glucose during the OGTT <sup>6</sup>.



98 The Matsuda index was calculated using the following formula:  $10^4/\sqrt{(\text{FGB} \times \text{FIRI} \times$   
99  $\text{mean BG during 75-g OGTT} \times \text{mean IRI during 75-g OGTT})^2}$ .

100 All pregnant women diagnosed with GDM were referred to diabetologists in  
101 the Kobe University Hospital and underwent self-monitoring of blood glucose (SMBG)  
102 and diet therapy. If FBG levels exceeded 100 mg/dL, or 2-hr BG levels exceeded  
103 120 mg/dL in SMBG regardless of diet therapy, an insulin therapy was started. Insulin  
104 doses were adjusted to achieve both FBG levels of <100 mg/dL and 2-hr BG levels of  
105 <120 mg/dL.

106 All pregnant women with GDM were instructed to undergo a 75-g OGTT at  
107 12 weeks after delivery. Using the WHO's 1999 criteria<sup>8</sup>, DM was diagnosed by either  
108 FBG levels of  $\geq 126$  mg/dL (7.0 mmol/L) or 2-hr BG levels of  $\geq 200$  mg/dL  
109 (11.1 mmol/L). IFG was diagnosed by FBG levels of  $\geq 110$  mg/dL (6.1 mmol/L), and  
110 IGT was diagnosed by 2-hr BG levels of  $\geq 140$  mg/dL (7.8 mmol/L). GI was defined by  
111 the presence of DM, impaired fasting glucose (IFG), or impaired glucose tolerance  
112 (IGT). FBG levels of <110 mg/dL (6.1 mmol/L) and 2-hr BG levels of <140 mg/dL  
113 (7.8 mmol/L) were identified as normal.

114 ***Statistical analysis***

115 Clinical characteristics were compared between pregnancies with GI during the early  
116 postpartum period and pregnancies without them. Differences between the two groups  
117 were analyzed using the Mann-Whitney *U* test, Fisher exact test, and  $\chi^2$  test. *P* values  
118 <0.05 were considered statistically significant. The stepwise approach was used to  
119 evaluate clinical factors and parameters in the antepartum 75-g OGTT associated with  
120 GI during the early postpartum period. **To avoid overfitting in multivariable logistic**  
121 **regression analyses, the number of variables in the final model of multivariable analyses**  
122 **was restricted to a maximum of 10% of the case number.** Variables with **the lowest and**  
123 **the second-lowest *P* values** in univariate logistic regression analyses were subjected to  
124 **the final model of** multivariable logistic regression analyses, and variables with *P* values  
125 <0.05 in **the final model of** multivariable logistic regression analyses were determined  
126 as clinical factors and parameters in the antepartum 75-g OGTT associated with GI  
127 during the early postpartum period in women with GDM. All statistical analyses were  
128 performed using the SPSS software, version 19 (SPSS Inc., Chicago, Illinois).

129

## 130 **Results**

131 **A flowchart of the subjects in this prospective cohort study is shown in Figure 1.** Of

132 2,370 pregnant women with singleton pregnancies who underwent screening for GDM  
133 at the Kobe University Hospital, 140 (5.9%) were diagnosed with GDM from January  
134 2011 to December 2018. The indications for the antepartum 75-g OGTT in the 140  
135 pregnant women with GDM were as follows: casual BG level  $\geq 100$  mg/dL and/or 1-hr  
136 BG level on a 50-g glucose challenge tests  $\geq 140$  mg/dL (n=99); casual BG level  
137  $\geq 100$  mg/dL (n=13); suspicion of polyhydramnios and/or HFD on ultrasound  
138 examinations during pregnancy (n=10); and presence of other risk factors of GDM,  
139 including a history of GDM, obesity, and persistent glycosuria (n=18). Twenty-five of  
140 the 140 women with GDM refused to receive a 75-g OGTT at 12 weeks after delivery.  
141 Therefore, 115 women with GDM were included in the analyses of risks for GI during  
142 the early postpartum period.

143 Twenty-two of the 115 (19.1%) pregnant women with GDM had GI at  
144 12 weeks after delivery, including one, two, and 19 women with DM, IFG and IGT,  
145 respectively.

146 **Table 1** shows the clinical characteristics and laboratory data in antepartum  
147 75-g OGTT of the subjects. The group of GDM women with postpartum GI (GI group)  
148 had a significantly higher 0.5-hr BG ( $p < 0.05$ ) and lower oral DI ( $p < 0.01$ ) than the group

149 without postpartum GI (non-GI group).

150 Univariate logistic regression analyses demonstrated that FBG (OR, 1.0; 95%  
151 CI, 1.0–1.1;  $p=0.04$ ), 0.5-hr BG (OR, 1.0; 95% CI, 1.0–1.1;  $p=0.02$ ) and oral DI (OR,  
152 0.1; 95% CI, 0.03–0.5;  $p<0.01$ ) were associated with the occurrence of GI during the  
153 early postpartum period in women with GDM (**Table2**). **The final model of**  
154 **multivariable** logistic regression analyses of the **2 factors with the lowest  $P$  value in**  
155 **univariate analyses** revealed that oral DI (OR, 0.2; 95% CI, 0.04–0.7;  $p<0.05$ ) was an  
156 independent factor associated with GI during the early postpartum period (**Table2**).

157

## 158 **Discussion**

159 This study used IADPSG criteria for diagnosing GDM <sup>4</sup>, and 140 of the 2,370 (5.9%)  
160 pregnant women were diagnosed with GDM. Because medians of the prevalence of  
161 GDM in Japan were reported to be 2.8%–13.0% <sup>9</sup>, the prevalence of GDM in this study  
162 was thought to be valid. In addition, the incidence of GI during the early postpartum  
163 period in women with GDM (19.1%) was also comparable to those (16.7%–36.6%) in  
164 previous studies <sup>3,10,11</sup>.

165           To the best of our knowledge, this prospective cohort study of pregnant women  
166 with GDM, for the first time, assessed both the clinical factors and parameters in the  
167 antepartum 75-g OGTT associated with GI during the early postpartum period by  
168 logistic regression analyses using a stepwise approach, and revealed that lower oral DI  
169 is an independent risk factor for postpartum GI.

170           A previous retrospective study also reported that oral DI in the antepartum 75-g  
171 OGTT was useful for identifying women with GDM at high risk of postpartum GI <sup>12</sup>. In  
172 addition, it was reported that among the Japanese-American adults, including males and  
173 non-pregnant women, the low oral DI was predictive of developing DM in the future <sup>13</sup>.  
174 DI represents a hyperbolic relationship between insulin secretion and insulin sensitivity  
175 <sup>6,14</sup>. Therefore, this parameter represents the insulin secretory capacity of pancreatic  $\beta$   
176 cells adjusted for insulin sensitivity <sup>13</sup>. An adequate insulin secretory response of  
177 pancreatic  $\beta$  cells adapting to changes in insulin sensitivity might be significant for the  
178 maintenance of normal glucose tolerance during the postpartum period. Pregnant  
179 women with low oral DI on the antepartum 75-g OGTT may be at high risk not only for  
180 GI during the early postpartum period, but also for DM in the future.

181           On the other hand, previous retrospective studies in Japan demonstrated that

182 low II and II/fasting IRI ratio in the antepartum 75-g OGTT were associated with  
183 postpartum GI in patients with GDM<sup>10,15</sup>. Our previous prospective cohort study of 72  
184 pregnant women with GDM, including 12 with postpartum GI, also demonstrated that a  
185 low II in the antepartum 75-g OGTT was an independent risk factor for developing GI  
186 during the early postpartum period<sup>3</sup>. In the present study, the levels of 0.5-h BG in  
187 antepartum 75-g OGTT in GI group were significantly higher than those in non-GI  
188 group, and oral DI in GI group was significantly lower than those in non-GI group.  
189 Whereas, there were no significant differences in FBG, FIRI, 0.5-h IRI and II between  
190 two groups. In addition, the numbers of women with GDM and postpartum GI in the  
191 present study (140 GDM and 22 postpartum GI) are almost two times larger than those  
192 in our previous study (72 GDM and 12 postpartum GI). The increase in the number of  
193 patients may lead to an increase in the number of GDM women with more impaired  
194 pancreatic  $\beta$  cell function, and therefore oral DI, but not II, may be selected as a risk  
195 factor for GI during the early postpartum period.

196 Previous studies evaluated associations between maternal clinical or laboratory  
197 findings of antepartum OGTT and postpartum GI. They demonstrated that higher FBG  
198 levels, higher AUC of glucose, lower fasting insulin concentration, decreased  $\beta$  cell

199 function, higher BMI prior to pregnancy, and family history of DM were risk factors for  
200 postpartum GI<sup>16,17</sup>. In addition, obesity and  $\beta$  cell function impairment were reported to  
201 be associated with type 2 DM at early postpartum<sup>18</sup>. In our present study, there were no  
202 clinical factors associated with postpartum GI, and oral DI was only associated with it.  
203 In these previous studies, not the new IADPSG criteria but previous one for GDM were  
204 used, and the race of the participants and the follow-up duration were different from  
205 those of our present study. Furthermore, not oral DI but HOMA- $\beta$  and insulin  
206 secretion/insulin resistance disposition index calculated by 100-g OGTT were evaluated  
207 as indicators of pancreatic  $\beta$  cell function in these studies. These facts may influence the  
208 differences in results between previous studies and our study. In addition, postpartum  
209 GI in women with GDM may be more closely associated with  $\beta$  cell function  
210 impairment rather than the clinical background or characteristics of the patients.

211         There are some potential limitations in this study. The indications for 75-g  
212 OGTT in this study varied among the participants, therefore the GW at diagnosis of  
213 GDM varied, and the facts may influence the results of this study. In addition, the scale  
214 of the study was not large enough. Therefore, further studies are required to confirm the  
215 conclusions of this study.

216           This prospective cohort study demonstrated that a low oral DI on the  
217 antepartum 75-g OGTT was an independent risk factor for GI during the early  
218 postpartum period in women with GDM. Measurements of oral DI in pregnant women  
219 with GDM may be useful for identifying GDM women at high risk for DM in the  
220 future.

221

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229

## 230 **Conflict of Interest**

231 The authors declare no conflict of interest.



232

233 **Author Contributions**

234 All listed authors meet the criteria for authorship and have contributed to the acquisition  
235 of data, supervision, manuscript writing and manuscript review.

236

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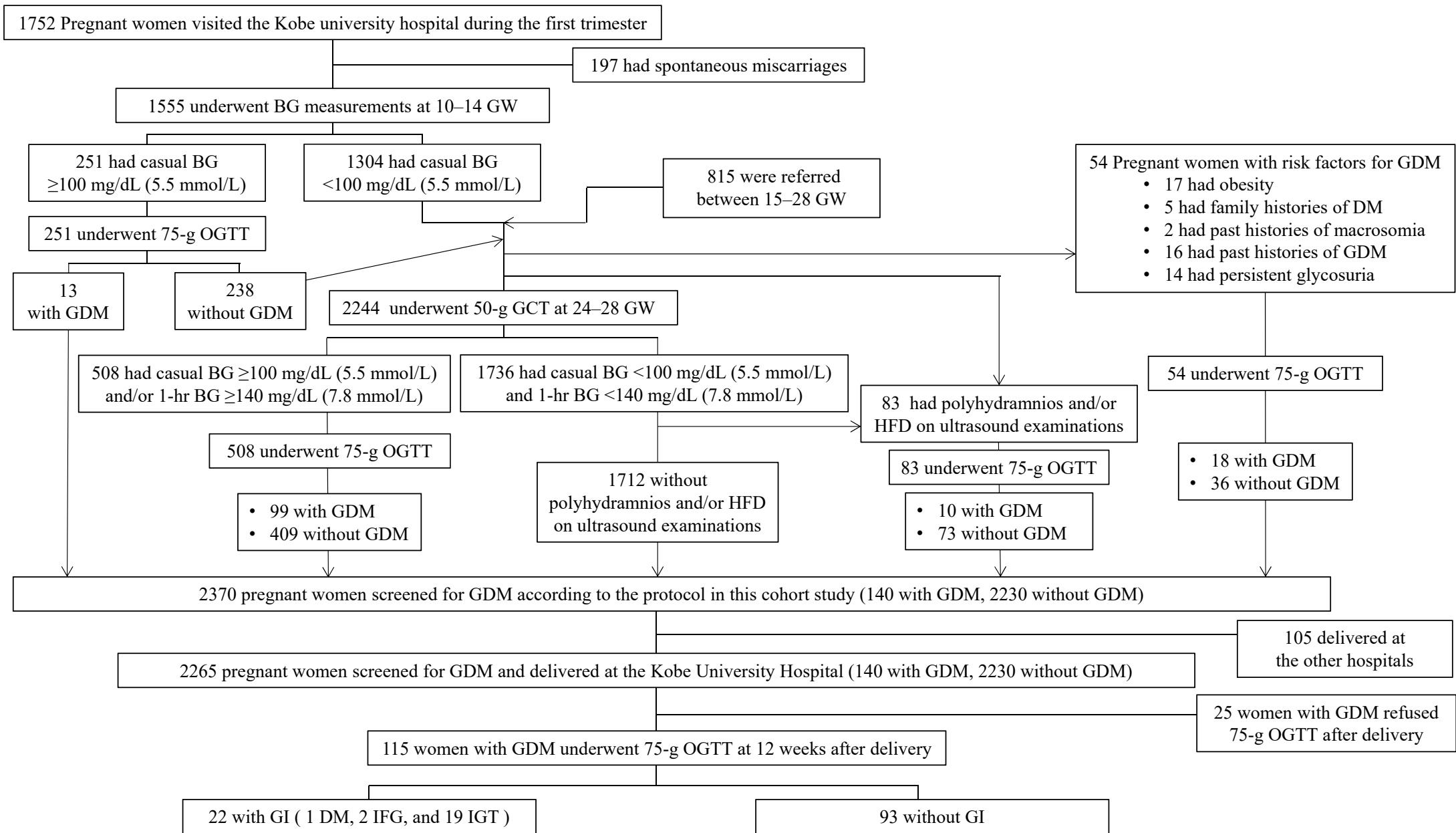
298 **Figure legends**

299 **Figure 1. Flow diagram for the study participants**

300 During the study period, 2370 pregnant women underwent screening for GDM and were  
301 enrolled in this study. Thirteen of the 251 (5.2%) pregnant women, who underwent 75-g  
302 oral glucose tolerance test (OGTT) due to a casual BG  $\geq$ 100 mg/dL (5.5 mmol/L) at  
303 10–14 gestational weeks (GW), were diagnosed with GDM. Ninety-nine of the 508  
304 (19.5%) pregnant women, who underwent 75-g OGTT due to a casual BG  $\geq$ 100 mg/dL  
305 (5.5 mmol/L) and/or 1-hr BG  $\geq$ 140 mg/dL (7.8 mmol/L) in the 50-g glucose challenge  
306 test (GCT) at 24–28 GW, were diagnosed with GDM. Ten of the 83 (12.0%) pregnant  
307 women, who underwent 75-g OGTT due to the presence of polyhydramnios and/or  
308 heavy for date (HFD) on ultrasound examinations, were diagnosed with GDM. Eighteen  
309 of 54 (33.3%) pregnant women, who underwent 75-g OGTT due to risk factors for  
310 GDM, were diagnosed with GDM. Total one hundred forty of the 2370 (5.9%) pregnant  
311 women screened for GDM by our study protocol were diagnosed with GDM. Finally,  
312 one hundred fifteen women with GDM underwent 75-g OGTT during the early  
313 postpartum period, and 22 of them (19.1%) were diagnosed with glucose intolerance  
314 (GI).

315 Abbreviations: BG, blood glucose; GW, gestational week; OGTT, oral glucose

316 intolerance test; GDM, gestational diabetes mellitus; DM, diabetes mellitus; HFD,  
317 heavy for date; GI, glucose intolerance; IFG, impaired fasting glucose; IGT, impaired  
318 glucose tolerance.  
319



**Table 1.** Clinical characteristics and laboratory data of the subjects.

| Variable                                    | postpartum GI<br>n=22 | non-postpartum GI<br>n=93 | <i>P</i> values |
|---|-----------------------|---------------------------|-----------------|
| Clinical findings of pregnant women         |                       |                           |                 |
| Age (years)                                 | 37 (29–42)            | 37 (21–45)                | 0.9             |
| Gravidity                                   | 2 (1–5)               | 2 (1–10)                  | 0.3             |
| Parity                                      | 1 (0–3)               | 0 (0–4)                   | 0.3             |
| BMI prior to pregnancy (kg/m <sup>2</sup> ) | 24.1 (16.4–33.9)      | 22.3 (16.4–34.7)          | 0.1             |
| Weight gain during pregnancy (kg)           | 5.0 (-9.0–13.2)       | 7.2 (-5–22.7)             | 0.1             |
| Family history of DM                        | 31.8%                 | 38.7%                     | 0.7             |
| GW at diagnosis of GDM                      | 28 (16–32)            | 29 (11–38)                | 0.4             |
| Insulin therapy during pregnancy            | 36.4%                 | 40.9%                     | 0.9             |
| Polyhydramnios                              | 4.7%                  | 4.3%                      | 1.0             |
| GW at delivery                              | 38 (32–40)            | 38 (31–41)                | 0.1             |
| Birth weight (g)                            | 2865 (2064–3850)      | 2938 (1580–3934)          | 0.6             |
| Birth weight > 90th percentile              | 4.7%                  | 9.6%                      | 0.7             |
| Birth weight < 10th percentile              | 4.7%                  | 11.8%                     | 0.5             |
| Diagnosis of HDP                            | 27.2%                 | 11.8%                     | 0.1             |
| Parameters in antepartum 75-g OGTT          |                       |                           |                 |
| FBG (mg/dl)                                 | 84 (76–138)           | 82 (55–112)               | 0.2             |
| 0.5-hr BG (mg/dl)                           | 155 (108–199)         | 145 (86–192)              | <0.05           |
| 1-hr BG (mg/dl)                             | 178 (123–226)         | 176 (120–235)             | 0.5             |
| 1.5-hr BG (mg/dl)                           | 174 (123–222)         | 171 (119–249)             | 0.5             |
| 2-hr BG (mg/dl)                             | 163 (122–206)         | 159 (86–248)              | 0.2             |
| Fasting IRI (μU/ml)                         | 8 (4–26)              | 7 (2–35)                  | 0.2             |
| 0.5-hr IRI (μU/ml)                          | 47 (20–115)           | 46 (7–243)                | 0.6             |
| 1-hr IRI (μU/ml)                            | 58 (22–109)           | 61 (27–307)               | 0.3             |
| 1.5-hr IRI (μU/ml)                          | 58 (18–146)           | 64 (20–340)               | 0.5             |
| 2-hr IRI (μU/ml)                            | 69 (20–150)           | 75 (15–501)               | 0.6             |
| AUC-glucose (mg min/dl)                     | 18735 (15345–23820)   | 18180 (14880–23970)       | 0.2             |
| AUC-insulin (μU min/ml)                     | 6713 (2205–12105)     | 6420 (2835–30060)         | 0.6             |
| AUC-insulin/glucose                         | 0.3 (0.1–0.6)         | 0.3 (0.2–1.8)             | 0.3             |
| HbA1c (%)                                   | 5.4 (4.8–6.2)         | 5.4 (4.9–6.2)             | 0.7             |
| HOMA-IR                                     | 1.7 (0.8–8.9)         | 1.4 (0.4–7.8)             | 0.2             |
| HOMA-β                                      | 140 (60–220)          | 127 (-1080–504)           | 0.8             |
| Insulinogenic index                         | 0.5 (0.2–1.5)         | 0.7 (0.0–3.6)             | 0.1             |
| Oral disposition index                      | 1.4 (0.5–2.2)         | 1.7 (0.7–3.5)             | <0.01           |

Data are expressed as the median (range) or percentage. Abbreviations: GI, glucose intolerance; BMI, body mass index; DM, diabetes mellitus; GW, gestational week; GDM, gestational diabetes mellitus; HDP, hypertension disorder during pregnancy; OGTT, oral glucose tolerance test; FBG, fasting blood glucose; BG, blood glucose; IRI, immunoreactive insulin; AUC, area under the curve; HOMA, homeostasis model assessment; IR, insulin resistance.



**Table 2.** Results of univariate and multivariate logistic regression analyses.

| Variable                                    | Univariate analysis |            |                 | Multivariable analysis |          |                 |
|---|---------------------|------------|-----------------|------------------------|----------|-----------------|
|   | Odds ratio          | 95% CI     | <i>P</i> values | Odds ratio             | 95% CI   | <i>P</i> values |
| Clinical findings of pregnant women         |                     |            |                 |                        |          |                 |
| Age (years)                                 | 1.0                 | 0.9–1.1    | 0.7             |                        |          |                 |
| Gravidity                                   | 0.8                 | 0.6–1.2    | 0.3             |                        |          |                 |
| Parity                                      | 1.3                 | 0.8–2.1    | 0.4             |                        |          |                 |
| BMI prior to pregnancy (kg/m <sup>2</sup> ) | 1.1                 | 1.0–1.2    | 0.2             |                        |          |                 |
| Weight gain during pregnancy (kg)           | 0.9                 | 0.8–1.0    | 0.1             |                        |          |                 |
| Family history of DM                        | 0.7                 | 0.3–2.0    | 0.5             |                        |          |                 |
| GW at diagnosis of GDM                      | 1.0                 | 0.9–1.1    | 0.7             |                        |          |                 |
| Insulin therapy during pregnancy            | 0.8                 | 0.3–2.2    | 0.7             |                        |          |                 |
| Polyhydramnios                              | 1.1                 | 0.1–10.0   | 1.0             |                        |          |                 |
| GW at delivery                              | 0.8                 | 0.6–1.0    | 0.1             |                        |          |                 |
| Birth weight (g)                            | 1.0                 | 0.9998–1.0 | 0.7             |                        |          |                 |
| Birth weight > 90th percentile              | 0.4                 | 0.1–3.7    | 0.5             |                        |          |                 |
| Birth weight < 10th percentile              | 0.4                 | 0.04–2.9   | 0.3             |                        |          |                 |
| Diagnosis of HDP                            | 2.8                 | 0.9–8.7    | 0.1             |                        |          |                 |
| Parameters in antepartum 75-g OGTT          |                     |            |                 |                        |          |                 |
| FBG (mg/dl)                                 | 1.0                 | 1.0–1.1    | 0.04            |                        |          |                 |
| 0.5-hr BG (mg/dl)                           | 1.0                 | 1.0–1.1    | 0.02            | 1.0                    | 1.0–1.05 | 0.2             |
| 1-hr BG (mg/dl)                             | 1.0                 | 1.0–1.02   | 0.8             |                        |          |                 |
| 1.5-hr BG (mg/dl)                           | 1.0                 | 1.0–1.03   | 0.5             |                        |          |                 |
| 2-hr BG (mg/dl)                             | 1.0                 | 1.0–1.03   | 0.2             |                        |          |                 |
| Fasting IRI (μU/ml)                         | 1.0                 | 1.0–1.1    | 0.3             |                        |          |                 |
| 0.5-hr IRI (μU/ml)                          | 1.0                 | 0.98–1.0   | 0.4             |                        |          |                 |
| 1-hr IRI (μU/ml)                            | 1.0                 | 0.98–1.0   | 0.2             |                        |          |                 |
| 1.5-hr IRI (μU/ml)                          | 1.0                 | 0.99–1.0   | 0.4             |                        |          |                 |
| 2-hr IRI (μU/ml)                            | 1.0                 | 0.98–1.0   | 0.3             |                        |          |                 |
| AUC-glucose (mg min/dl)                     | 1.0                 | 1.0–1.005  | 0.1             |                        |          |                 |
| AUC-insulin (μU min/ml)                     | 1.0                 | 0.9998–1.0 | 0.3             |                        |          |                 |
| AUC-insulin/glucose                         | 0.2                 | 0.01–2.4   | 0.2             |                        |          |                 |
| HbA1c (%)                                   | 1.2                 | 0.3–5.6    | 0.8             |                        |          |                 |
| HOMA-IR                                     | 1.3                 | 0.9–1.7    | 0.1             |                        |          |                 |
| HOMA-β                                      | 1.0                 | 0.997–1.0  | 1.0             |                        |          |                 |
| Insulinogenic index                         | 0.3                 | 0.1–1.3    | 0.1             |                        |          |                 |
| Oral disposition index                      | 0.1                 | 0.03–0.5   | <0.01           | 0.2                    | 0.04–0.7 | <0.05           |

Abbreviations: CI, confidence interval; BMI, body mass index; DM, diabetes mellitus; GW, gestational week; GDM, gestational diabetes mellitus; HDP, hypertension disorder during pregnancy; OGTT, oral glucose tolerance test; FBG, fasting blood glucose; BG, blood glucose; IRI, immunoreactive insulin; AUC, area under the curve; HOMA, homeostasis model assessment; IR, insulin resistance.