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Original Research

Importance of diagnosis time on pregnancy outcomes in pregnant women with pre-gestational diabetes mellitus

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Summary

Objective: To analyze the characteristics of pregnant women with pre-gestational diabetes mellitus (PGDM) who had missed diagnosis prior to pregnancy, and to evaluate the effects of diagnosis time on pregnancy outcomes in pregnant women with PGDM. *Materials and Methods:* A total of 822 pregnant women who were diagnosed with PGDM were conducted in this study. They were divided into two groups, including pre-pregnancy diagnosis group and pregnancy diagnosis group based on the initial diagnosis time. Then in the pregnancy diagnosis group, the cases diagnosed before 24 gestational weeks were defined as group A, and those diagnosed at or after 24 gestational weeks were defined as Group B. Maternal and pregnancy variables, as well as pregnancy outcomes, including delivery age of pregnant women, the rate of pregnancy loss, delivery gestational weeks, neonatal birth weight, the proportion of insulin treatment, the rate of pre-term, macrosomia, newborns transferred to pediatrics, the average of HbA1c level, and preeclampsia, were analyzed among groups by paired Student's *t*-test. *Results:* The rate of missed diagnosis before pregnancy was 68.1%. The proportion of insulin treatment and the rate of the cesarean section had a significant difference between pre-pregnancy diagnosis group and pregnancy diagnosis group. The characteristics and pregnancy outcomes in pregnancy diagnosis group A were not significantly different from those in the pre-pregnancy diagnosis group. However, in the pregnancy diagnosis group B, the proportion of pregnant women using insulin treatment and the average HbA1c level had a statistically significant difference, compared to pregnancy diagnosis group A, as well as the pre-pregnancy group. *Conclusions:* The rate of undiagnosed PGDM was high, and PGDM was significantly associated with multiple adverse pregnancy outcomes. Fasting plasma glucose should be used as a screening test to identify PGDM at pre-pregnancy or first antenatal care.

Key words: Pre-gestational diabetes mellitus; Pregnancy outcome; Diagnosis time.

Introduction

Pregnancies complicated by diabetes, including pre-gestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM), is one of the common pregnancy complications, which is increasing in recent years [1-3]. PGDM increases the risk of poor maternal and perinatal outcome, such as preeclampsia, fetal and neonatal death, macrosomia, preterm delivery, growth restriction, and so on [4-6]. Diabetes has become a major public health problem and its prevalence is increasing significantly among persons who are more than 20 years of age in China [7, 8]. However, due to the low proportion of regular physical examination, most diabetic patients are undiagnosed in China. In diabetic patients who have missed diagnosis before pregnancy, the control of blood glucose level is usually unsatisfactory, which will have adverse effects on maternal and perinatal outcome. However, there appears to be lack of studies on analysis of PGDM patients who have missed diagnosis before pregnancy.

Nowadays, the rising prevalence of diabetes increases the risk of diabetes for childbearing women in China, especially pregnant women [9, 10]. The study by Chan *et al.* demonstrated this epidemic is the result of the rapid societal transition, placing Chinese people at high risk of diabetes and multiple morbidities, and many are undiagnosed [9]. The pregnant women who had not been confirmed with diabetes before pregnancy with unsatisfactory blood glucose level management will lead to adverse pregnancy outcomes. For instance, Corrado *et al.* indicated the prevalence of fetal malformation and insulin requirements with PGDM first diagnosed during pregnancy were significantly higher compared with women with GDM [11]. Considering the high rate of missed diagnosis and risk of adverse pregnancy outcome, PGDM needs to be diagnosed in a timely fashion. The PGDM at different diagnosis time may affect the pregnancy outcome of pregnant women.

In the present study, the authors analyzed the clinical characteristics of PGDM pregnant women who were diagnosed during pregnancy (missed diagnosis before pregnancy). The maternal and perinatal outcomes were compared in women with PGDM who were diagnosed at different times.

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Materials and Methods

A total of 822 pregnant women who were diagnosed with PGDM were included between January 2011 and December 2017 in Yidu Central Hospital of Weifang. According to the diagnosis time of PGDM, all the participants were classified into pre-pregnancy diagnosis (PPD) group and pregnancy diagnosis (PD) group. Then the pregnancy diagnosis group was divided into group A (PGDM patients were diagnosed before 24 weeks) and group B (PGDM patients were diagnosed at 24 weeks or later). This study protocol was approved by the Medical Ethics Committee of Yidu Central Hospital of Weifang. Written informed consent was obtained from each participant.

The diagnosis of PGDM with pregnancy was based on the diagnostic criteria for GDM [12, 13]. It can be confirmed as PGDM when it conforms to either of the following two criteria: (1) a patient who has been diagnosed with diabetes before pregnancy or (2) pregnant women who are at high risk for diabetes and have not had a blood glucose examination before pregnancy should be confirmed with PGDM at the initial examination according to either of the following conditions. Firstly, fasting blood glucose level ≥ 7.0 mmol/L (126 mg/dL). Secondly, after the 75-gram oral glucose tolerance test (OGTT), the one with plasma glucose value more than 11.1 mmol/ L after two hours was considered positive. Thirdly, the one accompanied by typical hyperglycemia or hyperglycemia crisis symptoms, as well as a random blood glucose level ≥ 11.1 mmol/ L. Finally, the glycosylated hemoglobin (HbA1c) ≥ 6.5%.

In this study, the authors analyzed the following maternal and pregnancy variables: delivery age, diagnosis time of PGDM, blood glucose control level, insulin treatment, delivery gestational week, delivery mode, the history of pregnancy loss, the average of HbA1c levels, and preeclampsia. Fetal variables analyzed were: preterm birth (before 37 completed weeks), macrosomia, newborns transfer to pediatrics (NTP), and neonatal birth weight. According to these data, the authors designed the retrospective study of women diagnosed with PGDM.

The statistical analysis was carried out using the software of SPSS 21.0. Data are expressed as the mean ± standard deviation (SD). The differences between two groups were analyzed by paired Student's *t*-test. The association between PGDM and pregnant complication was analyzed by using the χ^2 test. Differences were considered significant when $p < 0.05$.

Results

In this study, the authors compared the clinical characteristics of pre-pregnancy diagnosis group and pregnancy diagnosis group, as well as among pre-pregnancy diagnosis group, and pregnancy diagnosis groups A and B. Among 822 pregnant women, 31.9% (262/822) pregnant women with PGDM were diagnosed before pregnancy, and 68.1% were diagnosed in pregnancy, of whom the rate of missed diagnosis of PGDM was 68.1%.

In pre-pregnancy diagnosis group and pregnancy diagnosis group, the delivery age of pregnant women was 32 ± 5 and 33 ± 4, the rate of pregnancy loss was 21.8% (57/262) and 17.8% (100 / 560), respectively. The information of delivery gestational weeks and neonatal birth weight are listed in Table 1. The clinical characteristic information, including delivery age, delivery gestational weeks, neonatal birth weight, and pregnancy loss, had no significant difference between pre-pregnancy group and pregnancy group (all $p > 0.05$, Table 1). Moreover, no positive difference in delivery age of pregnant women (32 ± 4, 33 ± 4, respectively), the rate of pregnancy loss (26/107, 74/453), delivery gestational weeks, and neonatal birth weight, was found between pregnancy diagnosis groups A and B (all $p > 0.05$, Table 1). In addition, the aforementioned clinical information in groups A and B of the pregnancy diagnosis group were compared with those in the pre-pregnancy diagnosis group, respectively, and both of the differences were not statistically significant (all $p > 0.05$).

In this study, insulin was used to control the blood glucose, and the level of HbA1c was detected to monitor the level of blood glucose control. Firstly, the authors compared the blood glucose control levels and pregnancy outcomes between pre-pregnancy diagnosis group and pregnancy diagnosis group. The average HbA1c level in pre-pregnancy diagnosis group was 6.3 ± 1.1%, which was higher than that in pregnancy diagnosis group. However, it had no statistically significant difference between the two groups. As shown in Table 2, the proportion of insulin treatment in pre-pregnancy diagnosis group was 89.7% (235/262), which was significantly higher than that in pregnancy diagnosis group (53.8%, 301/560, $p < 0.001$). The authors also compared the pregnancy outcomes between the two groups. As shown in Table 2, a statistically significant result was found in the rate of cesarean section in the pre-pregnancy group and pregnancy diagnosis group ($p < 0.001$). However there was no significant difference of other outcomes between the two groups, such as the rate of pre-term, macrosomia, newborns transfer to pediatrics, and preeclampsia (all $p > 0.05$, Table 2).

Secondly, the authors compared the related data between group A in pregnancy diagnosis group and pre-pregnancy diagnosis group. The average HbA1c level in group A was 6.4 ± 1.3%, which is higher than that in pre-pregnancy diagnosis group. However, as shown in Table 2, there was no significant difference between pre-pregnancy diagnosis group and pregnancy diagnosis group A (all $p > 0.05$). Then the pregnancy diagnosis group B was compared with the pre-pregnancy diagnosis group. As shown in Table 2, the average HbA1c level in group B was 6.0 ± 1.3%, and in pre-pregnancy diagnosis group it was 6.3 ± 1.1%. The blood glucose control level of group B was significantly lower than that of the pre-pregnancy diagnosis group, which had a significant difference between the two groups ($p = 0.005$). The comparison of insulin treatment between the two groups was also statistically significant ($p < 0.001$). The pregnancy outcome was also compared between the two groups. The rate of cesarean in group B (267/453, 58.9%) was lower than that in pre-pregnancy diagnosis group (190/262, 72.5%), which had a significant difference ($p < 0.001$). However, the pre-term rate, cesarean delivery

Table 1. — *Comparison of characteristics of PGDM pregnant women in the different groups.*

Variables	PGDM groups			p_1	p_2	p_3	p_4
	PPD (n = 262)	PD (n =560)					
		A (n = 107)	B (n = 453)				
Pregnancy loss	57 (21.8)	26 (25.7)	74 (16.3)	0.185	0.595	0.071	0.053
Delivery age (years)	32 ± 5	32 ± 4	33 ± 4	0.672	0.424	0.371	0.415
DGW (weeks)	38.5 ± 1.8	38.1 ± 1.7	38.3 ± 1.6	0.085	0.066	0.157	0.305
NBW (grams)	3,377 ± 422	3,308 ± 415	3,390 ± 387	0.060	0.152	0.667	0.051

Data in mean ± SD or number (%). PPD: pre-pregnancy diagnosis group; PD: pregnancy diagnosis group; DGW: delivery gestational weeks; NBW: neonatal birth weight. p_1: p value of the comparison between pre-pregnancy diagnosis group and pregnancy diagnosis group. p_2: p value of the comparison between pre-pregnancy diagnosis group and pregnancy diagnosis group A. p_3: p value of the comparison between pre-pregnancy diagnosis group and pregnancy diagnosis group B. p_4: p value of the comparison between pregnancy diagnosis groups A and B.

Table 2. — *Comparison of blood glucose control and pregnancy outcomes of PGDM pregnant women in the different groups.*

Therapy and Outcomes	Cases (n = 822)	PGDM groups			p_1	p_2	p_3	p_4
		PPD (n = 262)	PD (n =560)					
			A (n = 107)	B (n = 453)				
Insulin treatment					< 0.001	0.207	< 0.001	< 0.001
No	286	27	16	243				
Yes	536	235	91	210				
Term					0.460	0.823	0.422	0.731
Full-term	672	218	88	366				
Pre-term	150	44	19	87				
Cesarean					< 0.001	0.060	< 0.001	0.486
No	298	72	40	186				
Yes	524	190	67	267				
Macrosomia					0.535	0.801	0.513	0.835
No	752	242	98	412				
Yes	70	20	9	41				
NTP					0.826	0.897	0.828	0.986
No	544	172	71	301				
Yes	278	90	36	152				
Preeclampsia					0.854	0.682	0.938	0.704
No	752	239	99	414				
Yes	70	23	8	39				
HbA1c (%)		6.3 ± 1.1	6.4 ± 1.3	6.0 ± 1.3	0.091	0.263	0.005	0.002

PPD: pre-pregnancy diagnosis group; PD: pregnancy diagnosis group; NTP: newborns transferred to pediatrics; p_1: p value of the comparison between pre-pregnancy diagnosis group and pregnancy diagnosis group. p_2: p value of the comparison between pre-pregnancy diagnosis group and pregnancy diagnosis group A. p_3: p value of the comparison between pre-pregnancy diagnosis group and pregnancy diagnosis group B. p_4: p value of the comparison between pregnancy diagnosis groups A and B.

rate, the incidence of macrosomia, preeclampsia, and NTP in the two groups were not statistically significant (all $p > 0.05$, Table 2).

As shown in Table 2, the blood glucose control level of pregnant women in group A was significantly higher than that in group B, and the average HbA1c level had a significant difference ($p = 0.002$). The proportion of pregnant women using insulin treatment in group A was significantly higher than that in group B, and the difference was statistically significant ($p < 0.001$). The pre-term rate, cesarean delivery rate, the incidence of macrosomia, preeclampsia, and NTP in groups A and B were also respectively compared, and the difference was not statistically significant (all $p > 0.05$, Table 2).

Discussion

Pregnancy is a special stage of women's experience, and a variety of hormones secreted by the placenta during pregnancy lead to an increase of insulin resistance, which can cause the changes of maternal glucose metabolism, lipid metabolism, and protein metabolism [14, 15]. Insulin resistance is the central pathological process of metabolic syndrome and GDM [16, 17]. Accumulated studies have reported that both GDM and PGDM in pregnancy can increase the incidence of maternal and fetal complications, such as fetal macrosomia, neonatal hypoglycemia, perinatal mortality, and increased risk of cesarean delivery [1, 18-20]. PGDM includes both types 1 and 2 diabetes mellitus occurring prior to pregnancy, which is associated with an increased risk for maternal and fetal adverse outcomes than GDM [21, 22]. For instance, a study by Fong *et al.* demonstrated that PGDM was associated with significantly higher mortality when compa-

red to GDM [21]. In the Omani cohort, pregnant women with PGDM were also found at higher risk of developing obstetric and perinatal complications compared to GDM women [22]. Previous studies have shown that pre-pregnancy care for pregnant women with PGDM could improve the maternal and perinatal outcomes. For instance, Wahabi *et al.* demonstrated that pre-pregnancy care for women with pre-gestational type 1 or 2 diabetes mellitus was effective in improving rates of congenital malformations, perinatal mortality, and in reducing maternal HbA1c in the first trimester of pregnancy [23]. All these studies indicated the pivotal role of early screening and pre-pregnancy treatment of PGDM for maternal and perinatal outcomes.

In this study, among 822 pregnant women, 31.9% (262/822) pregnant women with PGDM were diagnosed before pregnancy, and 68.1% were diagnosed in pregnancy, of whom the rate of missed diagnosis of PGDM was 68.1%. The missed diagnosis rate of PGDM is consistent with the previous study by Yang *et al.* [7]. Even in developed countries with advanced medical technology and relatively complete regular physical examination system, such as the USA, among those with diabetes, the rate of undiagnosed diabetes was as high as 36.4% [24]. However, due to the incomplete periodic physical examination system in China, the rate of undiagnosed PGDM is more than 2/3 prior to pregnancy [25]. Due to the incidence of adverse pregnancy outcomes can be significantly reduced after blood glucose management before pregnancy, more strategies should be made to diagnose the PGDM.

To explore the effect of PGDM diagnosed at a different time on pregnancy outcome, the comparison among the pre-pregnancy diagnosis group, and pregnancy diagnosis groups A and B were analyzed. Firstly, the authors compared the pregnancy outcomes between pre-pregnancy diagnosis and pregnancy diagnosis groups. The average HbA1c level in pre-pregnancy diagnosis group was higher than that in pregnancy diagnosis group, but it had no statistically significant difference between the two groups. According to the results, the authors found that the proportion of insulin treatment and the rate of cesarean section were higher in pre-pregnancy diagnosis group than pregnancy diagnosis group, which had a significant difference. However, the rate of pre-term, macrosomia, newborns transfer to pediatrics, and preeclampsia showed no difference between the two groups. Further analysis revealed that the average HbA1c level in pregnancy diagnosis group A was higher than that in pre-pregnancy diagnosis group, but there was no significant difference between the two groups. Besides the average HbA1c level, the rate of insulin treatment, pre-term rate, cesarean delivery rate, the incidence of macrosomia, preeclampsia, and NTP were close to the pre-pregnancy diagnosis group. The reason might be that the pregnant women in the pregnancy diagnosis group A did not take good blood glucose control prior to pregnancy, and the risk of adverse pregnancy outcome was similar to that of in the pre-pregnancy diagnosis group.

The diagnosis of pregnancy diagnosis group B (PGDM pregnant women diagnosed at 24 weeks or after) was mainly based on the results of oral glucose tolerance test (OGTT). The results of the hyperglycemia and adverse pregnancy outcome study (HAPO) showed that center-to-center differences occurred in GDM frequency and relative diagnostic importance of fasting, one-, and two-hour glucose levels, for example, the proportion with only the two-hour value equal to or greater than threshold was just 6% in Bellflower but reached 29% in Hong Kong [26. 27]. The OGTT glucose metabolic is different in different regions or populations, whether the diagnosis of PGDM can be made by relying on OGTT two-hour blood glucose level remains to be further studied. The average level of HbA1c in pregnancy diagnosis group B was lower than those in pre-pregnancy diagnosis group and pregnancy diagnosis group A. At the same time, the proportion of pregnant women using insulin treatment was much lower in pregnancy group B than that of in pregnancy diagnosis group A, as well as pre-pregnancy diagnosis group. In addition, the rate of cesarean section was lower in pregnancy diagnosis group B than that in the pre-pregnancy diagnosis group. Taken together, there was a difference in pregnancy diagnosis group B when compared to the other two groups, and whether PGDM can be diagnosed according to the results of OGTT is still controversial. In considering the results of this study, the clinical data is limited, and more clinical parameters are needed to be involved in the further analyses. Furthermore, the postpartum follow-up data of PGDM pregnant women diagnosed at or later 24 weeks is needed to be analyzed in the further study.

In conclusion, the rate of undiagnosed PGDM was high, and PGDM was significantly associated with multiple adverse pregnancy outcomes. Fasting plasma glucose should be used as a screening test to identify PGDM at pre-pregnancy or first antenatal care. Using the abnormal value of two-hour plasma glucose after 24 gestational weeks as the only way to diagnose PGDM may not be suitable. The PGDM pregnant women who were diagnosed at or later 24 weeks were different from the PGDM pregnant women who were diagnosed at other times, whether the diagnosis of diabetes should be confirmed by a further postpartum review.

References

[1] Feig D.S., Hwee J., Shah B.R., Booth G.L., Bierman A.S., Lipscombe L.L.: "Trends in incidence of diabetes in pregnancy and serious perinatal outcomes: a large, population-based study in Ontario, Canada, 1996-2010". *Diabetes Care*, 2014, *37*, 1590.

[2] Jiang H., Wang X.: "Pregnancy outcomes in Chinese urban women at a very advanced maternal age". *Clin. Exp. Obstet. Gynecol.*, 2017, *44*, 56.

[3] Soytac Inancli I., Yayci E., Atacag T., Uncu M.: "Is maternal Vitamin

D associated with gestational diabetes mellitus in pregnant women in Cyprus?" *Clin. Exp. Obstet. Gynecol.*, 2016, *43*, 840.
[4] Siegel A.M., Tita A., Biggio J.R., Harper L.M.: "Evaluating gestational weight gain recommendations in pregestational diabetes". *Am. J. Obstet. Gynecol.*, 2015, *213*, 563 e1.
[5] Kanda E., Matsuda Y., Makino Y., Matsui H.: "Risk factors associated with altered fetal growth in patients with pregestational diabetes mellitus". *J. Matern. Fetal Neonatal Med*,. 2012, *25*, 1390.
[6] Bateman B.T., Bansil P., Hernandez-Diaz S., Mhyre J.M., Callaghan W.M., Kuklina E.V.: "Prevalence, trends, and outcomes of chronic hypertension: a nationwide sample of delivery admissions". *Am. J. Obstet. Gynecol*., 2012, *206*, 134 e1.
[7] Yang W., Lu J., Weng J., Jia W., Ji L., Xiao J., *et al.*: "Prevalence of diabetes among men and women in China". *N. Engl. J. Med.*, 2010, *362*, 1090.
[8] Xu Y., Wang L., He J., Bi Y., Li M., Wang T., *et al.*: "Prevalence and control of diabetes in Chinese adults". *JAMA*, 2013, *310*, 948.
[9] Chan J.C., Zhang Y., Ning G.: "Diabetes in China: a societal solution for a personal challenge". *Lancet Diabetes Endocrinol.*, 2014, *2*, 969.
[10] Yang W., Weng J.: "Early therapy for type 2 diabetes in China". *Lancet Diabetes Endocrinol.*, 2014, *2*, 992.
[11] Corrado F., Pintaudi B., D'Anna R., Santamaria A., Giunta L., Di Benedetto A.: "Perinatal outcome in a Caucasian population with gestational diabetes and preexisting diabetes first diagnosed in pregnancy". *Diabetes Metab*., 2016, *42*, 122.
[12] Yang H.X.: "Diagnostic criteria for gestational diabetes mellitus (WS 331-2011)". *Chin. Med. J. (Engl.)*, 2012, *125*, 1212.
[13] "Diagnosis and classification of diabetes mellitus". *Diabetes Care*, 2014, *37 Suppl 1*, S81.
[14] Dunietz G.L., Strutz K.L., Holzman C., Tian Y., Todem D., Bullen B.L., *et al.*: "Moderately elevated blood pressure during pregnancy and odds of hypertension later in life: the POUCHmoms longitudinal study". *BJOG*, 2017, *124*, 1606.
[15] Andolf E.G., Sydsjo G.C., Bladh M.K., Berg G., Sharma S.: "Hypertensive disorders in pregnancy and later dementia: a Swedish National Register Study". *Acta Obstet. Gynecol. Scand.*, 2017, *96*, 464.
[16] Tumurbaatar B., Poole A.T., Olson G., Makhlouf M., Sallam H.S., Thukuntla S., *et al.*: "Adipose tissue insulin resistance in gestational diabetes". *Metab. Syndr. Relat. Disord.*, 2017, *15*, 86.
[17] Li T., Chen K., Liu G., Huang L.P., Chen L., Wang Q.W., *et al.*: "Calorie restriction prevents the development of insulin resistance and impaired lipid metabolism in gestational diabetes offspring". *Pediatr Res.*, 2017, *81*, 663.
[18] Persson M., Fadl H.: "Perinatal outcome in relation to fetal sex in offspring to mothers with pre-gestational and gestational diabetes—a population-based study". *Diabet Med*, 2014, *31*, 1047.
[19] Macintosh M.C., Fleming K.M., Bailey J.A., Doyle P., Modder J., Acolet D., *et al.*: "Perinatal mortality and congenital anomalies in babies of women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland: population based study". *BMJ*, 2006, *333*, 177.
[20] Lin S.F., Kuo C.F., Chiou M.J., Chang S.H.: "Maternal and fetal outcomes of pregnant women with type 1 diabetes, a national population study". *Oncotarget*, 2017, *8*, 80679.
[21] Fong A., Serra A., Herrero T., Pan D., Ogunyemi D.: "Pre-gestational versus gestational diabetes: a population based study on clinical and demographic differences". *J. Diabetes Complications*, 2014, *28*, 29.
[22] Abu-Heija A.T., Al-Bash M., Mathew M.: "Gestational and Pregestational Diabetes Mellitus in Omani Women: Comparison of obstetric and perinatal outcomes". *Sultan Qaboos Univ. Med. J.*, 2015, *15*, e496.
[23] Wahabi H.A., Alzeidan R.A., Esmaeil S.A.: "Pre-pregnancy care for women with pre-gestational diabetes mellitus: a systematic review and meta-analysis". *BMC Public Health*, 2012, *12*, 792.
[24] Menke A., Casagrande S., Geiss L., Cowie C.C.: "Prevalence of and Trends in Diabetes Among Adults in the United States, 1988-2012". *JAMA*, 2015, *314*, 1021.
[25] Wei Y., Yang H., Zhu W., Hod M., Hadar E.: "Adverse pregnancy outcome among women with pre-gestational diabetes mellitus: a population-based multi-centric study in Beijing". *J. Matern. Fetal Neonatal Med.*, 2017, *30*, 2395.
[26] Sacks D.A., Hadden D.R., Maresh M., Deerochanawong C., Dyer A.R., Metzger B.E., *et al.*: "Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study". *Diabetes Care*, 2012, *35*, 526.
[27] Metzger B.E., Lowe L.P., Dyer A.R., Trimble E.R., Chaovarindr U., Coustan D.R., *et al.*: "Hyperglycemia and adverse pregnancy outcomes". *N. Engl. J. Med.*, 2008, *358*, 1991.

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