Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2020, 10, 1358-1369
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

Comparative Study on Clinical Characteristics and Outcomes of Overt Diabetes Mellitus and Gestational Diabetes Mellitus in Late Pregnancy

Rui Wang*, Suping Wu

Department of Clinical Nutrition, Beijing Anzhen Hospital, The Capital Medical University, Beijing, China
Email: *wangruiyyy@163.com

How to cite this paper: Wang, R. and Wu, S.P. (2020) Comparative Study on Clinical Characteristics and Outcomes of Overt Diabetes Mellitus and Gestational Diabetes Mellitus in Late Pregnancy. *Open Journal of Obstetrics and Gynecology*, **10**, 1358-1369.
https://doi.org/10.4236/ojog.2020.10100125

Received: August 27, 2020
Accepted: October 10, 2020
Published: October 13, 2020

Abstract

Background: With the rising prevalence in recent years, gestational diabetes mellitus has become one of the leading causes of maternal and child mortality and morbidity worldwide and has raised health concern. It is seriously detrimental to both the women and fetuses. However, there are limited evidences of two types of gestational diabetes mellitus on clinical characteristics and outcomes. Therefore, this study was aimed to explore the clinical characteristics and outcomes of patients with overt diabetes mellitus (ODM) and gestational diabetes mellitus (GDM) at the late pregnancy. **Methods:** From January 2015 to August 2016, totally 63 gestational diabetes mellitus from the Department of Clinical Nutrition in Beijing Anzhen Hospital were enrolled in the study. Patients were classified into two groups. 31 patients with gestational overt diabetes mellitus were grouped into ODM group and 32 patients with gestational diabetes mellitus were grouped into GDM group. Clinical characteristics and outcomes were compared between ODM and GDM. We collected records of the age, gestational week, family history, past history, pregnancy complications, insulin use, blood pressure, clinical nutrition indexes, blood pressure. Glycosylated hemoglobin (HbA1c), fasting blood glucose (FBG), total protein (TP), albumin (ALB), prealbumin (PALB), hemoglobin (HGB), urea nitrogen (BUN), serum creatinine (CREA), and dynamic blood glucose monitoring were measured. And we recorded the changes of blood glucose and the test data. We statistically analyzed the data of two groups. **Results:** In the ODM group, HbA1c, FBG, average blood glucose, two-hour postprandial blood glucose (2hPBG) after breakfast, 2hPBG after dinner, the number of hyperglycemic events and high blood glucose time ratio are significantly higher than those of GDM and two groups compared with statistical significance ($P < 0.05$). The number of patients treated with insulin (10/31) in ODM is significantly more than that in GDM (1/32) ($P < 0.05$). 45% (14/31)

of ODM have a family history of diabetes patients. The ratio is significantly higher than 13% (4/32) of GDM ($P < 0.05$). There was significant difference in urinary ketone positive rate between the two groups ($P < 0.05$), but there was no significant difference in urinary microalbumin abnormal rate between them ($P > 0.05$). The number of preeclampsia in ODM (8/31) is significantly higher than that of GDM ($P < 0.05$). The level of HGB in ODM is lower than that of GDM ($P < 0.05$). There was no difference in the pregnancy outcomes between the two groups. **Conclusion:** Late pregnancy women with ODM have obvious family history, higher HbA1c, higher FBG, higher glucose levels of two-hours after breakfast and dinner, higher average blood glucose, longer hypoglycemia time, higher probability of hyperglycemic events and greater opportunity to use insulin in the treatment of symptomatic patients, higher risk of preeclampsia, lower HGB level than GDM, while GDM has higher positive rate of urine ketone than ODM.

Keywords

Late Pregnancy, Gestational Diabetes Mellitus, Overt Diabetes Mellitus, Clinical Characteristics, Outcomes

1. Introduction

Gestational diabetes mellitus is defined as different degrees of abnormal glucose metabolism that occur or are recognized first during pregnancy. A global prevalence of 2% to 6% was estimated [1]. Gestational diabetes mellitus increases the risk of adverse events in pregnancy and jeopardizes long-term health of the mother and offspring [2]. Women with GDM are not only subjected to preeclampsia, gestational hypertension, polyhydramnios, premature rupture of membrane and caesarean section [3] [4], but also are at a higher risk of subsequent type 2 diabetes mellitus (T2DM) [5] and cardiovascular diseases [6] [7]. Babies born from mothers with GDM are prone to suffer from macrosomia, congenital deformities, hypoglycemia, respiratory distress syndrome and neonatal trauma [8]. Since 2010, the International Association of diabetes and pregnancy study group has divided gestational diabetes into two categories: overt diabetes mellitus (ODM) and gestational diabetes mellitus (GDM) [9]. ODM is defined as blood glucose ≥ 7.0 mmol/L or HbA1C ≥ 6.5% during the first prenatal examination. GDM is defined as 5.1 mmol/L ≤ FBG < 7.0 mmol/L at the time of the first pregnancy check-up and not diagnosed as ODM in the first 24 weeks of pregnancy, but meets the requirements of FBG ≥ 5.1 mmol/l, 1-hour PBG ≥ 10.0 mol/l or 2-hour PBG ≥ 8.5 mmol/l during the 75 g glucose tolerance test in 24 - 28 weeks of pregnancy. So far, there are few literatures comparing the clinical characteristics of these two types of patients. T. Sugiyama team had made a comparative analysis of the clinical outcomes of the two types, and found that pregestational body mass index was higher and gestational age at delivery was

earlier in overt diabetes than in gestational diabetes, glycated hemoglobin and glucose on 75-g oral glucose tolerance test and prevalence of retinopathy and pregnancy-induced hypertension were higher in overt diabetes than in gestational diabetes. They concluded that overt diabetes in pregnancy is significantly associated with maternal complications such as retinopathy and pregnancy-induced hypertension [10]. Meanwhile different nutritional interventions have been studied in the prevention of GDM. The Mediterranean diet or the Dietary Approaches to Stop Hypertension (DASH) and low glycaemic index diets were associated with decreases in seems to be effective in preventing GDM and other maternofoetal outcomes [11] [12]. A recent systematic review and meta-analysis analyzed different diet interventions used in GDM treatment as compared to standard diets on maternal glycaemic control and adverse events [13]. But there is still no agreement as to what the best dietary approach in the treatment of GDM is. Why? I think maybe because the research on clinical manifestations and outcomes in gestational diabetes is not deep enough, we can't reach a consensus on nutritional therapy. I think only if we have a thorough understanding of clinical characteristics such as nutritional indicators, dynamic changes of blood glucose etc., we can find a more targeted diet. So this study was carried out.

2. Materials and Methods

2.1. Materials

From January 2015 to August 2016, totally 63 gestational diabetes mellitus from the Department of Clinical Nutrition in Beijing Anzhen Hospital were enrolled in the study. The clinical records and data of the patients were obtained from the Department of Clinical Nutrition. According to diagnostic criteria of gestational diabetes mellitus, patients were classified into two groups. 31 patients with gestational overt diabetes mellitus were grouped into ODM group and 32 patients with gestational diabetes mellitus were grouped into GDM group. Inclusive criteria: 1) the diagnosis met the relevant diagnostic criteria of international organization for the study of gestational diabetes mellitus [14]; 2) those who had normal blood glucose before pregnancy; 3) those who had severe heart, lung, liver and kidney dysfunction, Cushing's syndrome, hyperthyroidism, pancreatitis and other diseases that may affect blood glucose were excluded; 4) those who did not use drugs affecting blood glucose metabolism.

2.2. Methods

The age, gestational week, family history, past history, pregnancy complications, insulin use, systolic and diastolic blood pressure were measured and recorded in ODM and GDM groups. At the same time, the fasting venous blood samples of the two groups were collected from the morning after admission, and the indexes of HbA1c, TP, ALB, PALB, HGB, BUN and CREA were detected. Morning urine, midday urine and bedtime urine were collected for three routine urine

tests. 24 h urine was collected for 24 h urine micro protein detection. The blood dynamic glucose of the two groups were detected by using the dynamic blood glucose monitoring system.FBG, average blood glucose, blood glucose fluctuation coefficient, hyperglycemia time ratio and hypoglycemia time ratio were recorded. According to the results of blood glucose monitoring, the number of hypoglycemia events, nighttime hypoglycemia events, daytime hypoglycemia events and hyperglycemia events were counted.

2.3. Statistical Analysis

All information was analyzed through the software Statistical Package for the Social Science (SPSS) version 23.0. Quantitative variables were presented through means and standard deviations, and qualitative variables were presented through absolute and relative frequencies. Once the normal distribution of the characteristics studied by the Kolmogorov-Smirnov test was confirmed, the T Test was applied to quantitative variables with normal distribution, and when the assumption of normality was rejected, the Mann Whitney nonparametric test was used. For qualitative variables, the Chi-square test (or Fisher's Exact test for frequencies less than 5) was applied.

3. Results

3.1. Comparison of General Conditions between the Two Groups

63 cases were grouped into two groups. 31 patients with gestational overt diabetes mellitus were grouped into ODM group and 32 patients with gestational diabetes mellitus were grouped into GDM group. In ODM group, the age was 32.16 ± 3.21 years old, gestational age was 31.77 ± 2.66 weeks, systolic blood pressure was 122.06 ± 10.24 mmHg, diastolic blood pressure was 73.90 ± 5.01 mmHg; in GDM group, the age was 30.56 ± 3.991 years old, gestational week was 31.50 ± 3.01 weeks, systolic blood pressure was 118.28 ± 11.03 mmHg, diastolic blood pressure was 72.19 ± 5.43 mmHg. There was no significant difference in basic data between the two groups ($P > 0.05$). See Table 1 for details.

3.2. Comparison of Blood Glucose Related Indicators between the Two Groups

HbA1c, FBG, average blood glucose, 2hPBG after breakfast, 2hPBG after dinner,

Table 1. Comparison of basic data between the two groups.

Indexes	ODM group	GDM group	P
Gestational weeks (week)	31.77 ± 2.66	31.50 ± 3.01	0.274
Age (year)	32.16 ± 3.21	30.56 ± 3.99	0.085
Systolic pressure (mmHg)	122.06 ± 10.24	118.28 ± 11.03	0.164
Diastolic pressure (mmHg)	73.90 ± 5.01	72.19 ± 5.43	0.198

number of hyperglycemic events and hyperglycemia time ratio in ODM group were significantly higher than in GDM group ($P < 0.05$). The number of patients using insulin in ODM group accounted for 32% (10/31), which was significantly higher than in GDM (1/32) ($P < 0.05$). The number of patients with family history of diabetes in ODM group accounted for 45% (14/31), which was significantly higher than in GDM group (4/32) ($P < 0.05$). There was no significant difference in effective blood glucose time, blood glucose fluctuation coefficient, total hypoglycemia events, night hypoglycemia events, daytime hypoglycemia events, hypoglycemia time ratio, and nighttime hypoglycemia segmented events between the two groups ($P > 0.05$). See Table 2 for details.

Table 2. Comparison of blood glucose related indexes in two groups.

Indexes	ODM group	GDM group	P
HbA1C (%)	5.99 ± 1.14	5.46 ± 0.53	0.019
Effective time (h)	67.89 ± 2.78	67.09 ± 3.06	0.279
Average blood glucose (mmol/L)	5.89 ± 0.96	5.28 ± 0.54	0.003
FBG (mmol/L)	5.29 ± 1.11	4.47 ± 0.49	<0.001
2hPBG after breakfast (mmol/L)	6.89 ± 1.49	5.95 ± 0.88	0.003
2hPBG after lunch (mmol/L)	6.51 ± 1.57	6.03 ± 1.06	0.162
2hPBG after dinner (mmol/L)	7.16 ± 1.57	6.33 ± 0.80	0.010
Blood glucose fluctuation coefficient (mmol/L)	1.33 ± 0.41	1.11 ± 0.32	0.120
High blood glucose time ratio (%)	14.29 ± 16.19	3.88 ± 5.01	<0.001
Hypoglycemia time ratio (%)	6.06 ± 8.59	7.94 ± 7.64	0.154
Number of high blood glucose events	3.06 ± 2.79	0.97 ± 1.09	<0.001
Number of hypoglycemic events	1.68 ± 1.16	2.13 ± 1.29	0.773
Number of nocturnal hypoglycemia events	1.16 ± 1.11	1.47 ± 1.17	0.810
Number of nocturnal hypoglycemia segment events (22 to 0 o'clock)	0.20 ± 0.50	0.17 ± 0.38	0.531
Number of nocturnal hypoglycemia segment events (0 to 3 o'clock)	0.36 ± 0.57	0.70 ± 0.70	0.129
Number of nocturnal hypoglycemia segment events (3 to 6 o'clock)	0.44 ± 0.65	0.50 ± 0.78	0.785
Number of hypoglycemic events during the day	0.52 ± 0.65	0.63 ± 0.96	0.154
Maximum blood glucose level (mmol/L)	9.40 ± 2.14	8.65 ± 1.62	0.125
Low blood glucose level (mmol/L)	3.34 ± 0.74	2.96 ± 0.75	0.057
Family history (positive number/total number) (%)	14/31 (45%)	4/32 (13%)	0.004
Insulin users (positive number/total number) (%)	10/31 (32%)	1/30 (3%)	0.002

3.3. Comparison of Nutrition Related Indexes between the Two Groups

HGB level in ODM group was lower than that in GDM group ($P < 0.05$). There was no significant difference in other nutrition related indexes between the two groups ($P > 0.05$). See Table 3 for details.

3.4, Comparison of Complications between the Two Groups

The positive rate of urinary ketone (14/32) in GDM group was higher than that in ODM group (5/31) ($P < 0.05$). There was no significant difference in 24-hour urinary microalbuminuria between the two groups ($P > 0.05$). The incidence of preeclampsia in ODM group (8/31) was significantly higher than that in GDM group ($P < 0.05$). See Table 4 for details.

3.5. Comparison of Pregnancy Outcomes

The comparison on the comparison of pregnancy outcomes of ODM and GDM groups was listed in Table 5. No significant differences were presented between two groups regarding the cesarean section (9/31 vs 7/32), premature infant (5/31 vs 4/32) and postpartum hemorrhage (5/31 vs 4/32), as well as abnormal birth process (3/31 vs 1/32), fetal growth restriction (2/31 vs 2/32), malformation (0/31 vs 1/32), giant (2/31 vs 1/32), neonatal hypoglycemia (5/31 vs 3/32), pathologic jaundice (5/31 vs 2/31), neonatal asphyxia (5/31 vs 3/32) and neonatal pneumonia (3/31 vs 3/32) ($P > 0.05$). See Table 5 for details.

Table 3. Comparison of nutritional indexes in two groups.

Indexes	ODM group	GDM group	P
TP (g/L)	62.55 ± 5.60	61.50 ± 4.65	0.423
ALB (g/L)	35.62 ± 4.39	34.33 ± 3.09	0181
PALB (g/L)	0.20 ± 0.03	0.21 ± 0.03	0.141
BUN (mmol/L)	3.53 ± 1.00	3.43 ± 1.89	0.734
CREA (umol/L)	49.65 ± 10.76	49.49 ± 9.24	0.950
HGB (g/L)	112.42 ± 19.19	120.09 ± 9.78	0.026

TP: Total protein; ALB: Albumin; PALB: Prealbumin; BUN: Urea nitrogen; CREA: Serum creatinine; HGB: Hemoglobin.

Table 4. Comparison of complications in two groups.

Indexes	ODM group	GDM group	P
Urine ketone (positive number/total number) (%)	5/31 (16)	15/32 (47)	0.009
24 hours urinary microalbumin	8/31 (26)	5/32 (16)	0.318
Preeclampsia	8/31 (26)	1/32 (3)	0.010

Table 5. Comparison of pregnancy outcomes in two groups.

Indexes	ODM group	GDM group	P
Cesarean section (positive number/total number) (%)	9/31 (29)	7/32 (22)	0.514
Premature infant	5/31 (16)	4/32 (13)	0.681
Postpartum hemorrhage	5/31 (16)	4/32 (13)	0.681
Abnormal birth process	3/31 (10%)	1/32 (3)	0.286
Fetal growth restriction	2/31 (6%)	2/32 (6)	0.974
Malformation	0/31 (0)	1/32 (3)	0.321
Giant	2/31 (6)	1/32 (3)	0.535
Neonatal hypoglycemia	5/31 (16)	3/32 (9)	0.421
Pathologic jaundice	5/31 (16)	2/32 (6)	0.212
Neonatal asphyxia	5/31 (16)	3/32 (9)	0.449
Neonatal pneumonia	3/31 (9)	3/32 (9)	0.967

4. Discussion

In recent years, with the deepening of medical research on gestational diabetes mellitus, it was found that premature birth, excessive amniotic fluid, postpartum hemorrhage, premature rupture of membranes, fetal macrosomia, neonatal hypoglycemia, cesarean section rate are very high in pregnant women with gestational diabetes mellitus [15], and the probability of postpartum evolution into type 2 diabetes mellitus is high [16]. Gunderson EP reported that 1035 cases of gestational diabetes mellitus were followed up for 2 years 11.8% became type 2 diabetes after 2 years [17]. Therefore, more and more medical workers paid attention to gestational diabetes mellitus. The International Diabetes Association pregnancy research group, the British National Institute of health and clinical optimization, and the Chinese Diabetes Association have developed guidelines for the management of gestational diabetes mellitus and its complications, which are gradually improved and revised with the progress of their research. Gestational diabetes mellitus can be divided into two types: gestational diabetes mellitus (ODM) and gestational diabetes mellitus (GDM). In China, the incidence rate of diabetes in pregnancy is about 1% - 5%. However, there are few reports on the detailed comparison of clinical characteristics between the two types. In this study, we compared and analyzed ODM and GDM from the aspects of blood glucose, nutrition, complications, genetic factors, whether insulin was used in treatment and so on.

In terms of blood glucose, this study showed that HbA1c, FBG, average blood glucose, 2hPBG after breakfast, 2hPBG after dinner, number of hyperglycemia events and hyperglycemia time ratio in ODM group were significantly higher than those in GDM patients. But there was no significant difference between the

two groups in blood glucose fluctuation coefficient. In short, except 2hPBG after lunch, the blood glucose level of ODM was higher than that of GDM in other points all day. In this study, the number of patients using insulin in ODM group accounted for 32%, and only one in GDM group used insulin treatment. The difference was significant. It showed that in addition to diet and exercise therapy patients with ODM had a greater chance to choose insulin therapy and most GDM might receive the effect of diet and exercise therapy. Other studies also showed that compared with those without family history of diabetes mellitus, the risk of GDM with family history increased by 4.91 times. The incidence of GDM in pregnant women with diabetes in first and second degree families was significantly higher than without family history, suggesting that GMD may be related to heredity. At present, it is confirmed that the rs7903146, rs13266634, rs2283228, rs5210 and rs179881 SNPs were found to be positively associated with GDM when calculated for genotype and allele frequencies [18]. Weaam Gouda *et al.* reported that The TT genotype of The SNPs in IGF-1 gene was associated with an elevated risk of GDM compared to controls [19]. These evidences indicated that genetic genes played an important role in the pathogenesis of GDM [20]. This study showed that 12% (4/32) of GDM has family diabetes mellitus history, which may be related to genetic factors. 48% of the GDM had a family history of diabetes mellitus. It was much higher than in GDM, which further indicates that ODM patients have a higher inheritance tendency than GDM patients. This is consistent with current reports.

There was no difference in pregnancy outcome between the two groups, which may be related to the synergistic effects of individualized diet and exercise therapy and insulin use. This study had some limitations. We did not consider the impact of diet and exercise on the clinical manifestations of both types of gestational diabetes mellitus. We will do further research.

Nutrition: 1) Several experiments have confirmed the correlation between HGB and insulin. The level of HGB is relatively high, and the risk of insulin resistance is high [21]. It has been proved that frequent blood donation and reduced HGB can reduce postprandial hyperinsulinemia in healthy volunteers, improve insulin sensitivity, and constitute a protective factor for the development of type 2 diabetes [22]. Other studies have shown that HGB in GDM patients is significantly higher than in non GDM patients [23]. We have known that insulin resistance (IR) is one of the basic mechanisms of diabetes and plays an important role in the pathogenesis of gestational hyperglycemia. Patients with gestational hyperglycemia already have IR before pregnancy, and the physiological IR during pregnancy makes the IR state show particularly obvious [24]. So is there any difference in HGB level in the case of common insulin resistance in ODM and GDM? This study confirmed that the level of HGB in GDM group was higher than that in ODM group, and the difference was statistically significant. This result reflected that there may be differences in insulin level and insulin resistance between these two types of GDM patients, and the specific me-

chanism needed further study. Whether it was related to iron metabolism needed further verification. However, at least the present experiment might suggest that the intake of iron rich food should be increased in the diet of ODM. 2) There was no significant difference in TP, ALB and PALB between ODM and GDM in this experiment, indicating that ODM protein nutrition metabolism in late pregnancy was basically equivalent to GDM.

In our study, the incidence of preeclampsia in ODM group was higher than that in GDM group. Some research also showed that the incidence rate of ODM complications was higher than that of GDM, such as retinopathy, gestational hypertension and so on [1]. It seemed that ODM was more harmful than GDM and had a greater impact on pregnancy outcome, which should be paid attention to. The detection rate of ketosis was higher than that of only detecting morning urine. Although there was no difference in hypoglycemia time ratio and hypoglycemic events between the two groups, the incidence of ketosis in ODM was lower than that in GDM. This result may be related to the higher hyperglycemia time ratio and the higher mean blood glucose value of ODM than GDM. Therefore, ODM showed better tolerance to hypoglycemia, but it was less prone to produce ketosis. Thus, it seemed that for patients with gestational hyperglycemia, especially GDM patients, clinical nutritional diet and exercise therapy should not only pay attention to whether the blood glucose value exceeds the standard, but also prevent the occurrence of ketosis. Our goal was not only to reduce hyperglycemia, but also to reduce ketosis. We should ensure that the blood sugar could reach the standard, but not too low. At the same time, we should increase the detection times of urine ketone so as to better prevent the occurrence of ketosis. This undoubtedly required the nutritionists to provide more accurate diet standards for GDM patients, so as to ensure adequate carbohydrate and total calorie intake.

After the more stringent new standard of gestational diabetes was proposed, the detection rate of patients with gestational diabetes increased significantly, which put forward new challenges for Clinical Nutrition Department and Obstetrics and Gynecology Department of each hospital. In order to provide patients with more individualized treatment such as diet and exercise therapy, we should have a deeper understanding of the clinical characteristics and outcomes of the two types of diabetes. We should also deeply understand its pathogenesis, so as to help patients control blood glucose reasonably and effectively. Only in this way can we finally reduce the risk of mother and child and ensure the safety of mother and child.

5. Conclusion

Through our research, we concluded that late pregnancy ODM had obvious family history, higher HbA1c, higher FBG, higher 2hPBG after breakfast and dinner, higher average blood glucose, longer hypoglycemia time, higher probability of hyperglycemic events and greater opportunity to use insulin in the

treatment of symptomatic patients, lower HGB level than GDM, while GDM had higher positive rate of urine ketone than ODM. Therefore, we could pay attention to the classification of gestational diabetes mellitus in individualized treatment of gestational diabetes mellitus, which might give us some guidance. For example, we should pay more attention to the control of blood glucose level for ODM patients, and more attention should be paid to the recurrent ketosis caused by substandard carbohydrate intake for GDM patients. Food ratio of each meal of ODM was different from GDM in order to better control hyperglycemia, especially breakfast and dinner. In view of our single center experiment, we need further experiments to prove this inference.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Groof, Z., Garashi, G., Husain, H., Owayed, S., AlBader, S., Mouhsen, H., Mohammad, A. and Ziyab, A.H. (2019) Prevalence, Risk Factors, and Fetomaternal Outcomes of Gestational Diabetes Mellitus in Kuwait: A Cross-Sectional Study. *Journal of Diabetes Research*, **2019**, Article ID: 9136250. https://doi.org/10.1155/2019/9136250

[2] Wendland, E.M., Torloni, M.R., Falavigna, M., Trujillo, J., Dode, M.A., Campos, M.A., Duncan, B.B. and Schmidt, M.I. (2012) Gestational Diabetes and Pregnancy Outcomes—A Systematic Review of the World Health Organization (WHO) and the International Association of Diabetes in Pregnancy Study Groups (IADPSG) Diagnostic Criteria. *BMC Pregnancy Childbirth*, **12**, Article No. 23. https://doi.org/10.1186/1471-2393-12-23

[3] McIntyre, H.D., Catalano, P., Zhang, C.L., Desoye, G., Mathiesen, E.R. and Damm, P. (2019) Gestational Diabetes Mellitus. *Nature Reviews Disease Primers*, **5**, Article No. 47. https://doi.org/10.1038/s41572-019-0098-8

[4] Najafi, L., Abedini, A., Kadivar, M., Khajavi, A., Bordbar, A., Noohi, A.H., Mashak, B., Hashemnejad, M., Khamseh, M.E. and Malek, M. (2019) Gestational Diabetes Mellitus: The Correlation between Umbilical Coiling Index, and Intrapartum as Well as Neonatal Outcomes. *Journal of Diabetes & Metabolic Disorders*, **18**, 51-57. https://doi.org/10.1007/s40200-019-00389-z

[5] Moon, J.H., Kwak, S.H. and Jang, H.C. (2017) Prevention of Type 2 Diabetes Mellitus in Women with Previous Gestational Diabetes Mellitus. *The Korean Journal of Internal Medicine*, **32**, 26-41. https://doi.org/10.3904/kjim.2016.203

[6] Kramer, C.K., Campbell, S. and Retnakaran, R. (2019) Gestational Diabetes and the Risk of Cardiovascular Disease in Women: A Systematic Review and Meta-Analysis. *Diabetologia*, **62**, 905-914. https://doi.org/10.1007/s00125-019-4840-2

[7] Shostrom, D.C.V., Sun, Y., Oleson, J.J., Snetselaa, L.G. and Bao, W. (2017) History of Gestational Diabetes Mellitus in Relation to Cardiovascular Disease and Cardiovascular Risk Factors in US Women. *Frontiers in Endocrinology*, **8**, 144. https://doi.org/10.3389/fendo.2017.00144

[8] Duong, V., Davis, B. and Falhammar, H. (2015) Pregnancy and Neonatal Outcomes in Indigenous Australians with Diabetes in Pregnancy. *World Journal of Diabetes*,

6, 880-888. https://doi.org/10.4239/wjd.v6.i6.880

[9] Frigeri, H.R., Martins, L.T., Auwerter, N.C., *et al.* (2014) The Polymorphism rs2268574 in Glucokinase Gene Is Associated with Gestational Diabetes Mellitus. *Clinical Biochemistry*, **4**, 346-348.

[10] Sugiyama, T., Saitoa, M., Nishigori, H., *et al.* (2014) Comparison of Pregnancy Outcomes between Women with Gestational Diabetes and Overt Diabetes First Diagnosed in Pregnancy: A Retrospective Multi-Institutional Study in Japan. *Diabetes Research and Clinical Practice*, **103**, 20-25. https://doi.org/10.1016/j.diabres.2013.10.020

[11] Assaf-Balut, C., *et al.* (2020) Detection, Treatment and Prevention Programs for Gestational Diabetes Mellitus: The St Carlos Experience. *Endocrinología*, *Diabetes y Nutrición*, **67**, 342-350. https://doi.org/10.1016/j.endinu.2019.06.007

[12] Assaf-Balut, C., Garcia de la Torre, N., Durán, A., *et al.* (2018) Medical Nutrition Therapy for Gestational Diabetes Mellitus Based on Mediterranean Diet Principles: A Subanalysis of the St Carlos GDM Prevention Study. *BMJ Open Diabetes Res Care*, **6**, e000550. https://doi.org/10.1136/bmjdrc-2018-000550

[13] Yamamoto, J.M., Kellett, J.E., Balsells, M., *et al.* (2018) Gestational Diabetes Mellitus and Diet: A Systematic Review and Meta-Analysis of Randomized Controlled Trials Examining the Impact of Modified Dietary Interventions on Maternal Glucose Control and Neonatal Birth Weight. *Diabetes Care*, **41**, 1346-1361. https://doi.org/10.2337/dc18-0102

[14] Tang, I.P., Shashinder, S., Kuljit, S., *et al.* (2007) Outcome of patients Presenting with Preauricular Sinus in a Tertiary Centre—A Five Year Experience. *Medical Journal of Malaysia*, **62**, 53-55.

[15] Muche A.A., Olayemi, O.O. and Get, Y.K. 2020 () Gestational Diabetes Mellitus Increased the Risk of Adverse Neonatal Outcomes: A Prospective Cohort Study in Northwest Ethiopia. *Midwifery*, **87**, Article ID: 102713. https://doi.org/10.1016/j.midw.2020.102713

[16] Parrettini, S., *et al.* (2020) Gestational Diabetes: A Link between Ogtt, Maternal-Fetal Outcomes and Maternal Glucose Tolerance after Childbirth. *Nutrition, Metabolism and Cardiovascular Diseases*.

[17] Gunderson, E.P., Hurston, S.R., Ning, X., *et al.* (2015) Lactation and Progression to Type 2 Diabetes Mellitus after Gestational Diabetes Mellitus: A Prospective Cohort Study. *Annals of Internal Medicine*, **163**, 889-898. https://doi.org/10.7326/M15-0807

[18] Khan, I.A., Jahan, P., Hasan, Q. and Rao, P. (2019) Genetic confirmation of T2DM Meta-Analysis Variants Studied in Gestational Diabetes Mellitus in an Indian Population. *Diabetes and Metabolic Syndrome Clinical Research and Reviews*, **13**, 688-694. https://doi.org/10.1016/j.dsx.2018.11.035

[19] Gouda, W., Mageed, L., Azmy, O., Okasha, A., Shaker, Y. and Ashour, E. (2019) Association of Genetic Variants in IGF-1 Gene with Susceptibility to Gestational and Type 2 Diabetes Mellitus. *Meta Gene*, **21**, Article ID: 100588. https://doi.org/10.1016/j.mgene.2019.100588

[20] Wei, H.X. (2016) Pathogenesis and Treatment Progress of Gestational Diabetes Mellitus. *World Latest Medical Information Digest*, **16**, 65-69.

[21] Fu, S.M., Li, F.F., Zhou, J.G. and Liu, Z.P. (2016) The Relationship between Body Iron Status, Iron Intake and Gestational Diabetes: A Systematic Review and Meta-Analysis. *Medicine*, **95**, 2383-2390.

[22] Ascherio, A., Rimm, E.B., Giovannucci, E., *et al.* (2001) Blood Donations and Risk

of Coronary Heart Disease in Men. *Circulation*, **103**, 52-57. https://doi.org/10.1161/01.CIR.103.1.52

[23] Afkhami-Ardekani, M. and Maryam, R. (2009) Iron Status in Women with and without Gestational Diabetes Mellitus. *Journal of Diabetes and Its Complications*, **23**, 194-198. https://doi.org/10.1016/j.jdiacomp.2007.11.006

[24] Jung Jung, E., Jung, E.S., Min, S.Y., *et al.* (2012) *Fibroblast Growth Factor Receptor* 2 Gene Amplification Status and Its Clinicopathologic Significance in Gastric Carcinoma. *Human Pathology*, **43**, 1559-1566. https://doi.org/10.1016/j.humpath.2011.12.002