Austin Journal of Clinical Immunology

Open Access

Austin Publishing Group

Original Article

High Free T3 Levels in the Second Trimester are Correlated with the Control of Gestational Diabetes Mellitus

Dunjuan Shen[1]; Lian Yang[2]; Mingyi Zhang[3]; Cuilan Zhang[1*]; Xiaoyan Wang[3*]

[1]Department of Obstetrics and Gynecology, Nanjing Jiangning Hospital, The Affiliated Jiangning Hospital of Nanjing Medical University, Nanjing, Jiangsu, 211100, China

[2]Department of Medical Imaging, Nanjing Jiangning Hospital, The Affiliated Jiangning Hospital of Nanjing Medical University, Nanjing, Jiangsu, 211100, China

[3]Department of Clinical Laboratory, Nanjing Jiangning Hospital, The Affiliated Jiangning Hospital of Nanjing Medical University, Nanjing, Jiangsu, 211100, China

***Corresponding author: Xiaoyan Wang; Cuilan Zhang**
Department of Clinical Laboratory, Nanjing Jiangning Hospital, The Affiliated Jiangning Hospital with Nanjing Medical University, Nanjing, Jiangsu, 211100, China.
Department of Obstetrics and Gynecology, Nanjing Jiangning Hospital, The Affiliated Jiangning Hospital with Nanjing Medical University,
Nanjing, Jiangsu, 211100, China.
Email: joyisme12@njmu.edu.cn; zcl591@126.com

Received: March 07, 2023
Accepted: April 27, 2023
Published: May 04, 2023

Abstract

Gestational Diabetes Mellitus (GDM) and abnormal thyroid function are two common endocrine disorders occurring during pregnancy. In this study, we evaluated the correlation between the levels of different thyroid hormones and blood glucose control in pregnant women with diet-controlled GDM. Mid-pregnancy serum samples were obtained from 439 participants with GDM controlled by diet for analyses of thyroid function. A 2-h 75-g oral glucose tolerance test was used to evaluate the effect of blood glucose controlled by diet. According to blood glucose levels before and 2h after a meal, mothers were grouped into GDM-A1 (≤5.3mmol/L, ≤6.7mmol/L, respectively) and GDM-A2 (>5.3 mmol, >6.7mmol/L, respectively) and these groups were compared to the associated thyroid levels using multivariate logistic regression analysis. Our results show that fT3 was positively associated with GDM-A2. The adjusted odds ratio (95% confidence interval) comparing the highest and lowest fT3 quartile was 3.12 (1.66, 15.87) at the second trimester. Neither TSH nor fT4 was significantly associated with GDM-A2. Higher FT3 levels during the second trimester of pregnancy are a risk for GDM-A2 incidence. This provides new ideas for the control of GDM.

Keywords: Blood glucose self-monitoring; Diet; Gestational diabetes mellitus; Second pregnancy trimester; Thyroxine; Triiodonine

Introduction

Gestational Diabetes Mellitus (GDM) and abnormal thyroid function are two common endocrine disorders occurring during pregnancy. During pregnancy, the size of the pregnant woman's thyroid increases by 10-40%, and the production of thyroid hormone increases by approximately 50% [1]. However, pregnant women with GDM have a higher incidence of thyroid disease than healthy individuals [2,3]. Insulin resistance and changes in carbohydrate metabolism are related to abnormal thyroid function [4,5]. Blood glucose levels during pregnancy are affected by various physiological hormones, which in turn are affected by thyroid hormones [6]. Therefore, abnormal thyroid hormones during pregnancy increase the risk of GDM [7-10].

GDM can be controlled by diet or insulin. Poor blood glucose control in women with GDM is also associated with poor neonatal prognosis and perinatal outcome [11,12]. Women with GDM with good glycemic control do not have increased risks of adverse maternal or neonatal outcomes [13,14]. Therefore, the effect of GDM control is particularly important. However, the effect of abnormal thyroid function on the control of GDM remains unknown.

In this study, we evaluated the correlation between the levels of different thyroid hormones (free triiodothyronine [fT3], free thyroxin [fT4], and Thyroid-Stimulating Hormone [TSH])

Citation: Shen D, Yang L, Zhang M, Zhang C, Wang X. High Free T3 Levels in the Second Trimester are correlated with the Control of Gestational Diabetes Mellitus. Austin J Clin Immunol. 2023; 9(1): 1054.

with the control of blood glucose in pregnant women with GDM that was controlled by diet.

Materials and Methods

Study Population and Data Collection

This study was approved by the Ethics Committee of the Jiangning Hospital, Nanjing, Jiangsu Province. This study was performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each woman with GDM at screening, and the patients agreed that their clinical data would be used for research purposes. This is a retrospective study including women with GDM at their second trimester antenatal screening and who planned to deliver at the Nanjing Jiangning Hospital from January 2018 to December 2019. Patients meeting the following criteria were included: 1) a single pregnancy; 2) complete data of a 2-h 75-g Oral Glucose Tolerance Test (OGTT) until deliver; and 3) delivery in the Nanjing Jiangning Hospital. Patients meeting the following criteria were excluded: 1) Diabetes before pregnancy; 2) Polycystic Ovary Syndrome (PCOS); 3) Personal history of thyroid disease; 4) Goiter; 5) Taking hormone drugs affecting thyroid function before or during pregnancy; 6) Multiple pregnancy; or 7) Incomplete medical data.

The Medical data of patients were obtained from databases. Approximately 717 pregnant women diagnosed with GDM in a second trimester antenatal screening were initially included in this study, and the following patients were excluded: 5 patients with diabetes history, 11 with history of thyroid disease, 6 with a history of thyroid disease, 12 taking drugs affecting thyroid function, 4 cases of twins, 3 with PCOS, 82 without OGTT results, and 111 with an incomplete medical record. Ultimately, 439 GDM women were included. The participants were followed up until delivery. The characteristics of the study population are shown in a flow chart in Figure 1.

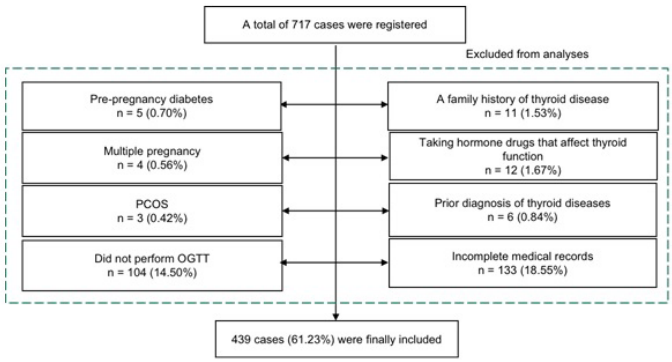

Figure 1: The characteristics of the study population are shown in a flow chart.

Thyroid Hormone Level Test

At the second antenatal visit (gestational age: 24-28 weeks), maternal serum samples were collected in 10-ml vacutainer tubes, centrifuged with 2000rpm for 10 minutes and stored in aliquots at –80°C until analyzed. Utilizing the electrochemiluminescence immunoassay method, levels of plasma TSH (mIU/L), fT3 (pmol/L), and fT4 (ng/dL) were measured with Roche reagents (Roche Diagnostics, Indianapolis, IN) on the Roche Cobas e602 analyzer. All assays were performed according to manufacturer's specifications.

Classification of GDM

Pregnant women diagnosed with GDM controlled by diet according to the International Federation of Gynecology and Obstetrics and American Diabetes Association criteria [15,16]. Women with blood glucose levels ≤5.3 and ≤6.7mmol/L before and 2h after a meal, respectively, were defined as GDM-A1 with well-controlled blood sugar. Patients with pre-meal blood glucose levels >5.3mmol/L or 2-h postprandial blood glucose levels >6.7 mmol/L were classified as GDM-A2 with poor blood glucose control. These blood glucose levels were evaluated by a 2-h 75-g oral glucose tolerance test.

Statistical Analysis

All statistical analyses were performed using SAS software (SAS Institute Inc., Cary, NC). A two-tailed Student's *t*-test analysis and a Pearson's χ^2 test of variance were used to evaluate the statistical significance of the measurement data. The relationship between thyroid hormone levels and GDM control was evaluated with Multivariate logistic regression. Odds Ratios (ORs) and 95% confidence intervals (95% CIs) are used to represent the results. Differences were considered to be statistically significant at P values <0.05.

Results

Clinical Characteristics of the Participants

The incidence of GDM-A2 tended to increase with age among the participants. The incidence of GDM also increased with increasing pre-pregnancy Body Mass Index (BMI). There were statistically significant differences in fetal weight and Fasting blood glucose (Fbg) (Table 1).

Table 1: Comparison of the clinical characteristics among women with GDM-A1 and GDM-A2.

	A1(%)	A2(%)	P
Age(years)			0.275
<25	25(8.48)	18(12.50)	
25–29	123(41.69)	50(34.72)	
30–34	89(30.17)	41(28.47)	
≥35	58(19.66)	35(24.31)	
Pre-pregnancy BMI(kg/m^2)			0.019
<18.5	24(8.13)	7(4.86)	
18.5–23.9	190(64.41)	79(54.86)	
≥24	81(27.46)	58(40.28)	
Pregnancy times			0.857
1	93(31.53)	42(29.17)	
2	90(30.51)	44(30.56)	
≥3	112(37.97)	58(40.28)	
Parity			0.509
1	142(48.14)	61(42.36)	
2	150(50.85)	81(56.25)	
3	3(1.02)	2(1.39)	
Delivery method			0.226
Vaginal delivery	154(52.20)	84(58.33)	
Cesarean section	141(47.80)	60(41.67)	
Gestational week(weeks)			0.483
<37	12(4.07)	8(5.56)	
37–42	283(95.93)	136(94.44)	
Fetal sex			0.405
Male	156(52.88)	68(47.22)	
Female	139(47.12)	76(52.78)	
Birth weight(kg)			
<2500	3(1.02)	3(2.08)	0.001*
2500–4000	271(91.86)	115(79.86)	
>4000	21(7.12)	26(18.06)	
Fbg(mmol/L)			0.002*
<5.10	154(52.20)	52(36.11)	
≥5.10	141(47.80)	92(63.89)	
1-h Glu(mmol/L)			
<10.0	188(63.73)	92(63.89)	0.791
≥10.0	107(36.27)	52(36.11)	
2-h Glu(mmol/L)			0.63
<8.5	169(57.29)	79(54.86)	
≥8.5	126(42.71)	65(45.14)	

BMI: Body Mass Index; Fbg: Fasting Blood Glucose; 1-h Glu: 1-h Postprandial Glucose Level; 2-h Glu: 2-h Postprandial Glucose.

Thyroid Hormone Levels in the Second Trimester in Women with GDM-A1 and GDM-A2

The levels of fT3 in mid-pregnancy were significantly higher in women with GDM-A2 than in women with GDM-A1 (P<0.0001). The difference in TSH and fT4 levels was not significantly different between the groups (Table 2).

Correlation Analysis between Different Thyroid Hormone Levels and the Risk of GDM-A2 in Mid-Pregnancy

We used a logistic regression analysis to investigate whether the levels thyroid hormone in mid-pregnancy affected the risk of GDM-A2 as shown in Table 3. The results showed that before adjusting for age, BMI, and delivery method, a fT3 level >3.89 pmol/L increased the risk of GDM-A2. After adjustment, using an fT3 level between 4.29 and 4.63pmol/L as a reference, we found that higher fT3 levels were associated with a increased risk of GDM-A2 (Table 3).

Relationship between GDM-A2 Clinical Parameters and fT3 and fT4 Levels

In patients with GDM-A2, fT3 and fT4 levels were associated with age. The fT3 level decreased with increasing age, while the fT4 level increased with increasing fasting blood glucose levels (≥5.1mmol/L) in the second trimester (Table 4).

Table 2: Comparison of thyroid hormone level in second trimester between women with GDM-A1 and GDM-A2.

	A1(n=295)	A2(n=144)	P
fT3, pmol/L	4.22(3.81, 4.54)	4.42(4.01, 4.74)	0.001
fT4, pmol/L	12.99(11.84, 1 4.93)	12.82(11.45,14.54)	0.26
TSH, mIU/L	1.85(1.39, 2.70)	1.99(1.38,2.73)	0.435

fT3: free T3; fT4: free T4; TSH: Thyroid-stimulating hormone.Data are presented as median(25th and 75th percentile).

Table 3: Adjusted odds ratio(95% confidence interval) for GDM-A2 according to quartiles of thyroid markers at gestational weeks 24-28.

	A1(n)	A2(n)	Crude model	P	Multivariable* model	P
fT3, pmol/L						
2.86–3.88	86	26	Ref		Ref	
3.89–4.28	74	34	1.52(1.17,2.06)	0.008	1.61(0.86,3.01)	0.139
4.29–4.63	73	35	1.60(1.19,2.17)	0.002	1.73(0.93,3.24)	0.086
4.64–6.61	62	49	2.61(1.95,3.46)	0	3.12(1.66,5.87)	0
P for trend				0		0.005
fT4, pmol/L						
7.44–11.70	66	41	Ref			
11.71–12.98	80	33	0.66(0.38,1.17)	0.154	0.55(0.30,1.01)	0.053
12.99–14.57	72	38	0.85(0.49,1.49)	0.564	0.69(0.38,1.24)	0.211
14.58–20.72	77	32	0.67(0.38,1.18)	0.165	0.45(0.24,0.84)	0.12
P for trend				0.413		0.072
TSH, mIU/L						
0.015–1.39	74	37	Ref		Ref	
1.40–1.91	78	32	0.82(0.46,1.45)	0.671	0.88(0.48,1.60)	0.082
1.92–2.69	69	39	1.13(0.65,1.97)	0.528	1.21(0.67,2.17)	0.158
2.70–10.39	74	36	0.97(0.56,1,71)	0.913	0.97(0.97,1.75)	0.63
P for trend				0.745		0.756

fT3: free T3; fT4: free T4; TSH: Thyroid-stimulating hormone.
*Adjusted for maternal age(years), pre-pregnancy body mass index.

Discussion

In this study, we provide evidence that thyroid function in the second trimester of pregnancy may be an indicator for assessing GDM control. An increased FT3 level was associated with a risk of poor GDM control, even after adjusting for potential confounders, such as pre-pregnancy BMI. Pre-pregnancy BMI and fasting blood glucose levels in the second trimester also correlated with the control of GDM. The birth weight was greater in patients with poor control of GDM than in patients with good control of GDM. In patients with GDM-A2, the fT3 and fT4 levels were associated with age. The fT3 level decreased with an increase in age. The fT4 level increased with an increased fasting blood glucose level(≥5.1mmol/L) in the second trimester.

BMI is an independent risk factor for GDM [17]. Obesity increases the risk of GDM and pre-eclampsia during pregnancy and increases the risk of metabolic syndrome in later life, strengthening the importance of weight control in women of childbearing age [18,19]. The risk of GDM is positively correlated with central obesity in pregnant women [20]. Obesity and obesity-related gene polymorphisms are associated with the risk of GDM, thus providing clues to study the mechanism of GDM [21]. The epidemiological association between GDM and dyslipidemia is caused by obesity in pregnant women, women with GDM are more likely to be obese, and the OR of dyslipidemia in women with obesity alone or with GDM only was not increased [22].

Previous studies mostly investigated the relationship between thyroid function in early pregnancy and the onset of GDM [10,23]. Among most pregnant women with GDM, the condition can be controlled by daily diet, and the condition is poorly controlled among some [15,16]. Poorly controlled GDM is more likely to have adverse neonatal outcomes [24]. In this study, the birth weight >4200kg of women with GDM-A2 was significantly more than that of fetus of women with GDM-A1. Low fT4 levels in the second trimester are related to the pathological process of GDM, but the role of fT3 in GDM is controversial. Some studies have indicated that low fT3 levels are related to GDM, while others consider that high fT3 levels are related to GDM [7,8,25]. In this study, high FT3 levels are correlated with the control of GDM, but FT4 not. Decreased free thyroid hormone levels in the normal range are associated with high glucose and insulin resistance [26]. In the present study, poor GDM control was associated with elevated fT3 levels, and the relationship between blood glucose and fT4 levels at 2h after a meal was stronger. Among the two thyroid hormones T3 and T4, T4 is considered to be the precursor of the biologically active form of T3. Eighty percent of T3 is derived from the conversion of T4 under the action of two deiodinases, and the rest is directly secreted by the thyroid. T3 is the main bioactive form for maintaining blood sugar homeostasis [27,28]. With age, the FT3 value of women and adults decreases, while the FT4 value remains stable [29]. This finding is consistent with our research.

There are some limitations still be noted in the study, (1) This is a retrospective single-centre study, which may result in selection bias. (2) The critical value of this study has not been verified in other study. Therefore, it is necessary to conduct a larger-scale multi-center clinical study to verify our research results.

In summary, this study suggested that a higher fT3 level may be involved in the control of GDM. The results of the study are limited by the small sample size and further studies of larger samples are needed.

Table 4: Relationship between GDM-A2 clinical parameters and fT3 and fT4 levels.

	FT3	P	FT4	p	TSH	P
Age(years)		0.035		0.02		0.759
<25	4.74(4.22–4.94)		12.61(11.71– 15.19)		1.61(1.31–2.32)	
25–29	4.47(4.11–4.97)		13.50(12.59–14.77)		1.86(1.37–2.93)	
30–34	4.33(3.81–4.61)		11.97(11.20–13.39)		2.03(1.38–2.76)	
≥35	4.29(3.94–4.69)		12.74(11.12–14.16)		2.16(1.60–2.56)	
Pre-pregnancy BMI(kg/m^2)		0.984		0.606		0.889
<18.5	4.56(4.05–4.82)		12.61(12.41–13.51)		1.89(1.43–2.43)	
18.5–23.9	4.42(4.08–4.79)		12.61(11.55–14.10)		2.02(1.42–2.71)	
≥24	4.39(4.01–4.71)		13.26(11.44–14.54)		1.97(1.28–2.81)	
Pregnancy times		0.186		0.325		0.108
1	4.33(3.96–4.82)		13.05(11.71–14.54)		1.99(1.43–2.86)	
2	4.60(4.11–4.97)		13.11(11.83–14.67)		2.11(1.45–3.79)	
≥3	4.35(3.99–4.66)		12.57(11.1–14.16)		1.94(1.26–2.45)	
Parity		0.158		0.985		0.634
1	4.48±0.56		13.06±2.37		2.41±1.77	
≥2	4.35±0.51		13.04±1.96		2.33±1.29	
Delivery method		0.718		0.263		0.94
Vaginal delivery	4.42±0.49		13.23±2.01		2.41±1.72	
Cesarean section	4.39±0.58		12.87±2.22		2.29±1.35	
Gestational week(weeks)		0.831		0.124	0.483	0.148
<37	4.38±0.34		11.78±2.21		1.91±1.33	
37–42	4.40±0.55		13.09±2.12		2.37±1.52	
Fetal sex		0.156		0.538		0.238
Male	4.47±0.55		13.11±2.04		2.49±1.63	
Female	4.34±0.53		12.94±2.23		2.21±1.40	
Birth weight(kg)		0.319		0.072		0.256
<2500	4.04(3.93–4.11)		10.70(9.37–12.34)		2.35(1.70–3.20)	
2500–4000	4.39(4.06–4.73)		13.00(11.75–14.54)		1.56(1.42–2.73)	
>4000	4.56(3.924–4.82)		11.71(11.03–13.38)		1.89(1.38–2.65)	
Fbg(mmol/L)		0.664		0.112		0.555
<5.10	4.37±0.53		12.58±1.98		2.27±1.09	
≥5.10	4.42±0.55		13.27±2.19		2.38±1.71	
1-h Glu(mmol/L)		0.695		0.22		0.628
<10.0	4.42±0.56		13.22±2.19		2.47±1.75	
≥10.0	4.37±0.51		12.64±2.06		2.09±0.89	
2-h Glu(mmol/L)		0.35		0.002		0.814
<8.5	4.45±0.56		13.55±2.16		2.45±1.80	
≥8.5	4.34±0.51		12.38±1.93		2.21±1.07	

BMI: Body Mass Index; Fbg: Fasting Blood Glucose; 1-h Glu: 1-h Postprandial Glucose; 2-h Glu: 2-h Postprandial Glucose.

Author Statements

Acknowledgements

Written informed consent was obtained from all patients before the collection of GDM samples.

There is no funding Not applicable.

We thank other colleagues in the Department of Laboratory Medicine for their support and help, and the Central Laboratory for their help in the Nanjing Jiangning Hospital, The Affiliated Jiangning Hospital with Nanjing Medical University.

Conflicts of Interest

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

Availability of Data and Material

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval

Ethical approval for this project was granted by the Ethics Committee of the Nanjing Jiangling Hospital, Nanjing Medical University. This study was performed in accordance with the principles of the Declaration of Helsinki.

References

1. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid. 2017; 27: 315-389.
2. Safian S, Esna-Ashari F, Borzouei S. Thyroid Dysfunction in Pregnant Women with Gestational Diabetes Mellitus. Curr Diabetes Rev. 2020; 16: 895-899.
3. Shah PB, Gupta K, Bedi M. Comparative Study on Different Hormones between Normal Pregnant Women and Women Experiencing Miscarriage. Int J Appl Basic Med Res. 2020; 10: 240-244.
4. Srivastava S, Mathur G, Chauhan G, Kapoor P, Bhaskar P, et al. Impact of Thyroid Dysfunction on Insulin Resistance: A Study from a Tertiary Care Center in India. J Assoc Physicians India. 2021; 69: 49-53.
5. Kocaturk E, Kar E, Kusku Kiraz Z, Alatas U. Insulin resistance and pancreatic beta cell dysfunction are associated with thyroid hormone functions: A cross-sectional hospital-based study in Turkey. Diabetes Metab Syndr. 2020; 14: 2147-2151.
6. Yuan N, Wang L, Li Z, Zhang X. Thyroid Diseases During Pregnancy: Bibliometric Analysis of Scientific Publications. Endocr Metab Immune Disord Drug Targets. 2022; 22: 247-258.
7. Yanachkova VE, Kamenov Z. The relationship between Thyroid dysfunction during pregnancy and Gestational diabetes mellitus. Endokrynol Pol. 2021; 72: 226-231.
8. Tang L, Li P, Zhou H, Li L. A longitudinal study of thyroid markers during pregnancy and the risk of gestational diabetes mellitus and post-partum glucose metabolism. Diabetes Metab Res Rev. 2021; e3441.
9. Zhang Y, Sun W, Zhu S, Huang Y, Huang Y, et al. The Impact of Thyroid Function and TPOAb in the First Trimester on Pregnancy Outcomes: A Retrospective Study in Peking. J Clin Endocrinol Metab. 2020; 105.
10. Yang S, Shi FT, Leung PC, Huang HF Fan J. Low Thyroid Hormone in Early Pregnancy Is Associated With an Increased Risk of Gestational Diabetes Mellitus. J Clin Endocrinol Metab. 2016; 101: 4237-4243.
11. Singh N, Madhu M, Vanamail P, Malik N, Kumar S. Efficacy of metformin in improving glycaemic control & perinatal outcome in gestational diabetes mellitus: A non-randomized study. Indian J Med Res. 2017; 145: 623-628.
12. Gonzalez-Quintero VH, Istwan NB, Rhea DJ, Rodriguez LI, Cotter A, et al. The impact of glycemic control on neonatal outcome in singleton pregnancies complicated by gestational diabetes. Diabetes Care. 2007; 30: 467-470.
13. Seshiah V, Kapur A, Balaji V, Shah SN, Das AK, et al. Targeting Glycemic Level in Gestational Diabetes Mellitus to that of Normal Pregnancy would result in a better Maternal-Fetal Outcome. J Assoc Physicians India. 2019; 67: 66-70.
14. Hochberg A, Pardo A, Oron G, Krispin E, Amikam U, et al. Perinatal outcome following induction of labor in patients with good glycemic controlled gestational diabetes: does timing matter? Arch Gynecol Obstet. 2019; 300: 299-303.
15. Hod M, Kapur A, Sacks DA, Hadar E, Agarwal M, et al. The International Federation of Gynecology and Obstetrics (FIGO) Initiative on gestational diabetes mellitus: A pragmatic guide for diagnosis, management, and care. Int J Gynaecol Obstet. 2015; 131: S173-S211.
16. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021; 44: S15-S33.
17. Yong HY, Mohd Shariff Z, Mohd Yusof BN, Rejali Z, Tee YYS, et al. Independent and combined effects of age, body mass index and gestational weight gain on the risk of gestational diabetes mellitus. Sci Rep. 2020; 10: 8486.
18. Poblete JA, Olmos P. Obesity and Gestational Diabetes in Pregnant Care and Clinical Practice. Curr Vasc Pharmacol. 2021; 19: 154-164.
19. West S, Ollila MM, Franks S, Piltonen T, Jokelainen J, et al. Overweight, obesity and hyperandrogenemia are associated with gestational diabetes mellitus: A follow-up cohort study. Acta Obstet Gynecol Scand. 2020; 99: 1311-1319.
20. Yao D, Chang Q, Wu QJ, Gao SY, Zhao H, et al. Relationship between Maternal Central Obesity and the Risk of Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis of Cohort Studies. J Diabetes Res. 2020; 6303820.
21. Yang FF, Han TB, Du WQ, Zhao F, Wang Y, et al, Association of fat mass and obesity associated gene polymorphism with the risk of gestational diabetes. Zhonghua Liu Xing Bing Xue Za Zhi. 2020; 41: 1097-1102.
22. O'Malley EQ, Reynolds CME, Killalea A, O'Kelly R, Sheehan SR, et al. Maternal obesity and dyslipidemia associated with gestational diabetes mellitus (GDM). Eur J Obstet Gynecol Reprod Biol. 2020; 246: 67-71.
23. Sert UY, Buyuk GN, Engin Ustun Y, Ozgu Erdinc AS. Is There Any Relationship Between Thyroid Function Abnormalities, Thyroid Antibodies and Development of Gestational Diabetes Mellitus (GDM) in Pregnant Women? Medeni Med J. 2020; 35: 195-201.
24. Moll U, Landin-Olsson M, Nilsson C, Ursing D, Strevens H. Pregnancy outcome in women with gestational diabetes - A longitudinal study of changes in demography and treatment modalities. Acta Obstet Gynecol Scand. 2020; 99: 333-340.
25. Rawal S, Tsai MY, Hinkle SN, Zhu Y, Bao W, et al. A Longitudinal Study of Thyroid Markers Across Pregnancy and the Risk of Gestational Diabetes. J Clin Endocrinol Metab. 2018; 103: 2447-2456.
26. Gu L, Yang J, Gong Y, Ma Y, Yan S, et al. Lower free thyroid hormone levels are associated with high blood glucose and insulin resistance; these normalize with metabolic improvement of type 2 diabetes. J Diabetes. 2021; 13: 318-329.
27. Maia AL, Goemann IM, Meyer EL, Wajner SL. Deiodinases: the balance of thyroid hormone: type 1 iodothyronine deiodinase in human physiology and disease. J Endocrinol. 2011; 209: 283-297.
28. Teixeira SD, Panveloski-Costa AC, Carvalho A, Monteiro Schiavon FP, Ruiz Marque AC, et al. Thyroid hormone treatment decreases hepatic glucose production and renal reabsorption of glucose in alloxan-induced diabetic Wistar rats. Physiol Rep. 2016; 4.
29. Chen X, Zheng X, Ding Z, Su Y, Wang S, et al. Relationship of gender and age on thyroid hormone parameters in a large Chinese population. Arch Endocrinol Metab. 2020; 64: 52-58.