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Association Between Maternal Thyroid Function in Early Pregnancy and Gestational Diabetes: A Prospective Cohort Study

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Introduction

- GDM is a **common** endocrine disease that occurs during pregnancy and results in glucose intolerance.

- The proportion of pregnant women with GDM has continued to **rise** in recent decades, resulting in a substantial impact on public health.

Introduction

- Thyroid function and metabolism of thyroid hormones undergo *significant changes* during pregnancy.

- Placental HCG is structurally **similar** to TSH and stimulates the thyroid gland directly through **TSH receptors**, so TSH secretion is briefly suppressed in the first trimester, while serum **FT4 and FT3** concentrations are **elevated in the first trimester**.

Introduction

- The thyroid gland's hormones are essential regulators of metabolic systems such as glucose, protein, and lipid metabolism, and type 2 diabetes in adults and thyroid disorders have been reported to be relate.

- *Hypothyroidism* in adults is associated with **resistance to insulin**, altered **glucose metabolism**, and being **overweight**, which each possibly contribute to the development of diabetes type 2.

Introduction

- Although the association between GDM and thyroid diseases and thyroid markers during pregnancy has been widely studied, findings are **not consistent**, and the specific mechanisms of the associations remain unclear.

Introduction

Fatima et al discovered significant positive connections between TSH and glucose levels during pregnancy and suggested that *SCH may affect glucose metabolism in pregnant women with diabetes*.

Introduction

Li et al reported that TPOAb positivity increased the occurrence of GDM and a research indicated that when TSH > 4.0 mIU/L, GDM incidence increased ***independent*** of thyroid antibody status, whereas GDM incidence ***depended*** on thyroid antibody status for TSH < 4.0 mIU/L.

Introduction

- However, the results of other studies do not support these correlations.

- As part of the present study's prospective cohort research, we investigated the correlations between hormone levels of the thyroid at **6-13+6 weeks** of gestation and **the incidence of GDM**, with a view to identifying women who are at a ***higher risk*** of suffering from GDM early and providing behavioral and/or therapeutic approaches that can prevent GDM from occurring.

Materials and Methods

Participants and Study Design

- This *prospective cohort* study was carried out at the Capital Medical University's Beijing Obstetrics and Gynecology Hospital.
- All the enrolled pregnant women received regular prenatal care during the first trimester at the hospital from **February 2018 to December, 2021**.
- A total of 36 256 pregnant women were initially enrolled on the basis of the **China Birth Cohort Study (CBCS)** inclusion criteria.

Materials and Methods

Patients were then excluded for the following reasons:

(1) withdrawal from the CBCS after recruitment (n = 513)

(2) non singleton pregnancy confirmed by ultrasound in the first trimester (n = 1094).

(3) pre pregnancy **thyroid disease** (including prepregnancy thyroid dysfunction, thyroid tumor, thyroid surgery, thyroiditis, or thyroid cysts; n = 2091).

(4) diabetes before conception or fasting venous blood glucose level ≥ 7.0 mmol/L in the first prenatal visit (n = 144).

Materials and Methods

(5) taking *medication* affecting thyroid function, glucose, or lipids before pregnancy (including L-T4, prednisone, methylprednisolone, dexamethasone, budesonide, lipid-lowering medicine, labetalol, or propylthiouracil; n = 165)

(6) TFT values not being ***accessible*** before week 14 of pregnancy (n = 2010)

(7) lacking *OGTT results* (n = 3497).

Ultimately, 26 742 pregnant women were enrolled in our study (Fig. 1).

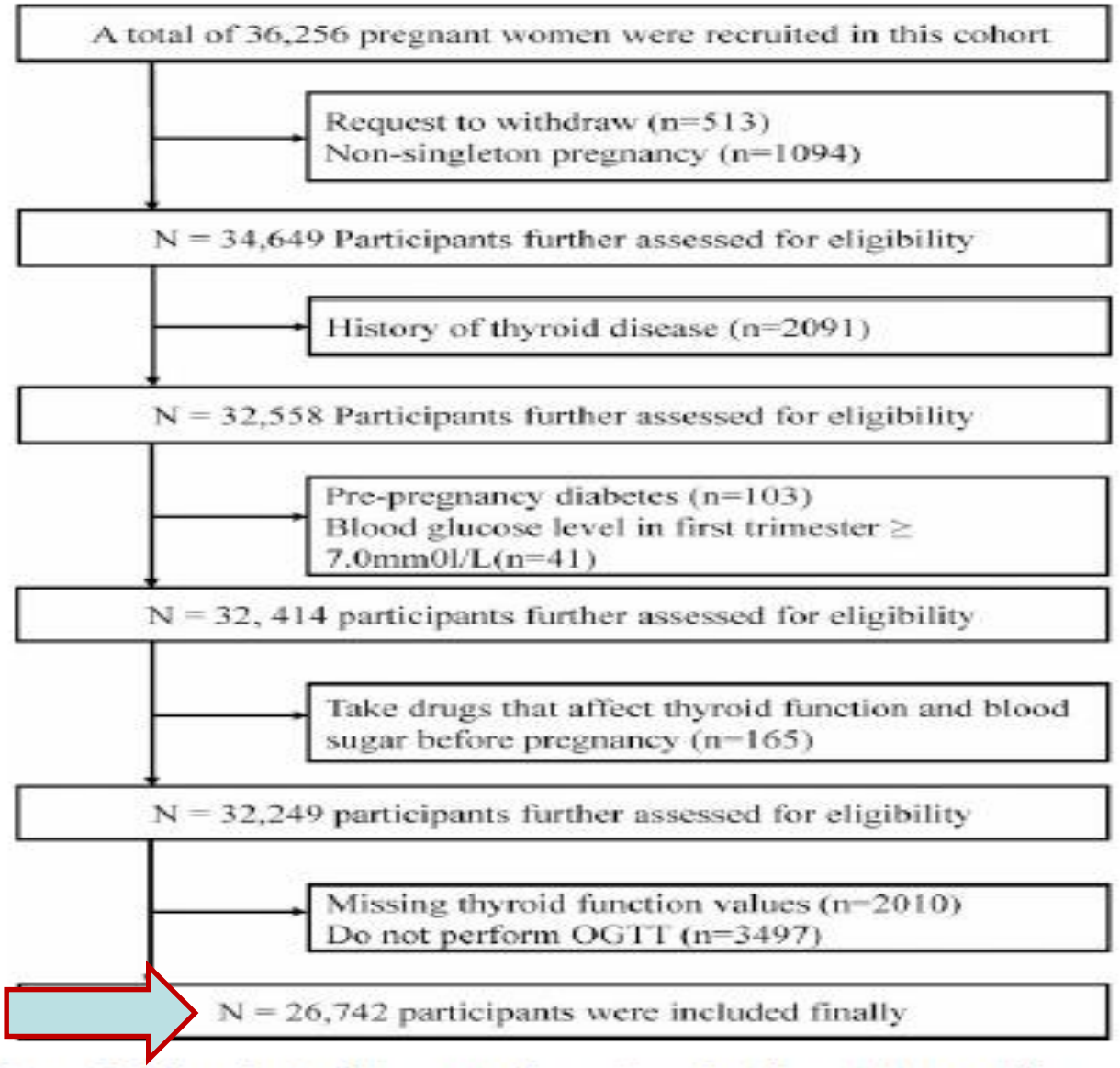

Figure 1. Flow chart of the protocol used to select the study population.

Materials and Methods

Data Collection

The following **demographic characteristics** were obtained using the CBCS-based enrollment questionnaire:

date **of birth**, height, prepregnancy **weight**, medication use, prepregnancy *thyroid disease*, smoking, **alcohol** consumption, and **mode of pregnancy** (classified as either **natural** pregnancy or with assisted reproductive technology).

Materials and Methods

- The enrolled pregnant women were placed in to 2 groups depending on their *age* (≥35 and <35 years old), and 3 groups that were defined by pre pregnancy BMI: obese, overweight, and normal (≥24.0 kg/m2, 24.0-28.0 kg/m2, <24.0 kg/m2).
- **Smoking and alcohol** consumption were classified as yes or no.
- The presence of **thyroid disease before** pregnancy was determined using **questionnaires and hospital** records**.**

Materials and Methods

Assessment of Thyroid Function

- At the **initial prenatal visit** (6-13+6 weeks of gestation), blood samples were collected from the pregnant women following ***overnight fasting of 8 to 10 hours***.

Materials and Methods

- Following the ATA suggestions from 2017, ***SCH*** was classified as having normal serum FT4 levels and ***TSH ≥ 4.0.***
- According to the standards of our hospital:
  - Normal range of FT4 in early pregnancy : 11.8-18.4 pmol/L.
  - Thyroid Ab positivity was indicated by TPOAb ≥ 60 U/mL.

Materials and Methods

GDM Diagnosis

- Between 24 and 28 weeks of gestation, all enrolled participants conducted a ***typical 2-hour***, **75-gram** OGTT.
- The OGTT measured intravenous glucose levels at 3 different time points: 0, 1, and 2 hours.
- According to the guidelines for diagnosis established by the ADA, GDM was diagnosed if **any** of these values were greater than or equal to ADA threshold values at the corresponding time points (0 hours, 5.1 mmol/L; 1 hour, 10.0 mmol/ L; and 2 hours, 8.5 mmol/L).

Materials and Methods

- Statistical Analysis

- Normally distributed continuous variables were expressed as mean -,+ SD and categorical data were expressed as percentages and number of cases.
- The 2-tailed Student's t test was applied to test for normally distributed continuous data, a nonparametric technique based on the **Mann- Whitney U test** was implemented for ordinal data with categories, and the **chi-squared or Fisher exact probability** test was performed for categorical data.

Materials and Methods

- Next, the **correlation** between the level of maternal thyroid hormone and GDM was determined using **multivariate logistic regression.**

Results

- Among the 26 742 pregnant women finally enrolled, **3985** had GDM (incidence of 14.90%).
- Participants who had GDM tended to be older than those in the group without it (33.26 -+ 4.01 vs 31.51 -+ years, *P* < .001) In comparison with the group that did not have GDM, the pre pregnancy BMI was higher in the GDM group(23.02 Vs 21.47,*P* < .001).

Results

- When compared with the group without GDM, the group with GDM had a greater incidence of **assisted reproduction** (9.2% vs 5.1%, *P* < .001), and the group with GDM contained many ***more*** pregnant women who had **previously smoked** compared with the group without GDM (4.2% vs 2.8%, *P* < .001).

Results

- However, there were no significant differences in the proportion of women with or without GDM who consumed alcohol or in ethnicity.

Table 1. Characteristics of the whole pregnant population and women with and without GDM

Demographics	Total (n = 26 742)	GDM (n = 3958)	Non-GDM (n = 22 784)	*P*
Age (years), mean ± SD	26 742	33.26 ± 4.01	31.51 ± 3.76	<.001[a]
Age (years), n (%)	26 742			<.001[a]
<35	20 465 (76.5)	2489 (62.9)	17 976 (78.9)	
≥35	6277 (23.5)	1469 (37.1)	4808 (21.1)	
Pre-BMI (kg/m^2), mean ± SD	26 742	23.02 ± 3.49	21.47 ± 3.07	<.001[a]
Pre-BMI (kg/m^2), n (%)	26 742			<.001[a]
<24	21 514 (80.5)	2606 (65.8)	18 908 (83.0)	
24-28	4092 (15.3)	1001 (25.3)	3091 (13.6)	
≥28	1136 (4.2)	351 (8.9)	785 (3.4)	
Ethnic				.334
Han	24 654	3664 (92.6)	20 990 (92.1)	
Others	2088	294 (7.4)	1794 (7.9)	
First pregnancy status, n (%)				<.001[a]
Yes	14 651 (54.8)	1922 (48.6)	12 729 (55.9)	
No	12 091 (45.2)	2036 (51.4)	10 055 (44.1)	
Pregnancy mode, n (%)				<.001[a]
Natural pregnancy	25 208 (94.3)	3592 (90.8)	21 616 (94.9)	
ART	1534 (5.7)	366 (9.2)	1168 (5.1)	
Smoking, n (%)				<.001[a]
Yes	796 (3.0)	165 (4.2)	631 (2.8)	
No	25 946 (97)	3793 (95.8)	22 153 (97.2)	
Drinking, n (%)				.172
Yes	1057 (4.0)	141 (3.6)	916 (4.0)	
No	25 685 (96.0)	3817 (96.4)	21 868 (96.0)	

Abbreviations: ART, assisted reproductive technology; GDM, gestational diabetes mellitus; pre-BMI, prepregnancy body mass index.
[a]$P < .05$ was considered to be statistically significant.

Correlation Between First-Trimester Thyroid Function (TPOAb, TSH, and FT4), SCH, and GDM

- The group with GDM had considerably higher TSH levels than the group without GDM (1.60-+ 1.28 vs 1.52-+ 1.38 mIU/L, *P* = .003), and this difference remained when comparing the intergroup relationship with TSH quintile spacing (*P* < .001).

Results

- Additionally, the **GDM** group's FT4 level was considerably lower than that of the group without GDM (16.27 - ,+2.34 vs 16.38-+ 2.51 pmol/L, *P* = .007), and this difference remained when comparing the intergroup relationship with FT4 quintile spacing (*P* = .012).
- Compared with the group without GDM, the TPOAb positive rate was greater in the group with GDM (11.3% vs 12.5%, *P* = .037).
- Furthermore, compared with the non-GDM group, more pregnant women with SCH were in the GDM group. However, the difference was not statistically significant (3.9% vs 3.4%, *P* = .063).

Table 2. Relationship between thyroid function in the first trimester and GDM

Thyroid function	GDM (n = 3958)	Non-GDM (n = 22 784)	*P*
TSH (mIU/L), mean ± SD	1.60 ± 1.28	1.52 ± 1.38	.002[a]
TSH (mIU/L), n (%)			<.001[a]
0-	732 (18.5)	4663 (20.5)	
0.61-	739 (18.7)	4640 (20.4)	
1.07-	830 (21.0)	4502 (19.8)	
1.55-	817 (20.6)	4485 (19.7)	
2.28-	840 (21.2)	4494 (19.7)	
FT4 (pmol/L), mean ± SD	16.27 ± 2.34	16.38 ± 2.51	.007[a]
FT4 (pmol/L), n (%)			.012[a]
4.18-	852 (21.5)	4526 (19.9)	
14.58-	774 (19.6)	4584 (20.1)	
15.63-	829 (20.9)	4498 (19.7)	
16.62-	748 (18.9)	4587 (20.1)	
17.90-	755 (19.1)	4589 (20.1)	
TPOAb (U/L), n (%)			.037[a]
<60	3464 (87.5)	20 201 (88.7)	
≥60	494 (12.5)	2583 (11.3)	
SCH, n (%)			.063
Yes	156 (3.9)	765 (3.4)	
No	3802 (96.1)	22 019 (96.6)	

Abbreviations: FT4, free thyroxine; GDM, gestational diabetes mellitus; SCH, subclinical hypothyroidism; TPOAb, thyroid peroxidase antibody; TSH, thyroid-stimulating hormone.
[a]$P < .05$ was considered to be statistically significant.

Results

As shown in Table 3, **after controlling** for *maternal age*, first pregnancy status, *pre pregnancy BMI*, pregnancy *mode*, and smoking status, the occurrence of GDM was significantly associated with:

TSH (a OR 1.030, 95% CI 1.007, 1.054, ***P* = .012**) but not with FT4 (a OR 0.998, 95% CI: 0.984, .012, *P* = .777) or TPOAb (a OR 1.079, 95% CI 0.970,1.200, *P* = .160).

Comparison of thyroid hormone levels in early pregnancy and SCH between GDM and non-GDM pregnant women

	OR (95% CI)	*P*	aOR (95% CI)	*P*
TSH	1.035 (1.012, 1.058)	.003[a]	1.030 (1.007, 1.054)	.012[a]
FT4	0.980 (0.966, 0.995)	.007[a]	0.998 (0.984, 1.012)	.777
TPOAb positive	1.115 (1.006, 1.236)	.037[a]	1.079 (0.970, 1.200)	0.160
SCH	1.181 (0.991, 1.408)	.063	1.211 (1.010, 1.451)	.039[a]

Abbreviations: aOR, adjusted odds ratio, adjusted for age, prepregnancy BMI, first pregnancy status, pregnancy mode, and smoking status; FT4, free thyroxine; GDM, gestational diabetes mellitus; non-GDM, not gestational diabetes mellitus; OR, odds ratio; SCH, subclinical hypothyroidism; TPOAb, thyroid peroxidase antibody; TSH, thyroid-stimulating hormone.

[a] $P < .05$ was considered to be statistically significant.

Results

- Subsequently, we classified all enrolled pregnant women into 2 groups: the SCH group and the non-SCH group.
- Binary logistic regression indicated that the rates of GDM and SCH did not correlate statistically significantly (OR 1.181, 95% CI 0.991, 1.408, *P* = .063).
- However, **after controlling** for maternal age, prepregnancy BMI, first pregnancy status, pregnancy mode, and smoking status, we found that **pregnant women with SCH had a greater risk of GDM** (aOR 1.211, 95% CI 1.010, 1.451, *P* = .039).

- Moreover, higher maternal **age**, higher prepregnancy **BMI**, ART conception, and **smoking** were noted **risk factors for GDM.**

Comparison of thyroid hormone levels in early pregnancy and SCH between GDM and non-GDM pregnant women

	OR (95% CI)	*P*	aOR (95% CI)	*P*
TSH	1.035 (1.012, 1.058)	.003[a]	1.030 (1.007, 1.054)	.012[a]
FT4	0.980 (0.966, 0.995)	.007[a]	0.998 (0.984, 1.012)	.777
TPOAb positive	1.115 (1.006, 1.236)	.037[a]	1.079 (0.970, 1.200)	0.160
SCH	1.181 (0.991, 1.408)	.063	1.211 (1.010, 1.451)	.039[a]

Abbreviations: aOR, adjusted odds ratio, adjusted for age, prepregnancy BMI, first pregnancy status, pregnancy mode, and smoking status; FT4, free thyroxine; GDM, gestational diabetes mellitus; non-GDM, not gestational diabetes mellitus; OR, odds ratio; SCH, subclinical hypothyroidism; TPOAb, thyroid peroxidase antibody; TSH, thyroid-stimulating hormone.

[a] $P < .05$ was considered to be statistically significant.

Relationships Between Early Pregnancy FT4, TSH, and TPOAb Levels and GDM Risk:

- To investigate the relationship between the function of the thyroid and the risk of GDM, all enrolled participants were separated into **quintile groups** dependent on their **TSH and blood FT4 levels**.

Results

- The TPOAb-negative group, the lowest quintile array of TSH, and the lowest quintile array of FT4 were utilized as references for logistic regression analysis, depending on the correlation findings.

- Because statistically significant variations in first pregnancy status, pregnancy mode, prepregnancy BMI, maternal age, and smoking status were observed between groups with and without DM, the **multiple logistic regression analysis was adjusted** for the above-mentioned influencing factors, and the results are shown in Table 4.

Results

- There were significant variations in the rate of GDM among the various TSH quintile groups (*P* for trend = .013). Furthermore, a greater level of TSH was related to a **higher GDM risk** (ORQ3: 1.174, 95% CI :1.055, 1.308,***P* = .003**; ORQ4: 1.160, 95% CI 1.042, 1.293, *P* = .007; ORQ5 : 1.191, 95% CI 1.070, 1.325, *P* = .001), and this association remained after controlling for first pregnancy status, maternal age, pre pregnancy BMI, pregnancy mode, and smoking status (ORQ3 1.124, 95% CI 1.006, 1.256, *P* = .039; ORQ5 1.124, 95% CI, 1.006, 1.256, *P* = .038).

Table 4. Risk of GDM at different levels of TSH and FT4 in all enrolled women

	GDM n (+/–)	Prevalence (%)	OR (95% CI)	*P*	aOR (95% CI)	*P*
TSH (mIU/L)						
Q1 (0-0.60)	732/4663	13.6	Ref		Ref	
Q2 (0.61-1.06)	739/4640	13.7	1.015 (0.909, 1.133)	.797	0.989 (0.883, 1.107)	.846
Q3 (1.07-1.54)	830/4502	15.6	1.174 (1.055, 1.308)	.003[a]	1.124 (1.006, 1.256)	.039[a]
Q4 (1.55-2.17)	817/4485	15.4	1.160 (1.042, 1,293)	.007[a]	1.102 (0.986, 1.232)	.086
Q5 (2.28-)	840/4494	15.7	1.191 (1.070, 1.325)	.001[a]	1.124 (1.006, 1.256)	.038[a]
P for trend		.013[a]				
FT4 (pmol/L)						
Q1 (4.18-14.57)	852/4526	15.8	Ref		Ref	
Q2 (14.58-15.62)	774/4584	14.4	1.144 (1.029, 1.272)	.013[a]	0.996 (0.892, 1.111)	.937
Q3 (15.63-16.61)	829/4498	15.6	1.026 (0.921, 1.144)	.639	0.945 (0.845, 1.056)	.319
Q4 (16.62-17.8)	748/4587	14.0	1.120 (1.007, 1.247)	.037[a]	1.069 (0.958, 1.194)	.232
Q5 (17.90-)	755/4589	14.1	0.991 (0.889, 1.105)	.873	0.946 (0.846, 1.059)	.334
P for trend		.934				

Abbreviations: aOR, adjusted odds ratio, adjusted for age, prepregnancy BMI, first pregnancy status, pregnancy mode, and smoking status; FT4, free thyroxine; GDM, gestational diabetes mellitus; non-GDM, not gestational diabetes mellitus; OR, odds ratio; TSH, thyroid-stimulating Hormone.
[a]$P < .05$ was considered to be statistically significant.

Results

- However, there were no discernible differences in the **incidence rate of GDM between the FT4** quintile groups (*P* for trend = .934).

- Moreover, there was no connection between TPOAb status and the occurrence of GDM.

In Fig. 2, restricted cubic splines were used to model and visualize the association of TSH and FT4 with the risk of GDM.

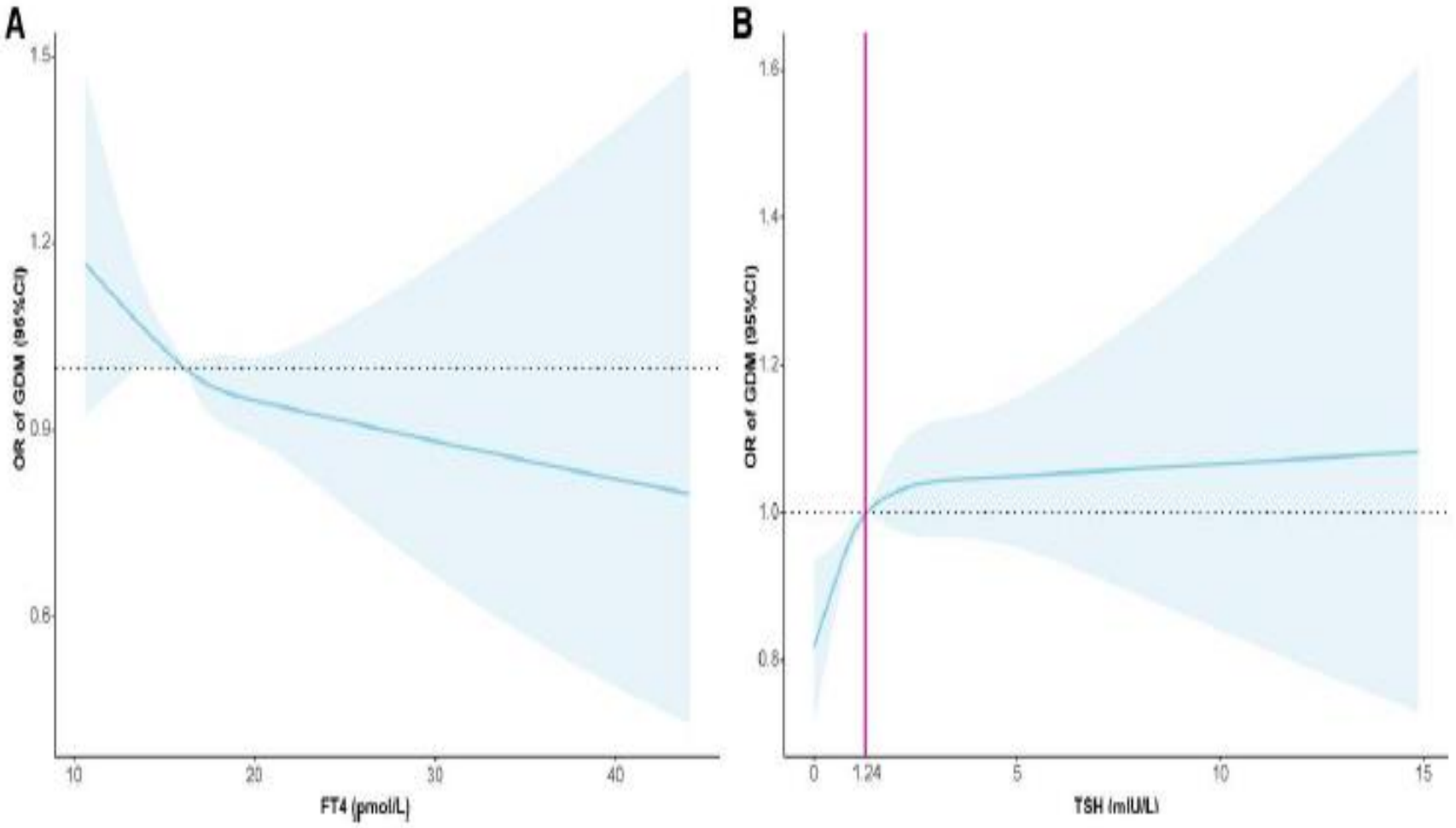

Figure 2. The association of FT4/TSH with the risk of GDM. (A) The relationship between FT4 and the risk of GDM. (B) The relationship between TSH and the risk of GDM. FT4, free thyroxine; GDM, gestational diabetes mellitus; OR, odds ratio; TSH, thyroid-stimulating Hormone.

Results

- Notably, we found a significant nonlinear relationship between TSH and GDM ($P < .05$) but not FT4 ($P > .05$).

- Figure 2B shows that TSH was positively correlated with the incidence of GDM, and the incidence of GDM when TSH ≤ 1.24 mIU/L increased rapidly with an increase in TSH.
- In contrast, when TSH > 1.24 mIU/L the increase in GDM was relatively stable with an increase in TSH.

The Association Between TSH and GDM Stratified by Age and Prepregnancy BMI

- Table 5 shows the association between TSH and GDM found by multiple logistic regression in different age and pre pregnancy BMI subgroups.
- ***In unadjusted*** models, there was a **significant linear trend** between **TSH and GDM** for the maternal age <35 years subgroup as well as for the pre pregnancy and BMI subgroups (*P* for trend < .05).

Table 5. The ORs and 95% CIs of the association between different TSH levels in first trimester and GDM, stratified by potential modifiers

	Q1	Q2 (OR 95% CI)	Q3 (OR 95% CI)	Q4 (OR 95% CI)	Q5 (OR 95% CI)	*P* for trend	*P* for interacti
Age (years)							
Unadjusted							.644
<35	1.000	1.071 (0.933, 1.229)	1.213 (1.060, 1.389)	1.243 (1.087, 1.422)	1.249 (1.092, 1.429)	<.001[a]	
≥35	1.000	0.933 (0.774, 1.125)	1.112 (0.925, 1.337)	1.039 (0.863, 1.250)	1.099 (0.914, 1.321)	.161	
Adjusted[b]							.571
<35	1.000	1.047 (0.911, 1.203)	1.162 (1.013, 1.333)	1.179 (1.028, 1.352)	1.177 (1.026, 1.349)	.005[a]	
≥35	1.000	0.901 (0.745, 1.090)	1.072 (0.889, 1.294)	0.985 (0.815, 1.190)	1.052 (0.872, 1.271)	.372	
Pre-BMI (kg/m^2)							
Unadjusted							.653
<24	1.000	0.948 (0.830, 1.082)	1.098 (0.965, 1.249)	1.072 (0.942, 1.219)	1.089 (0.957, 1.239)	.049[a]	
≥24	1.000	1.090 (0.892, 1.330)	1.223 (1.005, 1.489)	1.159 (0.951, 1.413)	1.257 (1.033, 1.531)	.021[a]	
Adjusted[c]							.652
<24	1.000	0.964 (0.843, 1.103)	1.115 (0.979, 1.271)	1.097 (0.962, 1.250)	1.110 (0.973, 1.265)	.026[a]	
≥24	1.000	1.100 (0.898, 1.347)	1.215 (0.995, 1.484)	1.159 (0.947, 1.417)	1.271 (1.040, 1.552)	.021[a]	

Abbreviations: GDM, gestational diabetes mellitus; OR, odds ratio; TSH, thyroid-stimulating Hormone.
[a]$P < .05$ was considered to be statistically significant.
[b]Adjusted model: adjusted for prepregnancy BMI, first pregnancy status, pregnancy mode, and smoking status.
[c]Adjusted model: adjusted for age, first pregnancy status, pregnancy mode, and smoking status.

Results

- **After adjusting** for confounding factors, this relationship disappeared in the subgroup <35 years of age.
- However, there was a stable and significant positive association between TSH and the occurrence of GMD in subgroups with **pre pregnancy BMI** (*P* for trend < .05).

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[b]Adjusted model: adjusted for prepregnancy BMI, first pregnancy status, pregnancy mode, and smoking status.
[c]Adjusted model: adjusted for age, first pregnancy status, pregnancy mode, and smoking status.

Results

After adjusting for confounding factors, TSH levels in the highest quintile of the prepregnancy BMI ≥ 24 kg/m2 subgroup were found to be associated with increased risk for GDM compared with the lowest quintile, and in the interaction analysis of age and pre pregnancy BMI on GDM, there were no statistically significant interaction between groups before or after adjusting for confounding factors (*P* for interaction > .05).

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Unadjusted							.653
<24	1.000	0.948 (0.830, 1.082)	1.098 (0.965, 1.249)	1.072 (0.942, 1.219)	1.089 (0.957, 1.239)	.049[a]	
≥24	1.000	1.090 (0.892, 1.330)	1.223 (1.005, 1.489)	1.159 (0.951, 1.413)	1.257 (1.033, 1.531)	.021[a]	
Adjusted[c]							.652
<24	1.000	0.964 (0.843, 1.103)	1.115 (0.979, 1.271)	1.097 (0.962, 1.250)	1.110 (0.973, 1.265)	.026[a]	
≥24	1.000	1.100 (0.898, 1.347)	1.215 (0.995, 1.484)	1.159 (0.947, 1.417)	1.271 (1.040, 1.552)	.021[a]	

Abbreviations: GDM, gestational diabetes mellitus; OR, odds ratio; TSH, thyroid-stimulating Hormone.
[a]$P < .05$ was considered to be statistically significant.
[b]Adjusted model: adjusted for prepregnancy BMI, first pregnancy status, pregnancy mode, and smoking status.
[c]Adjusted model: adjusted for age, first pregnancy status, pregnancy mode, and smoking status.

Discussion

- In the above results we observed an increase in the incidence of GDM with increasing **maternal age**, and the incidence of GDM also increased with an increase in **pre pregnancy BMI**.

- When the prepregnancy BMI ≥ 24 kg/m2, the being in the highest quintile of TSH level increased the risk of GDM compared with the lowest quintile.

- Moreover, the incidence of GDM in pregnant women with assisted reproduction was higher than in natural pregnancy.

Discussion

- The incidence of GDM was also higher in pregnant women who were previous or current smokers than in those who had never smoked.
- Furthermore, the participants in the GDM group had elevated first-trimester TSH levels compared with the corresponding participants without GDM.

Discussion

With rising TSH, the incidence of GDM rose as well, suggesting that a low level of TSH is protective against GDM.

When ***TSH ≤ 1.24*** mIU/L: GDM risk increased significantly with rising TSH, but this relationship was **not** obvious when ***TSH > 1.24*** mIU/L.

Discussion

Participants with **SCH** had a greater incidence of GDM than those without SCH.

These results indicate that high TSH level and SCH may be risk factors for GDM.

Discussion

- In our study population, the rate of development of GDM was **14.9%**, similar to a previous report.
- Wang et al reported that in China, diabetes prevalence increased from **10.9% in 2013 to about 12.4% in 2018**.
- In this study, the incidence of GDM exceeded those found in European and American populations, which may be because **East Asians have a limited ability to secrete insulin compared with these populations**.

Discussion

- Just a slight drop in the production of insulin could result in an acute decline in the level at which this resistance to insulin becomes a risk factor for developing diabetes.
- Mikhail et al found that for the same BMI, the incidence of GDM is greater in Asia than in the United States and Europe, which may be related to the higher rate of ***visceral fat in Asia.***

Discussion

- Based on the results of the present study, we propose that *higher TSH level is a risk factor for GDM*.

Discussion

- Similarly, in an investigation of 7258 pregnant participants in Tianjin, China, Leng et al discovered that the **levels of TSH** were strongly correlated with the incidence of GDM, especially in overweight or obese women.

Our study also found that pregnant women in the **SCH group had a higher percentage of GDM** than those without SCH.

Discussion

The possible mechanism by which TSH affects GDM is as follows:

- ✓ TSH directly decreases the capacity of pancreatic β cells to **generate and release insulin**, thereby increasing blood glucose levels.

- ✓ The TSH level is also thought to influence the development of resistance to insulin.

Discussion

- Furthermore, TSH may directly affect the metabolic parameters of human adipose tissue and stimulate leptin secretion .
- The existence of TSH receptors has been confirmed in human and animal cell tissues, and **adipocytes** also contain them.
- When TSH attaches to TSH receptors in adipocytes, it induces the production of **interleukin-6**, which regulates pre adipocyte and adipocyte **proliferation**, **differentiation, and leptin secretion.**

Discussion

- Leptin is a crucial neuroendocrine system regulator of TSH in terms of feedback control as it can either **directly** regulate the **gene expression** of TRH in the nucleus of the *paraventricular* or **indirectly** control the levels of TRH through the action of the *arcuate nucleus*.

Discussion

- Leptin levels have also been found to be associated with TSH and are known to be elevated in patients with hypothyroidism.

Discussion

- Leptin also plays a crucial role in glucose metabolism in the liver, where it has been found both to **promote and reduce** glycogen storage and promote gluconeogenesis.

This study has several strengths:

- First, this was a **prospective** cohort study with **a large sample**, and all enrolled pregnant women with **GDM were reliably diagnose** by clinicians based on OGTT results.

- Second, thyroid function was evaluated at **6-13+6 weeks** of pregnancy, greatly reducing the variation in thyroid function due to different gestational weeks.

However, even in light of these strengths several of our study's limitations warrant discussion.

- ✓ First, this was a **single-center study**, and therefore does not represent the whole population of China.

- ✓ Second, the study population was mainly **Han Chinese**; it is unknown to what extent the findings generalize to other ethnic populations.

Limitations:

- ✓ Third, **residual confounding** may have occurred due to untested factors.

- ✓ Fourth, this study did not measure **urinary iodine levels**, but all pregnant women enrolled lived in iodine adequate areas.

In conclusion

- ✓ our findings indicate that elevated TSH in early pregnancy is a risk factor for GDM, even when the TSH level is within the normal range, providing new evidence that thyroid function during pregnancy affects GDM.

- ✓ These results were further supported by the ***relatively high GDM rate in participants with SCH during pregnancy***.

Conclusion:

- ✓ Notably, higher TSH levels may increase the risk of GDM, especially when prepregnancy BMI ≥ 24 kg/m2.
- ✓ Moreover, our results suggest that women with BMI ≥ 24 kg/m2 before pregnancy can control their weight through *diet regulation and exercise* to reduce the incidence of GDM.
- ✓ Finally, our findings also illustrate the importance of TFT examination during early pregnancy.


Thank you for your attention