

Original Research

Association Between Maternal Thyroid-Stimulating Hormone Concentration in Early Pregnancy and Gestational Diabetes Mellitus: A Retrospective Cohort Study

Jiayi Zhang¹, Juanjuan Yang¹, Chunyu Wang¹, Yun Shi¹, Guoliang Jiang¹, Min Shen^{1,*}¹Department of Obstetrics, Suzhou Ninth People's Hospital, Suzhou Ninth Hospital Affiliated to Soochow University, 215000 Suzhou, Jiangsu, China*Correspondence: Szjyshenmin@163.com (Min Shen)

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Abstract

Background: Although the association between thyroid function in early pregnancy and gestational diabetes mellitus (GDM) has been explored, evidence remains inconsistent. This inconsistency necessitates further investigation to better clarify the potential relationship between maternal thyroid function in early pregnancy and subsequent GDM risk. **Methods:** A total of 1589 healthy pregnant individuals were enrolled in this study, all of whom had their initial prenatal visit from 10 to 13⁺₆ weeks of pregnancy at Suzhou Ninth Hospital affiliated to Soochow University from June to October 2023. Data were extracted from electronic medical records. GDM was diagnosed utilizing the 75 g oral glucose tolerance test (OGTT) at 24–28 weeks of gestation. To evaluate the independent association between early pregnancy thyroid function indicators and GDM, a series of analyses, including logistic regression, restricted cubic spline (RCS) analysis, correlation, and sensitivity analysis, was conducted. **Results:** Among 1589 pregnant women, 418 (26.31%) developed GDM. Multivariate logistic regression identified family history of diabetes, age, pre-pregnancy body mass index (BMI), fasting blood glucose (FBG), thyroid-stimulating hormone (TSH) (odds ratio [OR] = 1.23, 95% confidence interval [CI]: 1.09–1.38, $p < 0.001$), and triglycerides (TG) in early pregnancy as risk factors for GDM. RCS analysis demonstrated a significant dose-response correlation between TSH levels and GDM (p for overall association < 0.001 , p for nonlinearity = 0.441). Subgroup analysis revealed that among pregnant individuals with pre-pregnancy BMI ≥ 24 kg/m², each unit increase in early-pregnancy TSH was associated with a 1.61-fold increase in the odds of GDM (95% CI: 1.31–1.98, $p < 0.001$). **Conclusions:** Elevated odds of GDM may be associated with higher maternal TSH concentrations in the first trimester. This association was particularly pronounced among individuals with a pre-pregnancy BMI ≥ 24 kg/m².

Keywords: gestational diabetes mellitus; thyroid-stimulating hormone; oral glucose tolerance test

1. Introduction

Gestational diabetes mellitus (GDM) is a prevalent endocrine disorder characterized by abnormal glucose tolerance first identified during pregnancy. It poses both immediate and long-term health risks for mothers and offspring [1], including preeclampsia, birth trauma, neonatal respiratory distress syndrome, shoulder dystocia, and neonatal hypoglycemia [2]. An increased likelihood of developing type 2 diabetes later in life has been associated with GDM [3]. Independent of genetic and obesity-related risk factors, fetal exposure to maternal GDM predisposes offspring to obesity and diabetes in both childhood and adulthood [4]. The prevalence of GDM in China has demonstrated a significant increase over the past decade, with rates increasing from 4% in 2010 to 21% in 2020 [5], representing a growing public health concern that requires attention. To better understand the underlying mechanisms and associated risk factors, further studies are required, which may facilitate early prevention of GDM and decrease adverse maternal and neonatal outcomes.

Thyroid hormones are essential regulators of glucose, protein, and lipid metabolism. Changes in thyroid function

may be related to the onset of type 2 diabetes. Hypothyroidism is associated with insulin resistance (IR), impaired glucose metabolism, and obesity, resulting in type 2 diabetes [6]. Previous literature indicates that GDM and thyroid dysfunction, two of the most common disorders during pregnancy, are positively correlated [7]. Pregnant individuals exhibiting a higher free triiodothyronine (FT3)/free thyroxine (FT4) ratio at 26–28 weeks of gestation had significantly higher odds of GDM [8]. However, a delayed risk indicator is not conducive to early prevention of GDM. Given the established link between thyroid dysfunction and increased risk of adverse perinatal outcomes in GDM, combined screening of thyroid function and glucose metabolism has been proposed as a strategy to mitigate preterm birth, hypertensive disorders of pregnancy, and macrosomia [9].

Although the association between early-pregnancy thyroid function indicators and GDM risk has been explored, the evidence remains inconsistent. Following the 2017 American Thyroid Association (ATA) guidelines, which raised the recommended upper reference limit for thyroid-stimulating hormone (TSH) during early gestation from 2.5 to 4.0 mIU/L [10], numerous studies have recently investigated the correlation between first-trimester



TSH and GDM. For example, Fernández Alba et al. [11] demonstrated that higher TSH levels in early pregnancy may imply a higher risk of GDM. However, the highest tertile of TSH in Sağlam et al.'s study [12] showed an inverse association with GDM risk. Elevated serum concentrations of thyroid peroxidase antibody (TPOAb) and thyroglobulin antibodies during early- and mid-pregnancy are positively associated with an increased likelihood of GDM in pregnant individuals [13]. In contrast, other studies have not observed these associations [14,15]. Focusing on first-trimester thyroid function, particularly TSH, this study analyzed its association with GDM risk, aiming to contribute to GDM prevention strategies.

2. Materials and Methods

2.1 Study Population

This study involved a gestational population of 2169 individuals who attended their initial routine prenatal visit during 10–13⁺6 weeks of gestation at the Suzhou Ninth Hospital affiliated to Soochow University, from June to October 2023. For this retrospective analysis, data were extracted from the electronic medical records system. To mitigate potential data bias, the exclusion criteria include the following: non-singleton gestation confirmed by ultrasound ($n = 13$); termination of pregnancy in mid-trimester ($n = 14$); thyroid disease prior to conception, such as dysfunction, neoplasms (tumor/cysts), inflammation (thyroiditis), or a history of thyroid surgery ($n = 65$); pre-existing diabetes or fasting venous glucose concentration ≥ 7.0 mmol/L detected at the initial visit ($n = 20$); other endocrine system disorders or administration of medications that affect glucose, lipids, or thyroid function before pregnancy ($n = 8$); pre-existing chronic conditions such as hypertension, malignancy, connective tissue disease, hepatic or renal dysfunction, or psychiatric disorders ($n = 83$); absence of first trimester thyroid function test ($n = 132$); absence of oral glucose tolerance test (OGTT) ($n = 143$); and significant missing clinical data ($n = 102$, only medical records can be found in electronic information systems, without specific medical records and various test results, and cannot be obtained after multiple confirmations). Overall, 1589 pregnant women were enrolled in this study (Fig. 1).

Approval for this study protocol (Approval No. KYLW2026-011-01) was obtained from the Ethics Committee of the Suzhou Ninth Hospital affiliated to Soochow University. This study was conducted in accordance with the Declaration of Helsinki.

2.2 GDM Diagnosis

All enrolled pregnant individuals underwent one-step screening for GDM during gestational weeks 24–28. After at least 8 h fasting, 75 g of glucose was dissolved in 250–300 mL of warm water and consumed rapidly within 5 min. Glucose concentrations were measured at three specific time points: before ingestion of the glucose solu-

tion, and at 1 h and 2 h post-ingestion. Diagnostic criteria were based on the International Association of Diabetes and Pregnancy Study Group (IADPSG) consensus panel recommendations. According to these criteria, meeting or exceeding any single threshold value qualifies for a GDM diagnosis: $5.1 \leq$ fasting blood glucose (FBG) < 7.0 mmol/L, 1 h postprandial blood glucose ≥ 10.0 mmol/L, or 2 h postprandial blood glucose ≥ 8.5 mmol/L [16].

2.3 Variables

The selected variables were derived from a detailed review of preliminary studies, clinical knowledge, and established GDM risk factors reported in the literature. (1) Categorical variables included multiparous, family history of diabetes or hypertension, assisted pregnancy, Han Chinese ethnicity, and TPOAb positivity. (2) Continuous variables included age, pre-pregnancy body mass index (BMI), FT3, FT4, TSH, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), FBG, and the triglyceride-glucose (TyG) index.

Thyroid function indicators were assessed using the UniCel® DxI 800 Immunoassay System (Beckman Coulter, Inc., Brea, CA, USA). The reference range for FT4 was 7.64–16.03 pmol/L, and TPOAb ≥ 9 IU/mL was considered positive. Subclinical hypothyroidism (SCH) was defined as TSH > 4.0 mIU/L with FT4 within the reference range [10]. The other biochemical indicators were measured utilizing the ADVIA® 2400 Chemistry System (Siemens Healthcare Diagnostics Inc., Tarrytown, NY, USA), a fully automated biochemical analyzer. All procedures followed standard operating protocols.

The calculation formula for the TyG index was as follows:

$$\text{TyG index} = \text{Ln} [\text{fasting TG (mg/dL)} \times \text{FBG (mg/dL)} / 2] \text{ [17].}$$

2.4 Statistical Analyses

Normality of continuous variables was assessed via the Kolmogorov–Smirnov test. As the data were not normally distributed, continuous variables are reported as median (interquartile range, IQR). Categorical variables are presented as frequencies and percentages. For comparisons between the GDM and non-GDM groups, the Student's *t*-test or Mann–Whitney U test was employed, depending on data distribution. The chi-square test was conducted for categorical variables. Missing data were assumed to be missing at random (Supplementary Table 1) and were imputed using multiple imputation through the MICE package in R.

Initially, the correlation between GDM and each variable was evaluated using univariate logistic regression analysis. Collinearity diagnostics were conducted for variables with a $p < 0.05$ in univariate logistic regression analysis. A variance inflation factor (VIF) < 5 indicated no collinear-

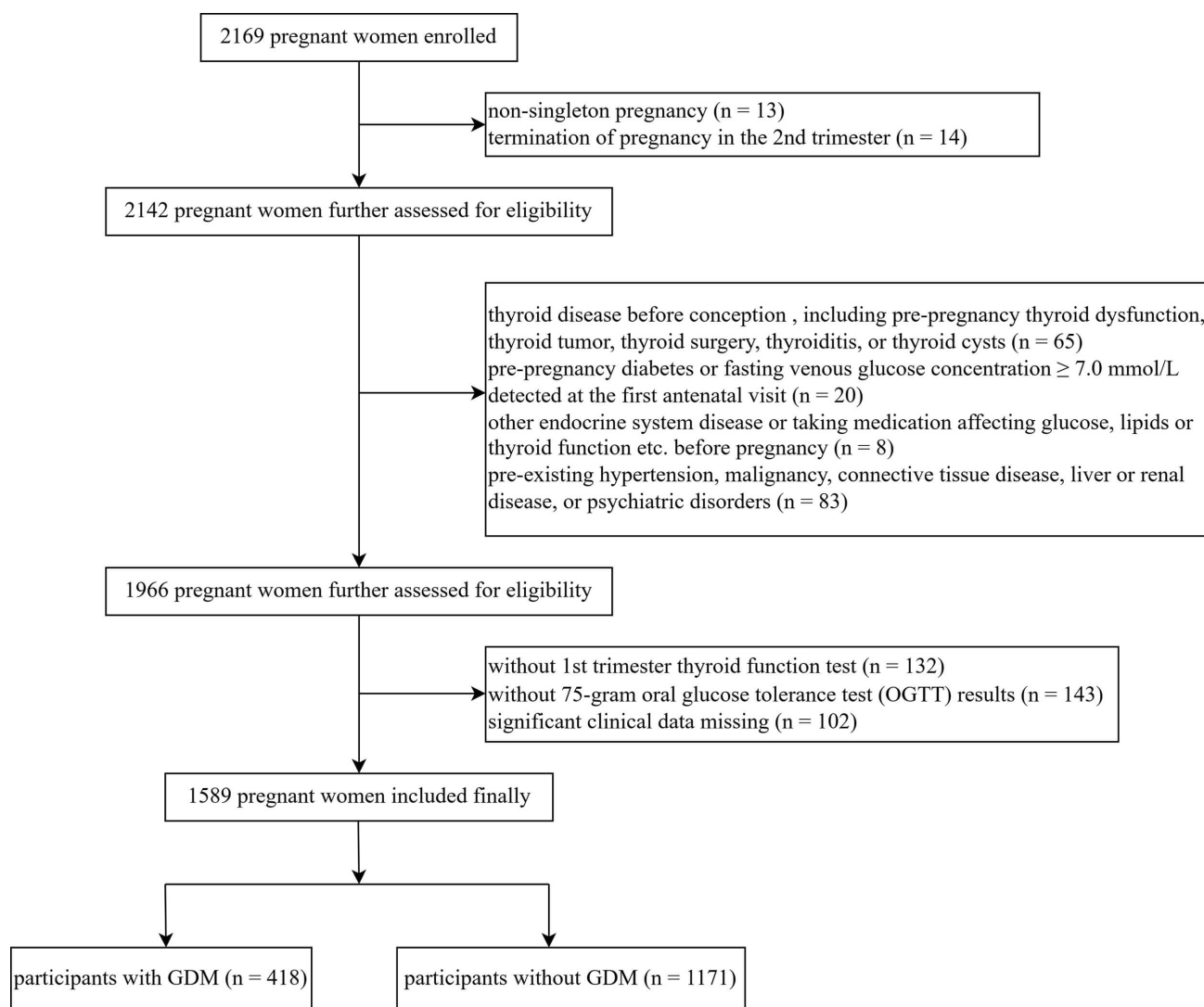


Fig. 1. Flowchart of participant selection. GDM, gestational diabetes mellitus.

ity between the independent variables; otherwise, severe collinearity existed. Based on these results, TG and other non-collinear variables ($p < 0.05$) were admitted into the multivariate logistic regression model. Spearman correlation analysis was used to assess the correlation among thyroid function indicators, lipid parameters, and the TyG index. Linear regression models were used to evaluate the associations of TG, TyG index, TG/HDL-C, TSH, FT3, FT4, TPOAb positivity, and the FT3/FT4 ratio with glucose concentrations at different time points during the OGTT.

The enrolled participants were stratified into quartile groups according to their TSH levels to further assess its association with GDM risk. Model 1 was unadjusted. Model 2 was adjusted for age and family history of diabetes. Model 3 additionally adjusted for pre-pregnancy BMI and TG in early pregnancy. Model 4 further adjusted for FBG in early pregnancy. FT3, FT4, the FT3/FT4 ratio, TyG index, and TG/HDL-C were also categorized into quartiles to evaluate their correlation with GDM risk. Due to collinear-

ity between TG and the TyG index and TG/HDL-C, TG was not included as an adjustment variable in the logistic regression models for these two parameters. Restricted cubic splines (RCS) analysis with four nodes (corresponding to the 5th, 35th, 65th, and 95th percentiles of TSH) was utilized to analyze the dose-response correlation and potential linear association between early-pregnancy TSH concentrations and GDM.

To investigate potential differences across various subgroups, all analyses were repeated stratified by pre-pregnancy BMI, age, TG, and TPOAb. Multiple sensitivity analyses were performed, including exclusion of participants with abnormal FT4 values during 10–13⁺6 weeks of gestation, missing FT4 values, and TSH >4 mIU/L during early pregnancy.

With 418 GDM events and 5 covariates in the final multivariate model, our study achieved an events-per-variable (EPV) of 83.6, which substantially exceeds the recommended minimum threshold of 10 [18].

Zstats software (Zhejiang Chinese Medical University, Hangzhou, Zhejiang, China; URL: <https://www.zstats.net>), Origin 2023 (OriginLab Corporation, Northampton, MA, USA), and R software (R Foundation for Statistical Computing, Vienna, Austria; version 4.4.0) were employed for data processing. Statistical significance was set at $p < 0.05$.

3. Results

3.1 Clinical Characteristics of Participants

Finally, the study included 1589 pregnant individuals, comprising 418 (26.31%) participants in the GDM group and 1171 (73.69%) participants with normal glucose tolerance in the non-GDM group. **Supplementary Table 2** presented baseline characteristics of 580 excluded individuals. As illustrated in Table 1, age, pre-pregnancy BMI, ALT, TG, TC, LDL-C, TyG index, TG/HDL-C, FBG, and OGTT values at different time points exhibited higher levels in the GDM group ($p < 0.05$). HDL-C was lower in the GDM group ($p < 0.05$). The GDM group exhibited significantly higher proportions of multiparous women and those with a family history of diabetes ($p < 0.05$). No significant differences were observed between groups for ethnicity, family history of hypertension, mode of conception, or AST level.

First-trimester FT3, TSH, and FT3/FT4 ratios were significantly higher in the GDM group than those in the non-GDM group (all $p < 0.05$). The proportion of TPOAb positivity was lower in the non-GDM group (8.03% versus 11.96%, $p = 0.016$). Participants in the non-GDM group exhibited higher FT4 concentrations ($p < 0.001$).

3.2 Outcomes of Univariate and Multivariate Analyses

Univariate logistic regression analysis was conducted to investigate factors associated with GDM occurrence from 24 to 28 weeks of gestation. As shown in Table 2, the following variables were included: family history of diabetes, multiparity, age, pre-pregnancy BMI, FBG, FT3, FT4, TSH, FT3/FT4 ratio, TPOAb positivity, ALT, TG, TC, HDL-C, LDL-C, TyG index, and TG/HDL-C. The variables with $p < 0.05$, including family history of diabetes, multiparity, age, pre-pregnancy BMI, FBG, FT4, TSH, TPOAb positivity, ALT, TG, HDL-C, and LDL-C, and confirmed as non-collinear (**Supplementary Table 3**), were analyzed by multiple logistic regression. As shown in **Supplementary Table 3**, TyG, TG/HDL-C, and TG all had VIF > 5 , indicating collinearity. Since both TyG and TG/HDL-C were derived from TG, we chose to include TG in the multivariate analysis. Multivariate analysis revealed that family history of diabetes (odds ratio [OR] = 1.79), age (OR = 1.08), pre-pregnancy BMI (OR = 1.07), FBG in early pregnancy (OR = 3.94), TSH (OR = 1.23), and TG (OR = 1.27) emerged as risk factors for GDM among pregnant individuals (all $p < 0.05$).

3.3 Correlation of Thyroid Function Parameters With Other Risk Factors

Supplementary Fig. 1 shows that FT3 and TSH presented a weak positive association with TG, the TyG index, and TG/HDL-C ($p > 0.05$). FT3/FT4 ratio was positively associated with TG, LDL-C, TyG index, and TG/HDL-C ($p < 0.05$). FT4 was negatively associated with TG, LDL-C, TyG index, and TG/HDL-C ($p < 0.05$). Lastly, there was no significant correlation between TPOAb and TG, HDL-C, LDL-C, TyG index, and TG/HDL-C ($p > 0.05$).

3.4 TG and Thyroid Parameters Associated With Glucose Concentrations at Specific OGTT Time Points

After adjusting for family history of diabetes, age, pre-pregnancy BMI, TSH, and FBG in the first trimester, TG, TyG index, and TG/HDL-C were all significantly associated with GDM ($p < 0.05$). The linear regression model revealed that TG, TyG index, and TG/HDL-C were positively correlated with 0 h-OGTT, 1 h-OGTT, and 2 h-OGTT in the second trimester (**Supplementary Table 4**).

Logistic regression model indicated a correlation between GDM and TSH, across various thyroid parameters, after adjustment for family history of diabetes, maternal age, pre-pregnancy BMI, and FBG during the first trimester (aOR = 1.27, 95% confidence interval [CI]: 1.15–1.41, $p < 0.001$). TSH was positively associated with 1 h-OGTT values ($\beta = 0.08$, 95% CI: 0.01–0.16, $p = 0.037$), but not significantly correlated with 0 h-OGTT and 2 h-OGTT values ($p > 0.05$). FT4 exhibited a negative association with 1 h-OGTT values ($\beta = -0.05$, 95% CI: -0.09 to -0.01 , $p = 0.016$) and 2 h-OGTT values ($\beta = -0.03$, 95% CI: -0.07 to -0.01 , $p = 0.040$). TPOAb was positively associated with 0 h-OGTT values ($\beta = 0.09$, 95% CI: 0.01–0.17, $p = 0.044$). Correlation between FT3 and the FT3/FT4 ratio and glucose concentration at different OGTT time points had no statistical significance ($p > 0.05$) (**Supplementary Table 5**).

3.5 Correlation Between TSH Quartiles and GDM Risk

The distribution of TSH quartiles varied significantly between GDM and non-GDM groups, as detailed in **Supplementary Table 6** ($\chi^2 = 32.72$, $p < 0.001$). In the GDM group, the highest percentage of pregnant individuals (35.41%) was observed in the Q4 TSH level. Using the Q1 group as the reference group, TSH levels at Q4 quartile were related to a heightened GDM risk (OR_{Q2}: 1.03, 95% CI: 0.73–1.43, $p = 0.879$; OR_{Q3}: 1.10, 95% CI: 0.79–1.53, $p = 0.580$; OR_{Q4}: 2.10, 95% CI: 1.54–2.88, $p < 0.001$) (Table 3). This association remained significant after adjustment for age, family history of diabetes, pre-pregnancy BMI, TG, and FBG in early pregnancy (OR_{Q4}: 1.92, 95% CI: 1.37–2.69, $p < 0.001$).

Fig. 2 demonstrates a linear dose-response correlation between TSH and GDM (p for overall < 0.001 , p for nonlinearity = 0.441). Across the full range of TSH values, each

Table 1. Demographic and clinical characteristics of the study participants.

Maternal characteristic	Total (n = 1589)	Non-GDM (n = 1171)	GDM (n = 418)	p-value
Age, M (Q ₁ , Q ₃), years	29.00 (27.00, 33.00)	29.00 (27.00, 32.00)	31.00 (28.00, 34.00)	<0.001
pre-pregnancy BMI, M (Q ₁ , Q ₃), kg/m ²	21.42 (19.61, 23.81)	21.06 (19.43, 23.31)	22.63 (20.61, 24.98)	<0.001
Ethnic, n (%)				0.883
Han	1545 (97.23)	1139 (97.27)	406 (97.13)	
Others	44 (2.77)	32 (2.73)	12 (2.87)	
Parity, n (%)				<0.001
Primiparous	891 (56.07)	700 (59.78)	191 (45.69)	
Multiparous	698 (43.93)	471 (40.22)	227 (54.31)	
Family history of hypertension, n (%)				0.813
Yes	226 (14.22)	168 (14.35)	58 (13.88)	
No	1363 (85.78)	1003 (85.65)	360 (86.12)	
Family history of diabetes, n (%)				0.013
Yes	94 (5.92)	59 (5.04)	35 (8.37)	
No	1495 (94.08)	1112 (94.96)	383 (91.63)	
Pregnancy mode, n (%)				0.381
Natural pregnancy	1528 (96.16)	1129 (96.41)	399 (95.45)	
ART	61 (3.84)	42 (3.59)	19 (4.55)	
FT3, M (Q ₁ , Q ₃), pmol/L	5.00 (4.65, 5.38)	4.97 (4.62, 5.36)	5.08 (4.69, 5.44)	0.025
FT4, M (Q ₁ , Q ₃), pmol/L	10.76 (9.70, 11.82)	10.90 (9.94, 11.96)	10.36 (9.16, 11.36)	<0.001
TSH, M (Q ₁ , Q ₃), mIU/L	1.35 (0.75, 2.00)	1.28 (0.72, 1.89)	1.56 (0.86, 2.53)	<0.001
FT3/FT4, M (Q ₁ , Q ₃)	0.47 (0.41, 0.52)	0.45 (0.41, 0.51)	0.50 (0.44, 0.55)	<0.001
TPOAb positive, n (%)				0.016
Yes	144 (9.06)	94 (8.03)	50 (11.96)	
No	1445 (90.94)	1077 (91.97)	368 (88.04)	
ALT, M (Q ₁ , Q ₃), U/L	11.00 (8.00, 16.00)	11.00 (8.00, 16.00)	12.00 (9.00, 16.00)	0.002
AST, M (Q ₁ , Q ₃), U/L	14.00 (13.00, 17.00)	14.00 (13.00, 17.00)	15.00 (13.00, 17.00)	0.683
TG, M (Q ₁ , Q ₃), mmol/L	1.23 (0.95, 1.60)	1.18 (0.91, 1.53)	1.38 (1.08, 1.78)	<0.001
TC, M (Q ₁ , Q ₃), mmol/L	4.31 (3.83, 4.85)	4.28 (3.81, 4.79)	4.40 (3.88, 4.97)	0.027
HDL-C, M (Q ₁ , Q ₃), mmol/L	1.69 (1.46, 1.95)	1.71 (1.48, 1.96)	1.64 (1.40, 1.93)	0.005
LDL-C, M (Q ₁ , Q ₃), mmol/L	2.14 (1.79, 2.54)	2.12 (1.77, 2.52)	2.21 (1.84, 2.66)	0.005
TyG index, M (Q ₁ , Q ₃)	8.44 (8.16, 8.72)	8.39 (8.12, 8.66)	8.58 (8.31, 8.87)	<0.001
TG/HDL-C, M (Q ₁ , Q ₃)	0.72 (0.53, 1.01)	0.69 (0.52, 0.96)	0.83 (0.61, 1.17)	<0.001
FBG in 1st trimester, M (Q ₁ , Q ₃), mmol/L	4.74 (4.49, 4.98)	4.69 (4.45, 4.92)	4.90 (4.63, 5.17)	<0.001
OGTT test in 2nd trimester, mmol/L				
0 h-OGTT, M (Q ₁ , Q ₃)	4.67 (4.47, 4.94)	4.60 (4.40, 4.78)	5.15 (4.78, 5.39)	<0.001
1 h-OGTT, M (Q ₁ , Q ₃)	8.09 (6.88, 9.34)	7.60 (6.61, 8.53)	10.07 (8.97, 10.85)	<0.001
2 h-OGTT, M (Q ₁ , Q ₃)	6.66 (5.84, 7.61)	6.33 (5.61, 7.10)	8.40 (7.05, 9.21)	<0.001

M (Q₁, Q₃), median (lower and upper quartiles); BMI, body mass index; ART, assisted reproductive technology; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid-stimulating hormone; TPOAb, thyroid peroxidase antibody; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; OGTT, oral glucose tolerance test; TyG index, triglyceride-glucose index.

1 mIU/L increase was associated with a 23% higher risk of GDM after multivariable adjustment (aOR = 1.23, 95% CI: 1.09–1.38). To further investigate data characteristics, we conducted an exploratory subgroup analysis based on the median TSH value. This analysis revealed a stronger correlation in the subgroup with higher TSH concentrations (≥ 1.35 mIU/L; OR = 1.42, 95% CI: 1.20–1.67, $p < 0.001$). In the subgroup with TSH below 1.35 mIU/L, the direc-

tion of the effect was consistent with the overall trend (OR = 1.11). However, it was not statistically significant ($p = 0.645$).

Additionally, we divided FT3, FT4, FT3/FT4 ratio, the TyG index, and TG/HDL-C into quartiles to examine associations between different levels of each parameter and GDM. As illustrated in **Supplementary Table 7**, when FT3 levels increased, the risk of GDM showed an upward trend

Table 2. Logistic regression analysis of risk factors for GDM.

Variables	Univariate regression analysis					Multivariate regression analysis				
	β	S.E	Z	p-value	Crude OR (95% CI)	β	S.E	Z	p-value	Adjusted OR (95% CI)
Family history of diabetes	0.54	0.22	2.46	0.014	1.72 (1.12~2.66)	0.58	0.29	2.03	0.042	1.79 (1.02~3.14)
Multiparous	0.57	0.11	4.95	<0.001	1.77 (1.41~2.21)	0.20	0.16	1.28	0.200	1.22 (0.90~1.66)
Age	0.10	0.01	7.19	<0.001	1.11 (1.08~1.14)	0.08	0.02	4.27	<0.001	1.08 (1.04~1.12)
Pre-pregnancy BMI	0.12	0.02	7.15	<0.001	1.13 (1.09~1.16)	0.07	0.02	2.96	0.003	1.07 (1.02~1.12)
FBG in 1st trimester	1.53	0.16	9.35	<0.001	4.61 (3.34~6.34)	1.37	0.20	6.91	<0.001	3.94 (2.67~5.82)
FT3	0.15	0.08	1.92	0.054	1.16 (1.00~1.36)	-	-	-	-	-
FT4	-0.16	0.04	-4.39	<0.001	0.85 (0.80~0.92)	-0.04	0.04	-1.24	0.217	0.96 (0.89~1.03)
TSH	0.27	0.05	5.51	<0.001	1.32 (1.19~1.45)	0.21	0.06	3.43	<0.001	1.23 (1.09~1.38)
FT3/FT4	0.65	0.42	1.56	0.120	1.92 (0.84~4.38)	-	-	-	-	-
TPOAb positive	0.44	0.19	2.39	0.017	1.56 (1.08~2.24)	0.34	0.21	1.61	0.107	1.41 (0.93~2.14)
ALT	0.02	0.01	2.18	0.029	1.02 (1.01~1.03)	0.01	0.01	1.02	0.306	1.01 (0.99~1.03)
TG	0.47	0.08	5.89	<0.001	1.59 (1.36~1.86)	0.24	0.09	2.54	0.011	1.27 (1.06~1.52)
TC	0.13	0.07	1.94	0.052	1.14 (1.00~1.29)	-	-	-	-	-
HDL-C	-0.38	0.16	-2.42	0.016	0.68 (0.50~0.93)	-0.21	0.20	-1.03	0.301	0.81 (0.55~1.20)
LDL-C	0.23	0.09	2.58	0.010	1.26 (1.06~1.51)	0.04	0.12	0.37	0.713	1.05 (0.83~1.32)
TyG	1.12	0.14	8.22	<0.001	3.06 (2.34~4.00)	-	-	-	-	-
TG/HDL-C	0.58	0.10	5.64	<0.001	1.79 (1.46~2.20)	-	-	-	-	-

OR, odds ratio; CI, confidence interval. Multivariate regression analysis, adjusted for family history of diabetes, multiparous, age, pre-pregnancy BMI, FBG in early pregnancy, FT4, TSH, TPOAb positive, ALT, TG, HDL-C, and LDL-C.

Table 3. GDM risk according to TSH quartile groups.

	Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
TSH quartile, GDM events (%)								
Q1 (0), 87/396 (21.97)	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Q2 (0.75), 89/397 (22.42)	1.03 (0.73~1.43)	0.879	1.04 (0.74~1.46)	0.828	0.96 (0.68~1.37)	0.826	1.08 (0.75~1.55)	0.684
Q3 (1.35), 94/398 (23.62)	1.10 (0.79~1.53)	0.580	1.04 (0.74~1.46)	0.821	0.91 (0.64~1.29)	0.595	0.98 (0.68~1.40)	0.900
Q4 (2.00), 148/398 (37.19)	2.10 (1.54~2.88)	<0.001	2.08 (1.51~2.86)	<0.001	1.81 (1.30~2.52)	<0.001	1.92 (1.37~2.69)	<0.001
p-value for trend	<0.001		<0.001		<0.001		<0.001	

Model 1: Crude. Model 2: Model 1 + age and diabetic family history. Model 3: Model 2 + pre-pregnancy BMI, and TG in early pregnancy; Model 4: Model 3+ FBG in early pregnancy.

(p for trend = 0.031). However, after further adjustment for FBG in the first trimester and TG in Models 3 and 4, this trend was no longer statistically significant (p for trend > 0.05). FT4 concentrations were negatively related to GDM risk. Compared to the Q1 group, the other groups all exhibited significantly reduced risks of GDM, with statistical differences observed in most models. The correlations were significant in Models 1 and 3 (p for trend < 0.05), whereas in Models 2 and 4, the p -values were slightly above 0.05. Higher FT3/FT4 ratio was correlated with progressively increased GDM odds (p for trend < 0.001), with the strongest association concentrated in the Q4 quartile (OR_{Q4}: 2.02, 95% CI: 1.37~2.99). This correlation and its trend remained significant after adjusting for covariates (OR_{Q4}: 1.55, 95% CI: 1.03~2.33, p = 0.038). For TyG index and TG/HDL-C, a clear dose-response correlation was consistently observed across all models (p < 0.05).

3.6 Subgroup Analysis

Subgroup analyses stratified by age, pre-pregnancy BMI, TG, and TPOAb examined the association between TSH and GDM (Table 4). In unadjusted models, significant associations were observed between TSH and GDM in early pregnancy in different subgroups. After controlling for relevant confounders, this correlation remained statistically significant. In interaction analysis of TSH and GDM in age, TG, and TPOAb subgroups, no interaction was observed between subgroups, before or after controlling for potential confounding variables (p for interaction > 0.05). Compared to the pre-pregnancy BMI <24 kg/m² subgroup, in the pre-pregnancy BMI ≥24 kg/m² subgroup, TSH exhibited an increased risk for GDM (OR = 1.61, 95% CI: 1.31~1.98 versus OR = 1.2, 95% CI: 1.07~1.35). After adjustment for age, family history of diabetes, FBG, and TG, the risk effect of TSH on GDM was more pronounced among individuals with pre-pregnancy BMI ≥24

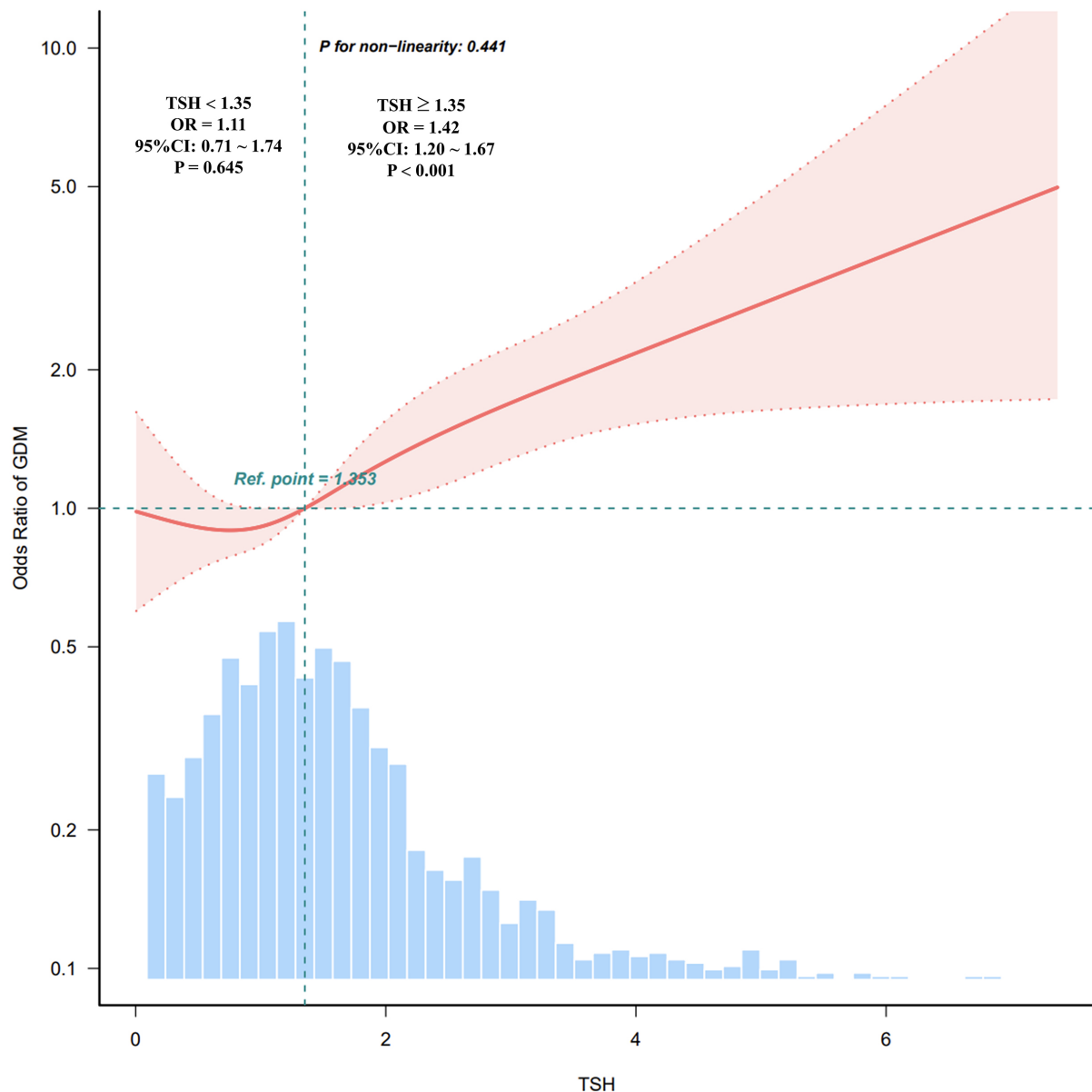


Fig. 2. RCS analysis demonstrated a significant linear association between TSH and GDM (p for overall < 0.001; p for non-linearity = 0.441). The model was adjusted for age, pre-pregnancy BMI, family history of diabetes, early pregnancy TG and FBG. A TSH concentration of 1.353 mIU/L (the median) was set as the reference. RCS, restricted cubic spline.

kg/m² (OR = 1.71, 95% CI: 1.36–2.14 versus OR = 1.17, 95% CI: 1.04–1.33). Significant interaction was observed across pre-pregnancy BMI subgroups (p for interaction = 0.012), which persisted after adjustment for confounders (p for interaction = 0.005). **Supplementary Table 8** illustrated that TSH at Q4 level exhibited an increased risk of GDM in subgroups with pre-pregnancy BMI < 24 kg/m² (aOR_{Q4} = 1.74, 95% CI: 1.17–2.58, p = 0.006). Notably, in the subgroup of pre-pregnancy BMI ≥ 24 kg/m², taking Q1 group as reference, when controlling for confounding variables, TSH at Q4 level exhibited greater odds of GDM (OR_{Q4} = 3.10, 95% CI: 1.69–5.69, p < 0.001; aOR_{Q4} = 4.24, 95% CI: 2.15–8.36, p < 0.001) (**Supplementary Table 9**).

3.7 Sensitivity Analyses

Table 5 shows that, to assess the robustness of results, several sensitivity analyses were performed. After excluding women with abnormal FT4 values (FT4 > 16.03 pmol/L, n = 27; FT4 < 7.64 pmol/L, n = 28, total = 55) and those with missing FT4 values (n = 344 participants, with only TSH results available), TSH remained positively associated with GDM in both crude (OR = 1.28, 95% CI: 1.15–1.42) and adjusted models (aOR = 1.26, 95% CI: 1.12–1.41; p < 0.05). The highest TSH quartile was associated with a 2.13-fold increased risk (aOR = 2.13, 95% CI: 1.45–3.15), showing a significant dose-response trend (p for trend < 0.001). Further exclusion of women with SCH (n = 54) yielded con-

Table 4. Subgroup analyses of the association between TSH and GDM risk.

	n (%)	GDM events (%)	OR (95% CI)	p-value	p for interaction
Pre-pregnancy BMI (kg/m ²)	1589 (100.00)	418 (26.31)	1.32 (1.19~1.45)	<0.001	
Unadjusted					0.012
<24	1217 (76.59)	280 (23.01)	1.20 (1.07~1.35)	0.002	
≥24	372 (23.41)	138 (37.10)	1.61 (1.31~1.98)	<0.001	
Adjusted ^a					0.005
<24	1217 (76.59)	280 (23.01)	1.17 (1.04~1.33)	0.011	
≥24	372 (23.41)	138 (37.10)	1.71 (1.36~2.14)	<0.001	
Age (years)	1589 (100.00)	418 (26.31)	1.32 (1.19~1.45)	<0.001	
Unadjusted					0.953
<35	1387 (87.29)	334 (24.08)	1.29 (1.16~1.44)	<0.001	
≥35	202 (12.71)	84 (41.58)	1.30 (1.03~1.65)	0.028	
Adjusted ^b					0.520
<35	1387 (87.29)	334 (24.08)	1.25 (1.11~1.40)	<0.001	
≥35	202 (12.71)	84 (41.58)	1.36 (1.06~1.75)	0.017	
TG (mmol/L)	1589 (100.00)	418 (26.31)	1.32 (1.19~1.45)	<0.001	
Unadjusted					0.829
<1.23	802 (50.47)	164 (20.45)	1.34 (1.17~1.55)	<0.001	
≥1.23	787 (49.53)	254 (32.27)	1.31 (1.14~1.51)	<0.001	
Adjusted ^c					0.852
<1.23	802 (50.47)	164 (20.45)	1.29 (1.11~1.49)	<0.001	
≥1.23	787 (49.53)	254 (32.27)	1.31 (1.12~1.52)	<0.001	
TPOAb positive	1589 (100.00)	418 (26.31)	1.32 (1.19~1.45)	<0.001	
Unadjusted					0.340
Yes	144 (9.06)	50 (34.72)	1.18 (0.94~1.47)	0.150	
No	1445 (90.94)	368 (25.47)	1.33 (1.19~1.49)	<0.001	
Adjusted ^d					0.441
Yes	144 (9.06)	50 (34.72)	1.15 (0.91~1.45)	0.255	
No	1445 (90.94)	368 (25.47)	1.28 (1.13~1.44)	<0.001	

a: adjustment for age, family history of diabetes, FBG, and TG in the first trimester. b: adjustment for family history of diabetes, pre-pregnancy BMI, FBG, and TG in the first trimester. c: adjustment for age, family history of diabetes, pre-pregnancy BMI, and FBG in the first trimester. d: adjustment for age, family history of diabetes, pre-pregnancy BMI, FBG in the first trimester, and TG.

sistent results. TSH remained significantly associated with GDM in both crude (OR = 1.37, 95% CI: 1.19–1.58) and adjusted models (aOR = 1.34, 95% CI: 1.15–1.56). The highest TSH quartile maintained elevated GDM risk (aOR = 1.84, 95% CI: 1.23–2.76, $p = 0.003$; p for trend = 0.004).

4. Discussion

GDM poses risks not only to maternal and neonatal health but also imposes a medical burden on health-care systems. At present, the recommended screening time for GDM in most countries is generally at 24–28 weeks of gestation. Early identification of high-risk individuals through a cost-effective screening approach, adjusting lifestyle modifications and timely interventions, may effectively reduce GDM incidence [19].

From the above results, elevated odds of GDM were associated with advanced age, family history of diabetes, higher pre-pregnancy BMI, elevated first-trimester TSH,

FBG, and TG concentrations. Maternal age at childbirth is on the rise worldwide, particularly in China. With the recent adjustment of China's birth policy and delayed childbearing caused by various social factors, the proportion of Chinese older pregnant women has shown a significant upward trend [20]. A prospective multicenter cohort study demonstrated a nonlinear positive correlation between maternal age and GDM, gestational hypertension, preeclampsia, placenta previa, preterm birth, macrosomia, cesarean section rate, and fetal congenital abnormalities [21]. It is crucial to encourage women of childbearing age to give birth at the appropriate age and enhance the management of older pregnant women in reducing adverse outcomes during the perinatal period for mothers and offspring. A family history of diabetes is a well-established predisposing factor for GDM [22,23,24]. Pregnant individuals with a family history of diabetes exhibited a 1.79-fold greater risk of GDM than their counterparts without a family history, as demonstrated in

Table 5. Association between TSH and GDM risk in sensitivity analyses across different clinical parameters.

GDM in Model 1 and 2 (n = 1190)		Model 1		Model 2		GDM in Model 3 and 4 (n = 1136)		Model 3		Model 4	
		OR (95% CI)	<i>p</i> -value	aOR (95% CI)	<i>p</i> -value			OR (95% CI)	<i>p</i> -value	aOR (95% CI)	<i>p</i> -value
TSH		1.28 (1.15~1.42)	<0.001	1.26 (1.12~1.41)	<0.001			1.37 (1.19~1.58)	<0.001	1.34 (1.15~1.56)	<0.001
Q1	65/298	1.00 (Reference)		1.00 (Reference)		62/284		1.00 (Reference)		1.00 (Reference)	
Q2	68/297	1.06 (0.72~1.57)	0.751	1.19 (0.78~1.80)	0.423	68/284		1.13 (0.76~1.67)	0.549	1.24 (0.81~1.90)	0.320
Q3	71/297	1.13 (0.77~1.65)	0.543	1.09 (0.72~1.64)	0.695	67/284		1.11 (0.75~1.64)	0.617	1.06 (0.69~1.63)	0.774
Q4	115/298	2.25 (1.57~3.23)	<0.001	2.13 (1.45~3.15)	<0.001	101/284		1.98 (1.36~2.87)	<0.001	1.84 (1.23~2.76)	0.003
<i>p</i> for trend			<0.001		<0.001				<0.001		0.004

Model 1 included sensitivity analyses excluding participants with abnormal FT4 values and missing FT4 values during 10–13⁺⁶ weeks of gestation.

Model 2 was adjusted for age, family history of diabetes, pre-pregnancy BMI, early pregnancy FBG, and TG, based on Model 1.

Model 3 exhibits sensitivity analyses excluding participants with abnormal FT4 values, missing FT4 values during 10–13⁺⁶ weeks of gestation, and SCH during early pregnancy.

Model 4 was adjusted for age, family history of diabetes, pre-pregnancy BMI, early pregnancy FBG, and TG, based on Model 3.

this study. Monod et al. [25] demonstrated that pregnant individuals with a family history of diabetes have a 1.91-fold higher risk of GDM, which is consistent with our findings. For pregnant individuals with normal early glycemic status, a correlation exists between first-trimester FBG and OGTT, as corroborated by several studies [26,27,28].

Our work focused on the correlation between early-pregnancy thyroid function and GDM. The results revealed that, as the TSH level increased during early gestation, the odds of GDM increased accordingly. Even after controlling for confounding factors, this effect still existed (aOR = 1.23, 95% CI: 1.09–1.38, $p < 0.001$). Several studies confirmed the association between abnormally elevated TSH and an increased risk of GDM [11,29,30,31]. The Spanish retrospective study, involving 6775 pregnant participants with normal first-trimester FT4 concentrations, indicated that the TSH concentrations ranging from 2.5 to 4.71 mIU/L exhibited 1.54-fold higher odds of developing GDM than those with TSH concentrations ranging from 0.31 to 2.49 mIU/L [11]. A meta-analysis revealed that maternal SCH during pregnancy correlates with a subsequent elevated risk of GDM [32]. However, the association between TSH and GDM remains inconsistent across studies. TSH concentrations were found to be negatively associated with the development of GDM, as reported by Zha et al. [33]. In Sağlam et al.'s study [12], the highest TSH tertiles during early- and mid-pregnancy displayed a decreased risk of GDM. The 2017 ATA guidelines increased the recommended upper reference limit for TSH in early pregnancy from 2.5 to 4.0 mIU/L [10]. In clinical practice, greater attention is typically given to individuals with abnormal TSH values and the metabolic status of pregnant individuals within the reference range (TSH <4.00 mIU/L) in early gestation is often overlooked, particularly those in the high-normal TSH range. We performed sensitivity analyses restricted to women with normal-range FT4 and TSH concentrations during early gestation. The results revealed that even high-normal TSH concentrations remained significantly correlated with a 1.84-fold higher risk of GDM (aOR = 1.84, 95% CI: 1.23–2.76, $p = 0.003$; p for trend = 0.004). This finding is consistent with the results by Yang et al. [30], which demonstrated that high-normal TSH ($1.04 < \text{TSH} < 4.0$ mIU/L) was a positive predictor of GDM in singleton pregnancies (aOR: 1.3, 95% CI: 1.0–1.6, $p = 0.024$). After further analysis, a significant linear dose-response correlation between TSH levels and GDM risk (p for overall < 0.001, p for nonlinearity = 0.441) was observed. The association appeared more significant at TSH levels above the median (≥ 1.35 mIU/L; OR = 1.42, 95% CI: 1.20–1.67), whereas the estimate below the median was not statistically significant (TSH <1.35 mIU/L; OR = 1.11, 95% CI: 0.71–1.74, $p = 0.645$). The discrepancies across subgroups may be attributed to a decrease in exposure variability within the low TSH range and a decrease in the inherent statistical power of subgroup analysis, which may limit accu-

rate effect estimation within this interval. Consequently, the overall linear association is considered the most robust core finding of this study, although subgroup results based on median cutoff points should be interpreted with caution. Huang et al. [29] demonstrated a nonlinear association between TSH and GDM ($p < 0.05$), with a threshold effect at 1.24 mIU/L. Below this threshold, the GDM risk increased with rising TSH, whereas above this level the upward trend was not evident. Maternal thyroid hormones changed with advancing gestation. In Huang et al.'s study [29], TSH was measured at 6–11 weeks of gestation, and the cohort included a proportion of multiple pregnancies, which may partly explain the differences between the two studies.

Furthermore, subgroup analysis revealed a significant interaction between pre-pregnancy BMI and TSH in relation to GDM risk (p for interaction = 0.005). Among women with pre-pregnancy BMI ≥ 24 kg/m², each one-unit increase in TSH was associated with a 71% higher risk of GDM (aOR = 1.71, 95% CI: 1.36–2.14, $p < 0.001$), compared with a 17% increase among those with pre-pregnancy BMI <24 kg/m² (aOR = 1.17, 95% CI: 1.04–1.33, $p = 0.011$). These results confirmed that obesity enhanced the correlation between TSH and GDM, consistent with those of Leng et al. [34]. TPOAb positivity was significantly linked to GDM in univariate analysis (OR = 1.56, 95% CI: 1.08–2.24, $p = 0.017$). However, after adjusting for confounders, this association was attenuated and became statistically nonsignificant (aOR = 1.41, 95% CI: 0.93–2.14, $p = 0.107$). The 2017 ATA guidelines recommend different management strategies for TPOAb-positive pregnant women based on their TSH levels. To investigate the association of TPOAb positivity with TSH levels and GDM risk, we conducted a subgroup analysis stratified by TPOAb status and determined that the interaction was nonsignificant (p for interaction = 0.441). Next, we examined the relevant literature and determined that the association between TPOAb and GDM may still warrant careful consideration. Li et al. [13] demonstrated that positive TPOAb is an independent factor for GDM. However, their analysis only included age and pre-pregnancy BMI as covariates. Studies, including those by Sitoris et al. [35] and Li et al. [36], did not consider the impact of lipid parameters in the development of GDM. According to Song et al. [14], positive TPOAb tests during 6–12 weeks of gestation did not differ significantly between the GDM and non-GDM groups. However, we acknowledged that, given that our cohort was a single-center cohort and the number of TPOAb-positive cases was small, only 9.06%, these findings need cautious interpretation. Future large-scale multicenter studies are warranted to clarify the interactions between thyroid autoimmunity, thyroid function, and GDM risk.

Consistent with multiple earlier studies [12,37,38], our research did not demonstrate a statistically significant association between first-trimester FT4 concentrations and overall GDM risk. However, some evidence suggests a

potential risk-reducing role of FT4 [39,40]. Further analysis revealed that FT4 levels were inversely correlated with 1-h postprandial and 2-h postprandial glucose during the OGTT, suggesting that FT4 may influence plasma glucose levels even when glycemia remains within the normal range. A previous study has demonstrated that an elevated FT3/FT4 ratio was linked to a higher odd of GDM, even after adjustment for potential confounders, including pre-pregnancy BMI and thyroid autoantibody status [40]. No significant relationship was detected when the FT3/FT4 ratio was examined as a continuous variable in our analysis. However, quartile analysis found that GDM risk was significantly elevated in pregnant women within the top quartile, with a significant trend across quartiles. This pattern supports the findings of Erkan Saglam et al. [12], who observed that in the first trimester, the highest tertile of the FT3/FT4 ratio increased the odds of GDM. FT3/FT4 ratio is regarded as an effective alternative biomarker for thyroid hormone metabolism and exhibits a significant association with IR [41]. A high FT3/FT4 ratio indicates the enhanced peripheral conversion of the less bioactive FT4 to the more bioactive FT3, potentially leading to a relative 'hypermetabolic' state and contributing to GDM development through mechanisms, including aggravated IR. In clinical practice, maintaining the FT3/FT4 ratio within an appropriate range may be more meaningful than focusing solely on its numerical value. Future prospective research with larger samples is essential to establish the optimal threshold of the FT3/FT4 ratio for predicting GDM.

Derived from FBG and TG, some studies suggest that the TyG index is positively associated with the homeostasis model of assessment for insulin resistance (HOMA-IR) index and may function as a potential surrogate marker for IR [42,43]. In a systematic review, Sánchez-García et al. [44] adopted a conservative position towards using the TyG index as a surrogate marker for IR, as the supporting evidence was limited to medium-to-low level. As a retrospective study, insulin levels were not assessed during early pregnancy, precluding direct calculation of HOMA-IR. Therefore, the TyG index was utilized as an indirect marker of IR. TSH was positively correlated with both TG and TyG index ($r = 0.036$ and 0.043 , respectively); however, these associations were not statistically significant. This may be attributed to several factors. First, most enrolled women were euthyroid, with only 3.40% (54/1589) exhibiting TSH levels >4 mIU/L. The limited variability of TSH within this normal range may have weakened its correlation with lipid parameters and the TyG index. IR is a core mechanism in the pathogenesis of GDM, directly driving lipid metabolism dysregulation (elevated TG and reduced HDL-C) and an increased TyG index. TSH may only indirectly influence lipid metabolism by regulating thyroid hormone levels, rather than exerting a direct effect. This indirect role may explain the weaker correlation between TSH and lipid parameters in euthyroid populations. Second, physiological

adaptations during early pregnancy may obscure these associations. The suppressive effect of human chorionic gonadotropin (hCG) on TSH, along with estrogen-induced increases in thyroxine-binding globulin [45], may potentially mask the direct relationship between TSH and lipid profiles. Notably, although the direct correlation between TSH and lipid parameters was not significant, our analyses revealed an interaction between TSH and pre-pregnancy BMI. This finding suggested that pre-pregnancy BMI, a marker of maternal metabolic reserve, could influence how TSH impacts GDM risk. Future investigation is warranted to explore the combined effects of BMI, thyroid parameters, and lipid indices on GDM development.

The mechanisms linking elevated TSH to GDM risk are multifactorial and possibly involve interactions between thyroid function, IR, inflammatory factors, and adipose tissue biology [46]. TSH has been shown to correlate positively with the HOMA-IR index, independent of type 2 diabetes [47]. In adipocytes, TSH can inhibit insulin signaling through the IRS-1/AKT/GLUT4 pathway, reducing glucose uptake, and contributing to IR [48]. This effect may be particularly relevant in overweight and obese individuals, as the enlargement and growth of adipocytes can lead to dysfunction of adipocytes, causing dysregulation of adipokines and proteins involved in lipid metabolism, blocking insulin signaling, and facilitating the occurrence of GDM [49,50]. Moreover, TSH receptors on adipocytes can stimulate the release of inflammatory cytokines, including interleukin-6, which may exacerbate IR [51,52]. The observed interaction between TSH and pre-pregnancy BMI indicates that individuals with elevated TSH and overweight or obesity may represent an especially high-risk group requiring closer monitoring and early lifestyle intervention.

This study has several strengths. First, thyroid function was assessed within a narrow gestational window (10–13⁺6 weeks), reducing variability in thyroid hormone levels attributable to advancing gestation, thereby enhancing the reliability of exposure assessment. Second, GDM was diagnosed based on OGTT performed at 24–28 weeks of pregnancy according to established diagnostic criteria, ensuring consistent outcome ascertainment. Third, sensitivity analyses restricted to euthyroid individuals with normal FT4 and TSH levels yielded consistent results. Fourth, multiple thyroid-related indicators—including TSH, FT3, FT4, FT3/FT4 ratio, and TPOAb—were comprehensively assessed, and the interaction between TSH and pre-pregnancy BMI was further investigated, providing novel insights into the synergistic effects of thyroid function and maternal metabolic status on GDM risk.

Limitations

Several limitations should be acknowledged. First, as this was a single-center study, its findings should be generalized with caution to populations with different racial, ge-

ographic, or socioeconomic backgrounds. Future multicenter studies across diverse populations are required to further confirm the generalizability of these conclusions. Second, despite statistical adjustments for multiple covariates, unmeasured potential confounding factors, including dietary composition, physical activity, educational level, and socioeconomic status, may still have introduced bias into the results. Third, selection bias cannot be completely ruled out. Although strict inclusion and exclusion criteria were implemented, the exclusion of certain individuals due to data completeness requirements (for example, 102 pregnant women with only outpatient records but substantial missing clinical data) may have affected the representativeness of the sample. Fourth, due to the lack of parameters associated with first-trimester IR, we were unable to systematically evaluate its effect on subsequent glycemic changes. Although we used proxy measures, including the TyG index and the FBG, the absence of direct IR data limits, to a certain extent, our ability to comprehensively characterize the underlying metabolic disturbances. Future studies should include additional metabolic markers to further clarify the potential interactions among IR, thyroid function, and GDM.

5. Conclusions

Elevated TSH concentrations during early gestation are independently associated with an increased likelihood of developing GDM, particularly among individuals with pre-pregnancy BMI ≥ 24 kg/m². This correlation remained robust in sensitivity analyses restricted to euthyroid women, suggesting that even high-normal TSH levels may have clinical relevance for GDM risk. Although no significant interaction was observed between TPOAb status and TSH, the limited number of TPOAb-positive cases warrants cautious interpretation. Moreover, although FT4 exhibited no significant association with overall GDM risk, its negative correlation with OGTT-derived glucose measures indicates a potential role in glycemic regulation. These findings emphasize the importance of thyroid function screening during early pregnancy and suggest that individuals with elevated TSH—particularly those with concurrent overweight or obesity—may benefit from closer monitoring and targeted lifestyle interventions to reduce GDM risk. Future multicenter prospective studies are needed to confirm these findings and establish optimal TSH cutoff values for GDM prediction across diverse populations.

Availability of Data and Materials

All data contained in this study can be obtained from the corresponding author upon reasonable request.

Author Contributions

JYZ, JJY, CYW, YS, GLJ and MS contributed to the study conception and design. JYZ, CYW, YS and JJY con-

tributed to data collection, collation and analysis. JJY and GLJ searched the literature. The first draft of the manuscript was written by JYZ and MS. MS was responsible for supervision, writing, reviewing and editing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was reviewed and approved by the Ethics Committee of the Suzhou Ninth Hospital affiliated to Soochow University (KYLW2026-011-01). Given the retrospective design of this study, the ethics committee formally granted a waiver of informed consent. All data were anonymized during data analysis, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.31083/CEOG50255>.

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