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Accuracy of HbA1c Levels as a Screening Tool for Gestational Diabetes Mellitus in Pregnant Women Prior to 20 Weeks of Gestation

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ABSTRACT

Objectives: To determine the diagnostic accuracy of hemoglobin A1c (HbA1c) measured before 20 weeks' gestation as a screening tool for gestational diabetes mellitus (GDM) in high-risk pregnancies, and to evaluate whether adding HbA1c to the conventional two-step algorithm (50-g glucose-challenge [50 g GCT] test followed by the 100-gram oral glucose tolerance test [100 g OGTT]) improves early detection.

Materials and Methods: This retrospective study included 282 pregnant women who met high-risk criteria for GDM. All participants underwent HbA1c measurement and a 50 g GCT at the first antenatal visit. Elevated HbA1c levels (≥ 5.7%) and/or abnormal GCT results (≥ 140 mg/dL) prompted patients to undergo a diagnostic 100g OGTT. Receiver operating characteristic curve analysis was used to identify the optimal HbA1c cutoff and to calculate sensitivity, specificity, PPV, NPV and accuracy. The screening performance of HbA1c was compared with 50 g GCT.

Results: Among 282 high-risk pregnancies, the overall prevalence of GDM was 29.8% (84/282), and 20.2% (57/282) were diagnosed before 20 weeks of gestation. Women with early-pregnancy HbA1c levels of 5.7–6.4% (38/282, 13.5%) had a significantly higher prevalence of GDM compared with those with HbA1c < 5.7% (71.1% vs 23.4%, respectively) and were more likely to require insulin therapy (13.2% vs 1.6%, $p < 0.001$). ROC analysis for HbA1c yielded an area under the curve of 0.716. Using an HbA1c threshold of ≥ 5.7% provided high specificity (92.9%) and overall accuracy (81.9%) but low sensitivity (38.6%), whereas the 50-g GCT demonstrated higher sensitivity (96.5%) with lower specificity (67.6%) and accuracy (73.4%).

Conclusion: HbA1c measured before 20 weeks in the 5.7–6.4% range could not replace glucose-based testing due to its limited sensitivity. However, with high specificity and an overall accuracy of 81.9%, it served as a valuable adjunct to the 50 g GCT within the two-step screening protocol, especially in cases where glucose loading was intolerant.

Keywords: hemoglobin A1c, early screening, gestational diabetes mellitus, 50-g glucose challenge test, oral glucose tolerance test

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ความแม่นยำของระดับฮีโมโกลบินเอวันซี (HbA1c) ในการเป็นเครื่องมือคัดกรองภาวะเบาหวานขณะตั้งครรภ์ก่อนอายุครรภ์ 20 สัปดาห์

ชัยวุฒ ไพบูลย์บริรักษ์

บทคัดย่อ

วัตถุประสงค์*: เพื่อประเมินความถูกต้องของการวัดระดับฮีโมโกลบินเอวันซี (HbA1c) ก่อนอายุครรภ์ 20 สัปดาห์ ในการคัดกรองภาวะเบาหวานขณะตั้งครรภ์ในสตรีกลุ่มเสี่ยงสูง และเสนอแนวทาง "HbA1c-first" ในกระบวนการตรวจคัดกรอง*

วัสดุและวิธีการ*: การศึกษาย้อนหลัง (retrospective cohort) ดำเนินการที่โรงพยาบาลกลาง สำนักการแพทย์ กรุงเทพมหานคร โดยคัดเลือกสตรีตั้งครรภ์ จำนวน 282 ราย (อายุ 18–45 ปี อายุครรภ์น้อยกว่า 20 สัปดาห์) ซึ่งมีปัจจัยเสี่ยงสูงต่อภาวะเบาหวานขณะตั้งครรภ์ ผู้เข้าร่วมได้รับการเจาะเลือดตรวจระดับ HbA1c และทดสอบ 50-g glucose challenge test (50g GCT) ในการฝากครรภ์ครั้งแรก หากผล 50g GCT ผิดปกติ (≥140 มก./ดล.) จะได้รับการตรวจยืนยันด้วยการทดสอบ 100-g oral glucose tolerance test (100g OGTT) ในกรณีที่พบ HbA1c ≥ ร้อยละ 6.5 ให้การวินิจฉัยเป็นเบาหวาน และส่งปรึกษาแพทย์ผู้เชี่ยวชาญ วิเคราะห์สมรรถนะของจุดตัด HbA1c ต่าง ๆ ด้วย receiver operating characteristic (ROC) เพื่อประเมินความไว ความจำเพาะ ค่าทำนายบวก และค่าทำนายลบ*

ผลการศึกษา*: พบอุบัติการณ์ของภาวะเบาหวานขณะตั้งครรภ์ ร้อยละ 29.8 โดยร้อยละ 20.2 ได้รับการวินิจฉัยก่อนอายุครรภ์ 20 สัปดาห์ กลุ่มที่มี HbA1c ร้อยละ 5.7–6.4 พบอัตราการเกิดภาวะเบาหวานขณะตั้งครรภ์สูงกว่ากลุ่ม HbA1c < ร้อยละ 5.7 อย่างมีนัยสำคัญ (ร้อยละ 71.1 เทียบกับร้อยละ 23.4, p < 0.001) และต้องใช้อินซูลินมากกว่า (ร้อยละ 13.2 เทียบกับร้อยละ 1.6, p < 0.001) การวิเคราะห์ ROC ให้ค่า area under the curve เท่ากับ 0.716 บ่งชี้ความแม่นยำที่ยอมรับได้ เมื่อใช้จุดตัด HbA1c ≥ ร้อยละ 5.7 ให้ความจำเพาะสูง (ร้อยละ 92.9) แต่ความไวต่ำ (ร้อยละ 38.6)*

สรุป*: การใช้ HbA1c ในช่วงร้อยละ 5.7–6.4 ตั้งแต่ก่อนอายุครรภ์ 20 สัปดาห์ มีประสิทธิภาพในการระบุกลุ่มเสี่ยงสูงที่ควรเข้ารับการตรวจยืนยันด้วย 50g GCT และ 100g OGTT ก่อนกำหนด ในทางกลับกัน หาก HbA1c ต่ำกว่าร้อยละ 5.7 อาจเลื่อนการตรวจแบบสองขั้นตอน ไปจนถึงช่วง 24–28 สัปดาห์ได้ แม้ว่าจะไม่สามารถใช้ HbA1c ทดแทนการประเมินระดับน้ำตาลด้วยกลูโคสได้ทั้งหมด แต่ด้วยความจำเพาะที่สูงจึงสามารถใช้เป็นเครื่องมือเสริมที่ช่วยเพิ่มประสิทธิภาพในการคัดกรองภาวะเบาหวานขณะตั้งครรภ์ได้เป็นอย่างดี*

คำสำคัญ*: ฮีโมโกลบินเอวันซี (HbA1c), การคัดกรองระยะแรก, เบาหวานขณะตั้งครรภ์, การทดสอบกลูโคส 50 กรัม (50-g GCT), การทดสอบกลูโคส 100 กรัม (OGTT)*

Introduction

Gestational diabetes mellitus is a significant pregnancy-related disorder that profoundly impacts maternal and fetal outcomes. Women diagnosed with GDM are more likely to develop type 2 diabetes mellitus (T2DM) later in life and face elevated risks of hypertensive disorders and preeclampsia[1]. Additionally, GDM is associated with adverse neonatal outcomes, including fetal macrosomia, birth trauma (e.g., brachial plexus injury and clavicular fractures), stillbirth, and neonatal hypoglycemia[2,3]. Children born to mothers with GDM are also more susceptible to obesity and metabolic diseases, such as T2DM[4]. Moreover, GDM increases healthcare utilization, underscoring the importance of accurate, early screening to mitigate potential adverse outcomes[5].

Currently, 6–8% of pregnant women are affected by GDM, a figure that rises to 7–14% among those with obesity[6]. Approximately 90% of these cases are first identified during pregnancy or at the initial antenatal visit[5,6]. GDM is defined as diabetes that is first diagnosed during pregnancy and includes both "true" gestational diabetes and previously undiagnosed pregestational diabetes[7]. This condition elevates risks for macrosomia, birth trauma, stillbirth, preeclampsia, increased cesarean delivery rates, and neonatal hypoglycemia[7, 8]. Consequently, early identification and effective management are paramount to safeguarding maternal and neonatal well-being.

Two principal approaches for diagnosing GDM currently exist: the one-step and the two-step methods. The two-step approach, recommended by the American College of Obstetricians and Gynecologists (ACOG), includes an initial 50g glucose challenge test (50g GCT) at 24–28 weeks, followed by a 100g oral glucose tolerance test (100g OGTT) if the 50g GCT result is abnormal (≥ 140 mg/dL)[7, 9]. Although both methods effectively detect GDM, they do so at different rates; however, research indicates no significant difference in maternal or neonatal complications between the two. Moreover, ACOG continues to endorse the two-step approach[7, 9-12]

Despite its effectiveness, the two-step approach primarily diagnoses GDM after 24–28 weeks of gestation and requires women to ingest glucose each time. Accordingly, both ACOG (2018) and the American Diabetes Association (ADA, 2023) suggest considering earlier screening (i.e., in the first trimester or at the first antenatal visit) for women at high risk of undiagnosed type 2 diabetes or early GDM—especially those with risk factors such as age over 35, obesity, a family history of diabetes, cardiovascular disease, or polycystic ovarian syndrome[9, 10]. Nevertheless, the optimal test for early screening remains undetermined[10].

Hemoglobin A1c (HbA1c) has drawn interest as a potential early screening tool because it reflects average blood glucose levels over the past 8–12 weeks[13]. It is widely used for diagnosing and monitoring nonpregnant patients with diabetes, generally applying an HbA1c ≥ 6.5% threshold to define diabetes[9, 14]. Furthermore, ADA (2023) guidelines advise HbA1c < 6.5% for women planning pregnancy to reduce congenital malformations, such as anencephaly, congenital heart disease, and renal anomalies, and to lower the risks of preeclampsia, fetal overgrowth, and preterm birth[10, 16–19]. During pregnancy, however, accelerated red blood cell turnover usually results in lower HbA1c levels than in nonpregnant individuals. Thus, ADA 2023 recommends an HbA1c target below 6.0% for most pregnant women, adjusting as needed to avoid maternal hypoglycemia[15].

Studies from multiple settings indicate that HbA1c might serve as an effective early screening test for GDM. One retrospective cohort study[20] showed that women with HbA1c values of 5.7–6.4% before 20 weeks were three times more likely to develop GDM than those with HbA1c < 5.7% (adjusted odds ratio 2.4). Another retrospective study[21] found that HbA1c ≤ 5.5% exhibited a negative predictive

value of 97%, demonstrating its capacity to rule out GDM early in pregnancy. Additional research comparing HbA1c with the 50g GCT[22] suggests that HbA1c has a lower threshold in pregnant women than in nonpregnant patients, making it a viable alternative for those unable to tolerate glucose ingestion. A prospective observational study[23] likewise supported HbA1c > 5.6% as a useful cutoff for detecting early GDM among high-risk pregnancies.

In summary, an internationally accepted strategy for early pregnancy GDM screening—particularly for high-risk women—has yet to be established. Emerging evidence nevertheless indicates that first-trimester HbA1c may reveal occult dysglycaemia well before the conventional 24-28 week window. On this premise, the present study measured HbA1c together with the 50 g GCT at the first antenatal visit in all high-risk pregnant women. Our primary objective was to determine the diagnostic accuracy of early pregnancy HbA1c as an adjunct to the conventional two-step screening strategy (50 g GCT followed by the 100 g OGTT reference test) and to quantify the incremental benefit that this combined approach offers for the early detection of gestational diabetes mellitus in Thai clinical practice.

Materials and Methods

This retrospective study was carried out at Bangkok Metropolitan Administration General Hospital (Klang hospital), to assess the accuracy of HbA1c for the early detection of GDM in women before 20 weeks of gestation. We reviewed the medical records of pregnant women who received antenatal care between 2023 and 2024. Participants were considered high-risk for GDM according to criteria adapted from both the Royal Thai College of Obstetricians and Gynecologists (RTCOG) and the ACOG Practice bulletin[10, 24]. The sample size was calculated based on the specificity of HbA1c at the 5.5% threshold (68%), as reported by Haddad et al[21], and an anticipated gestational diabetes mellitus (GDM) prevalence of 27.4% from institutional data. To estimate specificity with adequate precision (α = 0.05, d = 0.10), and accounting for a 20% attrition rate, a minimum of 139 participants was required.

Eligible individuals were 18–45 years of age, had a gestational age < 20 weeks, and fulfilled at least one high-risk criterion for GDM. These criteria included advanced maternal age (≥ 35 years), a first-degree relative with diabetes, a history of impaired glucose tolerance or HbA1c ≥ 5.7% before pregnancy, cardiovascular disease, or polycystic ovarian syndrome (PCOS). Obstetric risk factors encompassed previous GDM, a prior infant birth weight ≥ 4,000 g, unexplained stillbirth, recurrent pregnancy loss, and hydramnios. Physical-examination risk factors consisted of BMI ≥ 25 kg/m², hypertension (≥ 140/90 mmHg) coupled with BMI ≥ 23 kg/m², clinical signs of insulin resistance such as BMI ≥ 40 kg/m² or acanthosis nigricans, and glycosuria ≥ 1+ on at least two occasions[10, 24]. Women with preexisting diabetes, incomplete HbA1c or GDM screening data, or those who experienced fetal demise were excluded.

All included women underwent HbA1c testing at their first antenatal visit using the Cobas® Tina-quant Hemoglobin A1c Gen.3 assay, which is National Glycohemoglobin Standardization Program-certified and diabetes control and complications trial-standardized[25]. Based on established thresholds, HbA1c was categorized as < 5.7% (low risk), 5.7–6.4% (intermediate risk), or ≥ 6.5% (diabetes)[9, 14, 15]. Each participant also received the 50g GCT without fasting; a 1-hour blood glucose ≥ 140 mg/dL was considered abnormal[10]. Any woman with an abnormal 50g GCT underwent a 100g OGTT, interpreted using the Carpenter-Coustan criteria[12, 26].

Women with an HbA1c ≥ 6.5 % were classified as having overt diabetes mellitus and referred to an endocrinologist for definitive management. The diagnostic performance of early pregnancy HbA1c and the 50 g GCT was assessed against the 100 g OGTT, which served as the reference ("gold-standard") for GDM diagnosis. Women whose HbA1c fell between 5.7 % and 6.4 % or who produced an abnormal 50 g GCT result underwent a confirmatory 100 g OGTT. Participants with HbA1c < 5.7 % and a

normal 50 g GCT were re-screened at 24–28 weeks in accordance with the standard two-step ACOG protocol[9, 10]. A simplified outline of this screening strategy is shown in Fig. 1.

Data was analyzed using STATA 17.0. Continuous variables were reported as mean ± standard deviation (SD), while categorical variables were presented as frequencies (%). For comparisons, unpaired t-tests were used for continuous data, and chi-square or Fisher's exact tests were employed for categorical data. A p value < 0.05 was regarded as statistically significant. To identify the optimal HbA1c cutoff, we constructed a receiver operating characteristic (ROC) curve and computed sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The performance of HbA1c was compared to that of the 50g GCT, which is widely used in clinical practice but is not definitively considered a gold standard for early GDM screening[10, 23].

This study was approved by the Bangkok Metropolitan Administration Human Research Ethics Committee (BMAHREC). Because this research involved only the retrospective review of medical records, participants faced no additional risks, and all patient data were anonymized. Women diagnosed with GDM were managed according to institutional prenatal care guidelines, including self-monitoring of blood glucose, dietary counseling, and referral to specialists as needed.

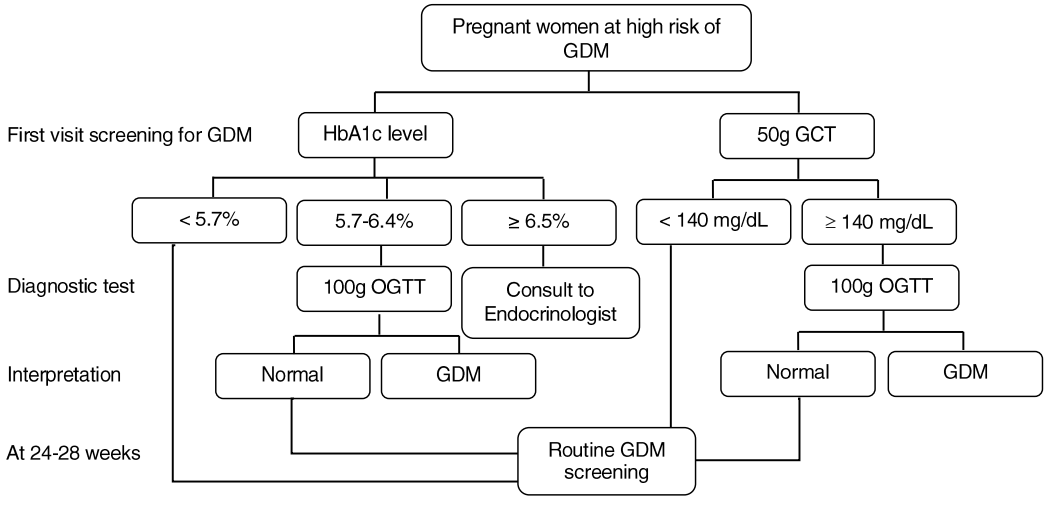

Fig. 1. Screening and diagnostic pathway for gestational diabetes mellitus (GDM) in high-risk pregnant women.

GDM: gestational diabetes mellitu, HbA1c: hemoglobin A1c, GCT: glucose challenge test, OGTT: oral glucose tolerance test

Results

A total of 463 pregnant women attended antenatal care (ANC) at Bangkok Metropolitan Administration General Hospital between January 2023 and April 2024. Following the inclusion criteria, 379 participants met the eligibility requirements for this study. A total of 97 women were excluded due to pre-existing diabetes (n = 21), lack of glucose screening (n = 4), fetal demise (n = 14), severe fetal anomalies leading to pregnancy termination (n = 2), molar pregnancy (n = 1), chromosomal abnormalities (n = 1), or incomplete data due to ANC transfer to other facilities (n = 54). This left 282 participants for final analysis (Fig. 2).

The baseline characteristics of the study population are summarized in Table 1. The mean maternal age was 30.71 ± 5.88 years, and the mean pre-pregnancy BMI was 25.69 ± 5.04 kg/m², with

55.3% (n = 156) classified as overweight or obese (BMI ≥ 25 kg/m²). Among the participants, 31.6% (n = 89) were primigravida, while 68.4% (n = 193) had previous pregnancies. The history of GDM in previous pregnancies was noted in 6.7% (n = 19) of cases. The mean HbA1c level was 5.19 ± 0.43%, and 45.4% (n = 128) had a positive 50g GCT (≥ 140 mg/dL). The overall GDM diagnosis rate was 29.8% (n = 84), with 20.2% (n = 57) diagnosed before 20 weeks of gestation and 9.6% (n = 27) diagnosed after 20 weeks. A small proportion, 3.2% (n = 9), required insulin therapy.

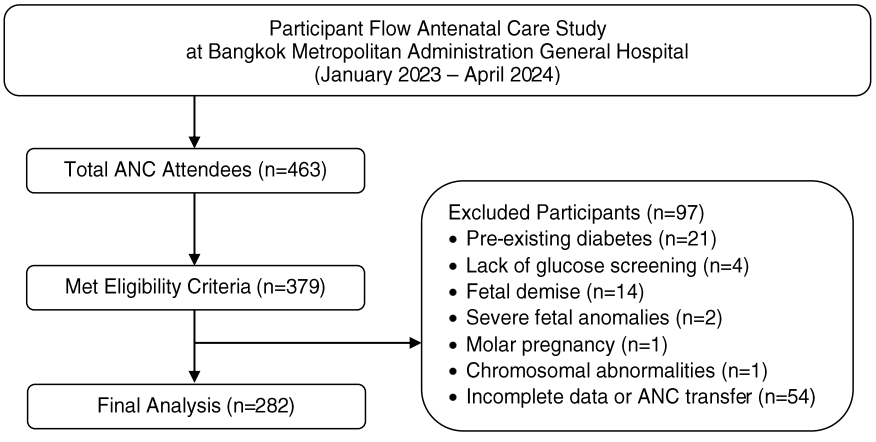

Fig. 2. Flowchart of participant selection for the study.

Table 1. Demographics of study population.

Demographics of study population	
Variable	**n = 282**
Age (years), mean ± SD	30.71 ± 5.88
Pre-pregnancy BMI (kg/m²), mean ± SD	25.69 ± 5.04
BMI ≥ 25 (kg/m²), n (%)	156 (55.3%)
Parity	
- Nulliparous, n (%)	89 (31.6%)
- Multiparous, n (%)	193 (68.4%)
Previous pregnancy GDM, n (%)	19 (6.7%)
HbA1c value (%), mean ± SD	5.19 ± 0.43
50 g GCT ≥ 140 mg/dL (screening test positive), n (%)	128 (45.4%)
GA at screening test	11 weeks 1 day
GDM diagnosis during pregnancy, n (%)	84 (29.8%)
Diagnosis GDM at GA ≤ 20 weeks, n (%)	57 (20.2%)
Diagnosis GDM at GA > 20 weeks, n (%)	27 (9.6%)
Need insulin treatment, n (%)	9 (3.2%)

BMI: body mass index, GDM: gestational diabetes mellitus, GCT: glucose challenge test, GA: gestational age, SD: standard deviation

Among the 282 participants, 38 women (13.5%) had HbA1c levels between 5.7–6.4%, while 244 women (86.5%) had HbA1c < 5.7%. The comparative analysis revealed significant differences in metabolic

parameters (Table 2).

Women in the HbA1c 5.7–6.4% group had significantly higher pre-pregnancy BMI ($p < 0.001$) and were more likely to have BMI ≥ 25 kg/m² ($p = 0.005$). The GDM diagnosis rate was significantly higher in this group (71.1% vs 23.4%, $p < 0.001$), with more cases diagnosed before 20 weeks ($p < 0.001$). The need for insulin therapy was also significantly increased ($p < 0.001$).

To assess whether HbA1c 5.7–6.4% could be a substitute for 50g GCT, a direct comparison was conducted between HbA1c 5.7–6.4% (n = 38) and GCT ≥ 140 mg/dL (n = 128), with key findings summarized in Table 3.

Table 2. Outcome based on screening test results between HbA1c < 5.7% and HbA1c 5.7 - 6.4%.

Outcome based on screening test results between HbA1c < 5.7% and HbA1c 5.7 - 6.4%			
Variable	**HbA1c < 5.7% (n = 244)**	**HbA1c 5.7 - 6.4% (n = 38)**	**p value**
Age (years), mean ± SD	30.62 ± 5.94	31.29 ± 5.51	0.516
Advanced maternal age (≥ 35-year-old)	73 (29.9%)	11 (28.9%)	0.903
Pre-pregnancy BMI (kg/m²), mean ± SD	25.27 ± 4.95	28.44 ± 4.82	< 0.001*
BMI ≥ 25 (kg/m²), n (%)	127 (52%)	29 (76.3%)	0.005*
Parity			0.261
- Nulliparous, n (%)	80 (32.8%)	9 (23.7%)	
- Multiparous, n (%)	164 (67.2%)	29 (76.3%)	
Previous pregnancy GDM, n (%)	15 (6.1%)	4 (10.5%)	0.317
GDM diagnosis during pregnancy, n (%)	57 (23.4%)	27 (71.1%)	< 0.001*
Diagnosis GDM at GA ≤ 20 weeks, n (%)	35 (14.3%)	22 (57.9%)	< 0.001*
Diagnosis GDM at GA > 20 weeks, n (%)	22 (9%)	5 (13.2%)	0.42
Need insulin treatment, n (%)	4 (1.6%)	5 (13.2%)	< 0.001*

SD: standard deviation, BMI: body mass index, GDM: gestational diabetes mellitus, GA: gestational age

Table 3. Baseline characteristics and pregnancy outcomes in participants with HbA1c 5.7–6.4% versus 50-g glucose challenge test (GCT ≥ 140 mg/dL).

Variable	HbA1c 5.7–6.4% (n = 38)	GCT ≥ 140 mg/dl (n = 128)	p value
Age (years), mean ± SD	31.29 ± 5.51	31.72 ± 5.65	0.68
Advanced maternal age (≥ 35-year-old), n (%)	11 (28.9%)	45 (35.2%)	0.477
Pre-pregnancy BMI (kg/m²), mean ± SD	28.44 ± 4.82	26.08 ± 4.85	0.009*
BMI ≥ 25 (kg/m²), n (%)	29 (76.3%)	71 (55.5%)	0.021*
Parity			0.325
- Nulliparous, n (%)	9 (23.7%)	41 (32%)	
- Multiparous, n (%)	29 (76.3%)	87 (68%)	
Previous pregnancy GDM, n (%)	4 (10.5%)	8 (6.3%)	0.371
GDM diagnosis during pregnancy, n (%)	27 (71.1%)	72 (56.3%)	0.102
Diagnosis GDM at GA ≤ 20 weeks, n (%)	22 (57.9%)	55 (43%)	0.105
Diagnosis GDM at GA > 20 weeks, n (%)	5 (13.2%)	17 (13.3%)	0.984
Need insulin treatment, n (%)	5 (13.2%)	9 (7%)	< 0.001*

SD: standard deviation, BMI: body mass index, GDM: gestational diabetes mellitus, GA: gestational age

The results indicated that women in the HbA1c 5.7–6.4% group had significantly higher pre-pregnancy BMI and were more likely to require insulin therapy compared to the GCT ≥ 140 mg/dL group ($p < 0.001$). However, the overall GDM diagnosis rate was not significantly different between the two groups ($p = 0.102$).

The ROC curve analysis was conducted to assess the diagnostic performance of HbA1c for early GDM detection, yielding an area under the curve (AUC) of 0.716 (95%CI 0.635–0.798), indicating acceptable diagnostic accuracy. Since an AUC between 0.7–0.8 suggests acceptable diagnostic accuracy, this supports the feasibility of HbA1c as a screening tool (Fig. 3).

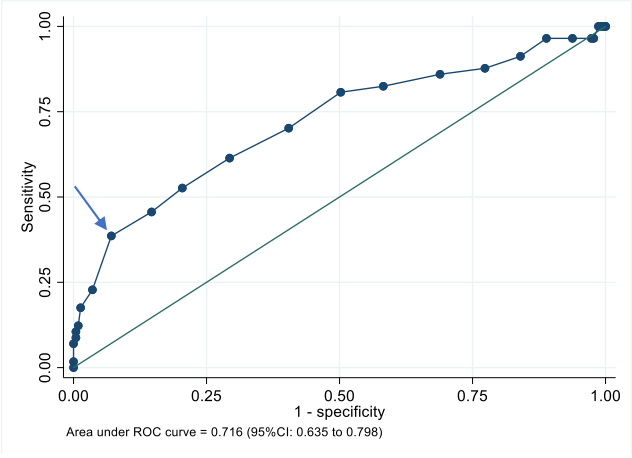

Fig. 3. Receiver operating characteristic curve for HbA1c cutoff in early GDM screening.

Further analysis using the Youden Index initially suggested that an HbA1c cutoff of ≥ 5.5% provided an optimal balance of sensitivity (52.6%), specificity (79.6%), and overall accuracy (74.1%). However, we selected ≥ 5.7% due to its notably higher specificity (92.9%), resulting in fewer false positives. Although this cutoff yields a lower sensitivity (38.6%)—and might therefore miss some early GDM cases—it remains effective for confirming high-risk pregnancies and reducing overdiagnosis. Meanwhile, HbA1c ≥ 6.0% demonstrated near-perfect specificity (99.1%) but very low sensitivity (12.3%), limiting its practicality for broad screening while underscoring its potential to identify severe cases.

Consequently, using HbA1c 5.7–6.4% as a threshold is a practical approach for pinpointing women who should undergo further evaluation

with the 50-g glucose challenge test (50g GCT) and, if indicated, confirmatory testing via the 100-g oral glucose tolerance test (OGTT) (Table 4).

Table 4. Receiver operating characteristic analysis for determining the optimal HbA1c cutoff in early gestational diabetes detection.

HbA1C cutoff ≥	True +	False +	False -	True -	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy	False positive rate (%)
3.6	57	224	0	1	100.0%	0.4%	20.3%	100.0%	20.6%	99.6%
3.8	57	223	0	2	100.0%	0.9%	20.4%	100.0%	20.9%	99.1%
4.1	57	222	0	3	100.0%	1.3%	20.4%	100.0%	21.3%	98.7%
4.4	55	220	2	5	96.5%	2.2%	20.0%	71.4%	21.3%	97.8%
4.5	55	219	2	6	96.5%	2.7%	20.1%	75.0%	21.6%	97.3%
4.6	55	211	2	14	96.5%	6.2%	20.7%	87.5%	24.5%	93.8%
4.7	55	200	2	25	96.5%	11.1%	21.6%	92.6%	28.4%	88.9%
4.8	52	189	5	36	91.2%	16.0%	21.6%	87.8%	31.2%	84.0%
4.9	50	174	7	51	87.7%	22.7%	22.3%	87.9%	35.8%	77.3%
5.0	49	155	8	70	86.0%	31.1%	24.0%	89.7%	42.2%	68.9%
5.1	47	131	10	94	82.5%	41.8%	26.4%	90.4%	50.0%	58.2%
5.2	46	113	11	112	80.7%	49.8%	28.9%	91.1%	56.0%	50.2%
5.3	40	91	17	134	70.2%	59.6%	30.5%	88.7%	61.7%	40.4%
5.4	35	66	22	159	61.4%	70.7%	34.7%	87.8%	68.8%	29.3%
5.5	30	46	27	179	52.6%	79.6%	39.5%	86.9%	74.1%	20.4%
5.6	26	33	31	192	45.6%	85.3%	44.1%	86.1%	77.3%	14.7%
5.7	22	16	35	209	38.6%	92.9%	57.9%	85.7%	81.9%	7.1%
5.8	13	8	44	217	22.8%	96.4%	61.9%	83.1%	81.6%	3.6%
5.9	10	3	47	222	17.5%	98.7%	76.9%	82.5%	82.3%	1.3%
6.0	7	2	50	223	12.3%	99.1%	77.8%	81.7%	81.6%	0.9%
6.1	6	1	51	224	10.5%	99.6%	85.7%	81.5%	81.6%	0.4%
6.2	5	1	52	224	8.8%	99.6%	83.3%	81.2%	81.2%	0.4%
6.3	4	0	53	225	7.0%	100.0%	100.0%	80.9%	81.2%	0.0%
6.4	1	0	56	225	1.8%	100.0%	100.0%	80.1%	80.1%	0.0%

PPV: positive predictive value, NPV: negative predictive value

The predictive capability of HbA1c 5.7–6.4% in estimating the likelihood of 50g GCT positivity (≥ 140 mg/dL) was analyzed, with the results presented in (Table 5).

Table 5. Predictive value of HbA1c 5.7–6.4% for 50g GCT (≥ 140 mg/dL) positivity.

Screening method	Sensitivity (%) (95%CI)	Specificity (%) (95%CI)	PPV (%) (95%CI)	NPV (%) (95%CI)	Accuracy (%) (95%CI)
HbA1c 5.7-6.4%	23.44 (16.41 - 31.74)	94.81 (90.02 - 97.73)	78.95 (62.68 - 90.45)	59.84 (53.39 - 66.04)	62.4 (56.5 – 68.1)

CI: confidence interval, PPV: positive predictive value, NPV: negative predictive value

Among individuals with HbA1c 5.7–6.4%, the probability of obtaining a positive 50g GCT result was reflected in the positive predictive value (PPV) of 78.9%, indicating that nearly four out of five women with HbA1c 5.7–6.4% were likely to have a GCT ≥ 140 mg/dL. Conversely, the negative predictive value (NPV) was 59.8%, suggesting that among those with HbA1c < 5.7%, approximately six out of ten women would have a GCT result below the threshold of 140 mg/dL.

The overall sensitivity of 23.4% implies that HbA1c 5.7–6.4% captures only a small proportion of those who will test positive on the 50g GCT, while the specificity of 94.8% demonstrates that those with HbA1c below 5.7% are highly unlikely to have GCT ≥140 mg/dL. The accuracy of 62.4% indicates moderate predictive reliability of HbA1c in estimating 50g GCT positivity.

These findings suggested that while HbA1c 5.7–6.4% strongly predicted a positive 50g GCT (high PPV), its low sensitivity limited its ability to detect all potential positive cases. This statistical insight can aid in understanding the role of HbA1c as a potential risk stratification marker for GDM screening.

Table 6 shows that an HbA1c threshold of 5.7–6.4% yields an overall diagnostic accuracy of 81.9% (95 %CI 76.9–86.2) to predict early GDM, surpassing the 73.4% (95 %CI 67.8–78.5) achieved with the conventional 50 g GCT. This 8.5 percentage point advantage was driven by the markedly higher specificity of HbA1c (92.9% vs 67.6%), which offset its lower sensitivity (38.6 % vs 96.5 %). Consequently, a positive HbA1c more reliably indicated true GDM (PPV 57.9% vs 42.9%), whereas a negative 50 g GCT remained superior for ruling out the condition (NPV 98.7%).

Table 6. Diagnostic performance of HbA1c 5.7–6.4% and the 50g GCT in early detection of gestational diabetes mellitus.

Screening method	Sensitivity (%) (95%CI)	Specificity (%) (95%CI)	PPV (%) (95%CI)	NPV (%) (95%CI)	Accuracy (%) (95%CI)
HbA1c 5.7 - 6.4%	38.6 (26 - 52.43)	92.89 (88.71 - 95.88)	57.89 (40.82 - 73.69)	85.66 (80.62 - 89.8)	81.91 (76.92 – 86.23)
50g GCT ≥ 140 mg/dL	96.49 (87.89 - 99.57)	67.56 (61.01 - 73.63)	42.97 (34.26 - 52.01)	98.7 (95.39 - 99.84)	73.4 (67.84 – 78.47)

CI: confidence interval, PPV: positive predictive value, NPV: negative predictive value

Discussion

This retrospective analysis of 282 high-risk Thai pregnant women revealed a significant burden of dysglycemia, with 29.8% diagnosed with gestational diabetes mellitus (GDM) and 20.2% identified by or before 20 weeks of gestation. These rates were higher

than the 14.4% early-GDM prevalence reported in a population-based first-trimester cross-sectional Thai study[27] and exceed the 16.4% total GDM prevalence found in the large prospective study[28]. This elevated prevalence was primarily attributable to the intentional recruitment of high-risk women (mean pre-pregnancy BMI 25.7 kg/m²; 55% overweight or obese) and systematic early screening with both HbA1c and the 50 g GCT at a median gestational age of 11 weeks. Early testing may have captured previously high risk for GDM, consistent with findings from Hinkle et al, who observed that 0.1% increase in first-trimester HbA1c was associated with a 22% increased risk of GDM[29].

Comparative data from Thai studies demonstrated a clear trend: elevated BMI was associated with a higher incidence of early GDM. Our study population's average BMI 25.7 kg/m² lied between the lean cohort (mean BMI 24.4 kg/m²)[30] and the heavier group[31], in which 78% had a BMI > 22.9 kg/m². This aligned with international findings suggesting that a first-trimester HbA1c ≥ 5.7% may reflect underlying beta-cell dysfunction even before full insulin resistance develops[32], highlighting the need for population-adapted screening thresholds.

The predictive performance of HbA1c at a threshold of 5.7% in our study demonstrated a specificity of 92.9%, sensitivity of 38.6%, and an area under the curve (AUC) of 0.716, indicating acceptable discriminative ability. This compares favourably with previously reported thresholds, such as 5.4% (AUC 0.706, sensitivity 61.8%, specificity 68.3%)[33], 5.45% (AUC 0.84, sensitivity 54.8%, specificity 96.8%)[28], and 5.8% (specificity 100%, sensitivity 17.1%)[30], although the latter studies involved participants screened beyond 24 weeks' gestation. In contrast, the 50 g GCT at a threshold of ≥ 140 mg/dL yielded a sensitivity of 96.5%, specificity of 67.6%, PPV of 43.0%, NPV of 98.7%, and overall accuracy of 73.4%. HbA1c testing, by comparison, offered higher specificity and superior overall accuracy (81.9%). These findings illustrated the trade-off between maximizing case detection and minimizing false positives and support the role of HbA1c at 5.7% as an efficient and practical early adjunct to conventional GDM screening. This approach may be particularly advantageous in resource-limited settings or for pregnant women unable to tolerate oral glucose ingestion.

A unique strength of our study was the generation of a detailed ROC matrix encompassing HbA1c values from 3.6% to 6.4% increments in 0.1%. This provided a flexible framework for customizing screening thresholds based on institutional prevalence rates and local resource availability. For example, high-risk maternal-fetal clinics aiming to minimize false negatives may adopt a threshold of 5.4% (sensitivity ≈ 60%, likelihood ratio (LR) 0.59), consistent with data[33], facilitating timely referral for OGTT. Conversely, community hospitals facing OGTT overcapacity may choose a threshold of 5.7% to achieve specificity > 90% (LR+ ≈ 5.4), as reported[28, 32], where HbA1c ≥ 5.7% effectively predicted insulin requirement (odds ratio ≈ 4) and correlated with a 2- to 4-fold increased risk of delivering large for gestational age neonates.

Strengths of this study included its real-world, resource-conscious design, targeted focus on high-risk Asian populations, and early gestational data collection. Limitations comprised its retrospective single-center nature, modest sample size, and the potential for ethnic bias in HbA1c interpretation. Additionally, which limited the generalizability of specificity and overall accuracy estimates. Nonetheless, post hoc 95%CI for specificity (88.7–95.9%) and accuracy (76.9–86.2%) supported the internal validity of our findings. Future prospective studies in broader-risk populations with larger sample sizes are warranted to refine the HbA1c cutoff and validate these performance indices.

Conclusion

In conclusion, HbA1c measured before 20 weeks in the 5.7–6.4% range cannot replace glucose-based testing due to its limited sensitivity. However, with high specificity and an overall accuracy of 81.9%, it served as a valuable adjunct to the 50 g GCT within

the two-step screening protocol. First-trimester HbA1c enhances diagnostic precision, facilitates early risk stratification, and offers a pragmatic alternative when glucose loading is intolerant (e.g., severe hyperemesis gravidarum), thereby improving both clinical efficiency and the quality of GDM detection in high-risk Thai pregnancies.

Potential conflicts of interest

The author declares no conflicts of interest.

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