



การศึกษาเปรียบเทียบระหว่างระดับฮีโมโกลบินเอวันซี และระดับน้ำตาลในเลือดหลังอดอาหารในผู้รับบริการ ตรวจสุขภาพประจำปี

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A Comparative Study of HbA1c and Fasting Plasma Glucose in Annual Health Check-Up Participants

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บทคัดย่อ

ภูมิหลังและวัตถุประสงค์: จำนวนผู้ป่วยเบาหวานมีแนวโน้มเพิ่มขึ้นทั่วโลก การวินิจฉัยเบาหวานทำได้ทั้งวัดระดับน้ำตาลในเลือดหลังอดอาหารและฮีโมโกลบินเอวันซี ในประเทศไทยโดยเฉพาะภาคอีสานพบภาวะฮีโมโกลบินผิดปกติชนิด อี ได้มาก ทำให้รบกวนการวินิจฉัยเบาหวานด้วยระดับฮีโมโกลบินเอวันซี การศึกษานี้มีวัตถุประสงค์เพื่อศึกษาเปรียบเทียบการวินิจฉัยเบาหวานโดยใช้ระดับฮีโมโกลบินเอวันซี และระดับน้ำตาลในเลือดหลังอดอาหารรวมถึงผลกระทบของภาวะฮีโมโกลบินผิดปกติต่อการแปลผล

วิธีการศึกษา: การศึกษาภาคตัดขวางในกลุ่มบุคลากรในโรงพยาบาลขอนแก่น ที่ได้รับการตรวจสุขภาพประจำปีระหว่างเดือนกันยายนถึงเดือนธันวาคม 2561 จำนวน 893 รายที่ได้รับการตรวจทั้งระดับน้ำตาลในเลือดและระดับฮีโมโกลบินเอวันซี วิเคราะห์ข้อมูลทางสถิติใช้ Stata version 6.0 ใช้ค่าความถี่ ร้อยละ ค่าเฉลี่ย ส่วนเบี่ยงเบนมาตรฐาน Pearson Chi-square test, two-tailed tests, และ logistic regression

ผลการศึกษา: จากผู้มาตรวจสุขภาพประจำปี 893 ราย เป็นเพศหญิงร้อยละ 57.7 อายุเฉลี่ย 47.6 ปี ดัชนีมวลกายเฉลี่ย 24.5 กก./ม.² ส่วนใหญ่ไม่มีโรคประจำตัว (ร้อยละ 78.5) ไม่ได้รับประทานยาเป็นประจำ (ร้อยละ 89.5) พบการวินิจฉัยเบาหวานโดยใช้ระดับน้ำตาลในเลือด ร้อยละ 4.6 ภาวะก่อนเบาหวานร้อยละ 13.2 ส่วนการวินิจฉัยเบาหวานโดยใช้ระดับฮีโมโกลบินเอวันซีพบมากกว่าคือร้อยละ 10.1 และภาวะก่อนเบาหวานร้อยละ 18.0 โดยพบว่าทั้ง 2 วิธีให้ผลสอดคล้องกันจาก kappa 0.38, 95%CI: 0.35-0.40 พบความชุกของภาวะฮีโมโกลบินผิดปกติอยู่ที่ร้อยละ 37.8 โดยพบ Hb E trait (ร้อยละ 30.2) และ homozygous Hb E (ร้อยละ 3.6) มากที่สุด ทั้งนี้ไม่พบความแตกต่างอย่างมีนัยสำคัญ ในการวินิจฉัยเบาหวานระหว่างกลุ่มที่มีและไม่มีภาวะผิดปกติของฮีโมโกลบิน ทั้งการใช้เกณฑ์ระดับน้ำตาลในเลือดหลังอดอาหาร (p=0.44) และฮีโมโกลบินเอวันซี (p=0.15)

สรุป: การวินิจฉัยเบาหวานด้วยระดับฮีโมโกลบินเอวันซีและระดับน้ำตาลในเลือดหลังอดอาหารมีความสอดคล้องกันระดับปานกลาง โดยไม่ได้รับผลกระทบจากภาวะฮีโมโกลบินผิดปกติ แต่ด้วยความชุกของภาวะฮีโมโกลบินผิดปกติชนิด อี และต้นทุนที่สูงกว่า จึงควรใช้ฮีโมโกลบินเอวันซีเพื่อยืนยันผลมากกว่าใช้คัดกรอง

คำสำคัญ: ระดับน้ำตาลในเลือดหลังอดอาหาร, ฮีโมโกลบินเอวันซี, การวินิจฉัยเบาหวาน, ภาวะความผิดปกติของฮีโมโกลบิน

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Abstract

Background and objective: The number of diabetes patients is escalating worldwide. Currently criterion for diagnosing diabetes used fasting plasma glucose or HbA1c. In Thailand, especially the northeast region had high prevalence of HbE. Hemoglobinopathies affect the immunoassays used for HbA1c measurement. In this study, we evaluate the concordance between HbA1c and FPG criteria in the diagnosis of diabetes and explores the prevalence of hemoglobinopathies that may affect HbA1c interpretation.

Methods: A cross-sectional analytical study was conducted on Khon Kaen Hospital staff undergoing annual health check-ups between September and December 2018. Total 893 participants were evaluated both FPG and HbA1c. Statistical analyses were performed using Stata version 6.0 by percentages, means, standard deviations, Pearson Chi-square test, two-tailed tests, and logistic regression.

Results: A total of 893 participants, 57.7% were female, mean ages of 47.6 years, and mean BMI was 24.5 kg/m². Most participants had no underlying disease (78.5%) and were not taking medication regularly (89.5%). When using FPG criteria, the prevalence of diabetes was 4.6% and prediabetes was 13.2%. There were relatively higher prevalence using HbA1c criteria, with diabetes was 10.1% and prediabetes was 18.0%. However, the correlation between these 2 diagnostic criteria was fair by kappa coefficient of 0.38, 95%CI; 0.35 to 0.40. Prevalence of hemoglobinopathies was 37.8% with high prevalence of homozygous Hb E (3.6%) and Hb E trait (30.2%). Diabetes diagnosis did not differ significantly by hemoglobinopathy status for both FPG (OR 1.29; 95% CI 0.67–2.47, $p=0.44$) and HbA1c (OR 1.61; 95% CI 0.85–3.05, $p=0.15$) criteria.

Conclusions: HbA1c and FPG showed fair to moderate agreement for diabetes diagnosis, unaffected by hemoglobinopathy status. However, due to the high prevalence of HbE and higher costs, HbA1c is more suitable as a confirmatory test than a screening tool.

Keywords: FPG, HbA1c, diagnosis of diabetes, hemoglobinopathies

Introduction

The number of diabetes patients is escalating worldwide, especially in the Western Pacific Region of Asia. In 2025, the International Federation of Diabetes estimated that 589 million adults worldwide had diabetes, and the number will rise to 853 million in 2050. Western Pacific is the IDF region with the highest number of adults living with diabetes (215 million) or over a third (37%), with prevalence ranging from 3% to 47.3% across countries. Thailand is among the countries in this region with a high prevalence of diabetes [1]. Every year, more than 200,000 deaths among the Thai populace are caused by chronic noncommunicable diseases, of this number, about 30,000 deaths are owing to diabetes, a leading cause of death in Thailand [2]. Thai National Health Examination Surveys (NHES) have shown that the age-adjusted prevalence of diabetes increased from 8.9% in 2014 to 9.5% in 2020 and 10.6% in 2025 (9.7% among men and 11.3% among women) [3] with a majority of diabetes being undiagnosed clinically. The regional burden of diabetes is anticipated to become an even greater concern in the future due to late diagnosis and inadequate follow-up or compliance [4]. Early identification of high-risk individuals is considered the best strategy to contain the burden and costs of diabetes and its associated complications in the general population [4,5].

Previously, fasting plasma glucose (FPG) was used as a criterion for diagnosing diabetes, alone or during an oral glucose tolerance test where 2 hours glucose level is also a criterion. This method is sensitive but has poor reproducibility and patients must fast overnight prior to either test. In recent years, glycated hemoglobin (HbA1c), initially discovered by Rahbar et al in 1969 [6], was recommended as a tool for the diagnosis and monitoring of treatment of diabetes. In 2009, the International Expert Committee recommended using an HbA1c >6.5% (48 mmol/mol) threshold to diagnose diabetes [7], and this position was also endorsed by the American Diabetes Association [8]. Recent data from Ho Chi Minh City

showed significant discordance in the diagnosis of diabetes between FPG and HbA1c measurements [9]. The mean HbA1c levels are different between ethnicities, with Asians having higher levels than Caucasians [3,8]. Factors that affect the lifespan of red blood cells affect the HbA1c level. Hemoglobinopathies not only affect red blood cells lifespan but also affect the immunoassays used for HbA1c measurement. Some current HbA1c measurement methods show clinically significant interference with samples containing hemoglobin E (HbE), hemoglobin F (HbF), hemoglobin S (HbS) and hemoglobin C (HbC) [10]. There is a high prevalence of hemoglobinopathies in Thailand, especially the northeast region. The average carrier rates for common thalassemia and Hb disorders in Thailand are 2.2–9% for α^0 -thalassemia, 8–30% for α^+ -thalassemia, 1–3% for β -thalassemia, 10–50% for HbE and <1% for HbS [11]. In northeastern Thailand, average carrier rates are 13.6% for α -thalassemia, 6% for β -thalassemia and 20–60% for HbE [12]. In the presence of Hb E, HbA1c may not be detectable by ionexchange chromatography (highpressure liquid chromatography) but may be estimated by immunoassay technique and boronate affinity chromatography. However, the result may be underestimated when correlated with plasma glucose [13].

Hemoglobin variants among thalassemia and hemoglobinopathies patient were the serious factors for the accuracy of HbA1c quantification in the diabetes clinic. Immunoassays, ion-exchange high performance liquid chromatography (HPLC) method have been favored and developed to the analysis of HbA1c because of their precision and no interference of hemoglobinopathies. However, in study from Surin hospital showed HbA1c levels were significantly lower in diabetic patients with homozygous HbE [14], that reflects interference of this method. Other HbA1c measurement technique with capillary electrophoresis (CE) method does not only report the HbA1c level but also detects hemoglobin variants by examination of the electropherograms [15]. However, this method of HbA1c measurement is not included in standard

annual health check-up and cannot be reimbursed by the government, despite its more diagnostic benefits of diabetes.

Because controversial data in Diabetes diagnostic criteria in Asian especially in South-east Asia and HbA1c test by HPLC method can interference from hemoglobinopathies. This study aims to evaluate the diagnostic concordance between HbA1c and FPG in detecting diabetes in Thai health check-up participants. It also explores the prevalence of hemoglobinopathies that may affect HbA1c interpretation.

Methods

Participants and study design

A cross-sectional analytical study was conducted on the hospital personnel of Khon Kaen Hospital including physicians, pharmacists, nurses, allied health professionals and back-office staff who were assigned to have routine physical yearly check-up between September 2018 and December 2018. The use of the hospital's Electronic Health Records ensures access to precise, centralized laboratory results and medical histories, eliminating recall bias.

The sample size was determined by the number of specimens provided from the health hospital personnel during the period with Daniel formula [16] below

$$n = \frac{N \times Z_{\alpha/2}^2 \times p(1-p)}{d^2(N-1) + Z_{\alpha/2}^2 \times p(1-p)}$$

$d = 0.05$ and $p = 9.7\%$ for diabetes and 34.6% for prediabetes (data from Ho-Pham LT et al. [9]).

Totals of at least 733 samples were calculated. The inclusion criteria included aged between 20 and 65 years. We excluded individuals who had blood loss from any cause within six months before blood collection, active tuberculosis, renal failure, liver impairment, malignancy, known cases of hemolytic diseases other than hemoglobinopathies.

FPG, HbA1c, lipid profile, complete blood count including hemoglobin concentration (Hb), BUN, creatinine, ALT, and AST were collected on the same day. Hemoglobin typing was performed, if HbA1c measured by capillary electrophoresis suggested abnormal hemoglobin variants. HbA1c was examined by Sebia Capillarys HbA1c on Capillarys 2 Flex Piercing (Sebia, Paris, France). FPG, Lipid profile consists of serum cholesterol level (CHOL), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL). CHOL and TG were measured by enzymatic colorimetric assay (Roche Diagnostics, Mannheim, Germany). HDL and LDL were measured by homogenous enzymatic colorimetric assay (Roche Diagnostics, Mannheim, Germany). Hemoglobin type was determined using a standard capillary electrophoresis system (Capillarys 2FP).

Patients were classified into three groups: normal, pre-diabetes, and diabetes groups. Each group was classified by Thai Diabetic Guideline criteria [17]. An individual was diagnosed with diabetes if the individual's HbA1c $\geq 6.5\%$ (48 mmol/mol). Pre-diabetes was defined as HbA1c value between 5.7% and 6.4% . In addition, and for comparison, diabetes was also diagnosed as individuals with FPG $\geq 126 \text{ mg/dl}$, and pre-diabetes was classified as FPG between 100 and 125 mg/dl (i.e., impaired fasting glucose)

This study received approval from a research ethics committee of Khon Kaen Hospital with approval reference number was KE61130.

Statistical analysis

Results were analyzed using Stata version 6.0. Data were described in percentages, means, and standard deviations (SD). The Pearson Chi-square test was used to compare differences between nominal variables. Fisher's exact test and continuity correction were used as appropriate. Two-tailed tests were used to determine the statistical significance at p -value less than 0.05 . Logistic regression was used to compare between groups and reported as odds ratios

and 95% confidence interval (CI). The distributions of data were evaluated by Kolmogorov-Smirnov test. Kruskal-Wallis test was used to determine differences between means in each group. Factors that affected diabetes and pre-diabetes diagnosis were analyzed by logistic regression and adjusted odds ratio with 95% CI.

Results

Demographic data

A total of 1,061 persons had yearly check-up but only 893 persons were eligible and included for

analysis. Of 893 participants, 57.7% were female, mean age was 47.6 years, mean body weight was 63.9 kg, and mean BMI was 24.5 kg/m², smoker 8.3% and alcohol consumption 28.8% (table 1). Most participants had no underlying disease (78.5%) while, 8.7% had hypertension, 2.4% had hyperlipidemia and 11.4% had other disease such as chronic kidney disease, liver cirrhosis, gouty arthritis and rheumatoid arthritis. Ninety-four participants (10.5%) were taking medication such as antihypertensive agent, lipid lowering agent, uric lowering agent or steroid as shown in Table 1.

Table 1 Demographics data in number (%)

Characteristics	Total, n = 893
Age, years*	47.6 ± 10.7
Female	378 (57.7)
Weight, kg*	63.9 ± 12.4
BMI, Kg/m ² in median (IQR)	24.5 (22.8-27.0)
Waist circumference, cm* (IQR)	32.5 (30 - 35)
Underlying disease	192 (21.5)
- Hypertension	78 (8.7)
- Dyslipidemia	21 (2.4)
- gouty arthritis	6 (0.7)
- CKD stage 3 and below	1 (0.1)
- others disease	102 (11.4)
Medication	94 (10.5)
- Antihypertensive agent	67 (7.5)
- Lipid lowering agent	20 (2.2)
- Uric lowering agent	3 (0.3)
- steroid	1 (0.1)
- others medication	33 (3.7)
Smoking	74 (8.3)
Alcohol drinking	257 (28.8)
Systolic BP, mmHg*	124.2 ± 16.1
Diastolic BP, mmHg*	77.1 ± 12.3

Abbreviation: KG, kilogram; cm, centimeter; BMI, body mass index; IQR, interquartile range; CKD, chronic kidney disease; BP, blood pressure; mmHg, millimeter of Mercury

*Mean ± standard deviation

Laboratory values, mean hemoglobin was 13.3 ± 1.6 g/dl, mean corpuscular volume was 80.6 ± 9.6 fL, Red blood cell distribution width was 14.3 ± 2.3 %, fasting plasma glucose was 93.0 ± 22.2 mg/dl and mean HbA1c was 5.5 ± 0.8 % as shown in Table 2.

Table 2 Laboratory values in mean ± standard deviation

Test (n)	Result; mean± SD
Hemoglobin, g/dl (892)	13.3 ±1.6
Hematocrit, % (892)	40.3 ± 4.7
MCV, fL (892)	80.6 ± 9.6
MCH, pg (892)	26.9 ± 3.9
RDW, % (805)	14.3 ± 2.3
Fasting plasma glucose, mg/dl (893)	93.0 ± 22.2
HbA1c, gm% (893)	5.5 ± 0.8
Total Cholesterol, mg/dl (891)	204.9 ± 39.5
Triglyceride, mg/dl (684)	130.7 ± 106.1
High density lipoprotein, mg/dl (358)	56.1 ± 14.7
c-LDL, mg/dl (21)	145.1 ± 40.3
d-LDL, mg/dl (130)	144.8 ± 40.8
Creatinine, mg/dl (714)	0.9 ± 0.4
eGFR, mL/min/1.73 m ² (714)	92.7 ± 14.3
AST, IU/L (662)	23.4 ± 10.6
ALT, IU/L (670)	22.2 ± 16.2

Abbreviation: MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; c-LDL, calculated low density lipoprotein; d-LDL, direct low-density lipoprotein; eGFR, estimated glomerular filtration rate; AST, aspartate transaminase; ALT, alanine transaminase

Primary outcomes

Among 893 participants, using fasting plasma glucose criteria for diagnosis of diabetes, 41 (4.6 %) participants had diabetes, 118 (13.2%) participants had prediabetes, and 734 (82.2%) participants were normal. While using HbA1c criteria for diagnosis of diabetes, 90 (10.1%) participants had diabetes, 161 (18.0%) participants had prediabetes, and 642 (71.9%) participants were normal. HbA1c has 65.8 % Sensitivity (95% CI 49.4-79.9) and 92.6% specificity (95% CI 90.6-

94.3) in diabetes diagnosis, Positive Predictive Value (PPV) was 30.0% (95% CI 23.6-37.2) and Negative Predictive Value (NPV) was 98.3% (95% CI 97.4-98.8). There still were relatively higher prevalence of diabetes and prediabetes in HbA1c criteria than fasting plasma glucose criteria, but the agreement of these 2 diagnostic criteria was fair to moderate: kappa 0.38, 95%CI; 0.35 to 0.40, p<0.01, Table 3.

Table 3 Diagnostic of diabetes by FPG and HbA1c criteria in number (%)

HbA1c	FPG				Kappa (95%CI)	p-value
	Normal	Pre-diabetes	Diabetes	Total		
Normal	589 (80.3)	45 (38.1)	8 (19.5)	642 (71.9)	0.38 (0.35 – 0.40)	<0.01
Pre-diabetes	105 (14.3)	50 (42.4)	6 (14.6)	161 (18.0)		
Diabetes	40 (5.5)	23 (19.5)	27 (65.9)	90 (10.1)		
Total	734 (82.2)	118 (13.2)	41 (4.6)	893 (100)		

Secondary outcomes

Of the 893 participants, 845 (94.6%) were measured by CE method testing for HbA1c and had reported Hemoglobin typing data which giving 37.8 % prevalence of Hemoglobinopathies with dividing to Beta thalassemia trait was 0.7, Homozygous Hb E was 3.6, Hb E trait 30.2, Hb H disease was 0.2 and Hb Constant Spring was 1.1 respectively. Among 128 of 845 participants were tested for Hb typing method by standard capillary electrophoresis, which gave prevalence of Hemoglobinopathies was 38.3% with dividing to Beta thalassemia trait was 0.8, Homozygous Hb E was 3.9, Hb E trait 24.2, Hb H disease was 0.8 and Hb Constant Spring was 3.9 respectively. The agreement of these 2 techniques was almost perfect, kappa 0.91 (95%CI 0.83-0.92, $p<0.01$).

No statistically significant difference was found in the diagnosis of diabetes between the hemoglobinopathies group and the normal hemoglobin typing group. This held true for both FPG criteria (OR 1.29; 95% CI 0.67–2.47, $p=0.44$) and HbA1c criteria (OR 1.61; 95% CI 0.85–3.05, $p=0.15$).

Discussion

Among 893 participants who came to routine physical yearly check-up at Khon Kaen Hospital between September 2018 and December 2018, prevalence of diabetes was 4.6% and pre-diabetes was 13.2% when used fasting plasma glucose criteria, while using HbA1c criteria we found prevalence of diabetes and pre-diabetes were 10.1% and 18.0% respectively. Prevalence of Diabetes and Pre-diabetes in this study is similar to Thai National Health Examination Surveys 2025 [3].

The study demonstrated a high specificity (92.6%) and NPV (98.3%) for HbA1c, yet its low PPV (30.0%) and fair agreement with FPG (Kappa = 0.38) indicate significant diagnostic discordance. This finding was nearly concordant with previous study from Vietnam [9]. Notably, 40 participants were classified as diabetic by HbA1c despite having normal FPG, suggesting a high risk of over-diagnosis in this Hb E-prevalent population. These findings imply that while HbA1c is effective for ruling out diabetes, it should not be used as a standalone marker. Clinically, a combined approach using FPG, HbA1c, or confirmatory tests like OGTT is essential to ensure diagnostic accuracy and avoid inappropriate treatment. However, HbA1c should be a confirmatory test rather than a screening test because of high specificity and higher cost than FPG.

In addition, we found that prevalence of Hemoglobinopathies was 37.8%: beta thalassemia trait was 0.7%, homozygous Hb E was 3.5%, Hb E trait 30.2%, Hb H disease was 0.2% and Hb Constant Spring was 1.1%. This finding was consistent when compare with previous study by Leckngam [12], and there was still high prevalence of hemoglobinopathies, especially HbE disorder in the northeastern region same as previous study at Surin Hospital shown the prevalence of homozygous Hb E and Hb E trait were 9.0% and 38.2%, respectively [14].

Hb E contains a substitution of lysine for glutamic acid at position 26 of the β chain. Hb E is found primarily in people from Southeast Asia especially in the northeastern region of Thailand. Subjects with homozygous E disease and heterozygous

E trait are usually completely asymptomatic. Most common techniques of HbA1c measurement were Immunoassay technique: It uses an antibody that recognizes the structure of the Nterminal glycated amino acids, usually the first 4–10 amino acids on the Hb β chain. Hb E disease usually does not affect the immunoassay technique of HbA1c estimation, as the mutation tends to be farther away on the β chain than 4–10 amino acids. However, it does interfere with the ionexchange HPLC method, as the mutation tends to alter the ionic charges on the Hb. Thus, a physician may be unaware that their patient with diabetes has Hb E disease or Hb E trait, and their HbA1c result may be incorrect [13]. In this study, HbA1c was measured using CE method, which significantly minimizes analytical interference from Hb E. Unlike immunoassays, the CE method provides high resolution by clearly separating Hb E peaks from HbA1c on electropherograms, ensuring accurate measurements in individuals with Hb E trait. However, a limitation remains in cases of homozygous Hb E or Hb E/beta-thalassemia, where the absence of HbA or shortened red blood cell lifespan may still lead to clinically unreliable HbA1c results, therefore, we still caution when using HbA1c criteria for diagnosis of diabetes.

When focus on factors that affected pre-diabetes diagnosis by HbA1c criteria. Older age, male gender, high waist circumference and high level of alanine transaminase were shown correlation effect, but only low serum creatinine had affected on diabetes diagnosis by HbA1c criteria. At the same time, male gender, high systolic BP, low serum creatinine and high level of alanine transaminase were shown correlation effect to pre-diabetes diagnosis by fasting plasma glucose criteria. But only high waist circumference and low serum creatinine were shown correlation effect to diabetes diagnosis by fasting plasma glucose criteria. Other information was shown in supplement tables 1.1 and 1.2.

After adjusting the effect of several factors by Forward stepwise, this study highlights several key factors significantly associated with diabetes risk, specifically older age, increased waist circumference (WC), and elevated serum triglycerides that affect diabetes diagnosis by both HbA1c and fasting plasma glucose criteria. Other information was shown in Table 4.

Table 4 Factors by forward stepwise multivariable analysis

Factors	Pre-diabetes		Diabetes	
	Adjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
HbA1c				
Age	1.08 (1.05 - 1.10)	<0.01	1.04 (1.01 - 1.07)	0.01
WC	1.14 (1.07 - 1.21)	<0.01	1.13 (1.05 - 1.21)	<0.01
TG	1.00 (1.00 - 1.01)	0.01	1.00 (1.00 - 1.01)	0.01
Cr	0.29 (0.08 - 1.02)	0.05	0.03 (0.01 - 0.19)	<0.01
FPG				
Age	1.05 (1.03 - 1.07)	<0.01	1.05 (1.01 - 1.09)	0.02
SBP	1.02 (1.01 - 1.04)	<0.01	1.02 (0.99 - 1.04)	0.21
WC	1.05 (1.00 - 1.12)	0.06	1.09 (1.02 - 1.17)	0.02
TG	1.00 (1.00 - 1.01)	<0.01	1.01 (1.00 - 1.01)	<0.01

Abbreviation: WC, waist circumference; TG, triglyceride; Cr, creatinine; SBP, systolic blood pressure.

Advance age can independently influence HbA1c levels. Previous research suggests that HbA1c levels tend to increase with age even in non-diabetic populations, potentially due to changes in red blood cell (RBC) turnover or glycation rates [18]. Consequently, using a fixed HbA1c threshold for the elderly may lead to a decrease in diagnostic specificity, and age-adjusted reference ranges may be necessary to avoid overdiagnosis. Increased waist circumference (WC) was identified as a strong predictor of diabetes, reflecting the critical role of central adiposity, serves as a more direct proxy for visceral fat, which is metabolically active and releases pro-inflammatory cytokines and free fatty acids that impair insulin signaling [19]. However, WC itself does not typically interfere with the laboratory measurement of the HbA1c molecule but rather reflects the underlying chronic hyperglycemic state. Elevated TGs are often a hallmark of the “atherogenic dyslipidemia” seen in metabolic syndrome, which is closely linked to insulin resistance [20]. Primarily, elevated TGs serve as a surrogate marker for poor glycemic control rather than a direct measurement confounder.

Strengths of our study were large sample size and was done on a single site with universal standardization by ISO. Another, our study was evaluation hemoglobinopathies by capillary electrophoresis with perfect agreement to standard method. Furthermore, we analyze several factors that affected diabetes and pre-diabetes diagnosis. This study has several limitations, first, the study’s use of a single laboratory measurement, which may inflate the reported prevalence and reduce diagnostic accuracy due to a lack of confirmatory testing. Second, several laboratory data were missing because there were not done in some yearly check-up participants program. Third, since the cohort consisted solely of hospital staff who typically have higher health literacy and better access to care these results may not be fully generalized to the broader population. Furthermore, our study collected data in 2018, due to the lack of timeliness of this data, the applicability of the findings should be interpreted with caution.

Future studies should employ longitudinal designs with repeat testing to enhance diagnostic precision. To improve generalizability, research should involve more diverse, community-based populations. Furthermore, validating alternative glycemic markers, such as fructosamine or glycated albumin, is recommended to establish more reliable diagnostic tools for populations with high hemoglobinopathy prevalence.

Conclusion

The level of agreement between diabetes diagnoses using HbA1c and FPG is fair to moderate. Furthermore, no statistically significant difference was found in the diagnosis of diabetes between individuals with and without hemoglobinopathies. However, given the high prevalence of hemoglobinopathies, particularly Hb E, in the Northeast region, HbA1c should be utilized as a confirmatory test rather than a screening tool due to its high specificity and higher cost compared to FPG.

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Conflict of Interest

Author(s) declared none.

References

1. Duncan BB, Magliano DJ, Boyko EJ. IDF Diabetes Atlas 11th edition 2025: global prevalence and projections for 2050. *Nephrol Dial Transplant* 2025;41(1):7-9.
2. Porapakham Y, Rao C, Pattaraarchachai J, Polprasert W, Vos T, Adair T, et al. Estimated causes of death in Thailand, 2005: implications for health policy. *Popul Health Metr* 2010;8:14. doi:10.1186/1478-7954-8-14.

3. Patanavanich R, Aekplakorn W. Thai National Health Examination Survey VII (2024-2025). Nonthaburi: Health Systems Research Institute (HSRI); 2025.
4. Huang OS, Tay WT, Ong PG, Sabanayagam C, Cheng CY, Tan GS, et al. Prevalence and determinants of undiagnosed diabetic retinopathy and vision-threatening retinopathy in a multiethnic Asian cohort: the Singapore Epidemiology of Eye Diseases (SEED) study. *Br J Ophthalmol* 2015;99(12):1614-21. doi:10.1136/bjophthalmol-2014-306492.
5. Narayan KM, Chan J, Mohan V. Early identification of type 2 diabetes: policy should be aligned with health systems strengthening. *Diabetes Care* 2011;34(1):244-6. doi:10.2337/dc10-1952.
6. Rahbar S, Blumenfeld O, Ranney HM. Studies of an unusual hemoglobin in patients with diabetes mellitus. *Biochem Biophys Res Commun* 1969;36(5):838-43. doi:10.1016/0006-291X(69)90685-8.
7. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care* 2009;32(7):1327-34. doi:10.2337/dc09-9033.
8. American Diabetes Association Professional Practice Committee for Diabetes*; 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2026. *Diabetes Care* 2026;49 (Supplement_1):S27–S49. doi:10.2337/dc26-S002.
9. Ho-Pham LT, Nguyen UDT, Tran TX, Nguyen TV. Discordance in the diagnosis of diabetes: Comparison between HbA1c and fasting plasma glucose. *PLoS One* 2017;12(8):e0182192. doi:10.1371/journal.pone.0182192.
10. Little RR, Rohlfing CL, Hanson S, Connolly S, Higgins T, Weykamp CW, et al. Effects of hemoglobin (Hb) E and HbD traits on measurements of glycated Hb (HbA1c) by 23 methods. *Clin Chem* 2008;54(8):1277-82. doi:10.1373/clinchem.2008.103580.
11. Viprakasit V, Lee-Lee C, Chong QT, Lin KH, Khuapinant A. Iron chelation therapy in the management of thalassemia: the Asian perspectives. *Int J Hematol* 2009;90(4):435-45. doi:10.1007/s12185-009-0432-0.
12. Leckngam P. Thalassemia and Hemoglobinopathies in Thailand: A Systematic Review. *J Health Sci Altern Med* 2023;5(3):18-26.
13. Yedla N, Kuchay MS, Mithal A. Hemoglobin E disease and glycosylated hemoglobin. *Indian J Endocr Metab* 2015;19:683-5. doi:10.4103/2230-8210.163211.
14. Srisurin W. Prevalence and effect of hemoglobin E disorders on Hba1c and lipid profile of diabetic patients at Surin Hospital. *J Med Assoc Thai* 2011; 94(1):36-42.
15. Rohlfing C, Hanson S, Weykamp C, Siebelder C, Higgins T, Molinaro R, et al. Effects of hemoglobin C,D,E and S traits on measurements of hemoglobin A1c by twelve methods. *Clin Chim Acta* 2016; 455:80-83. doi:10.1016/j.cca.2016.01.031.
16. Daniel WW, Cross CL. *Biostatistics: A Foundation for Analysis in the Health Sciences*. 10th edition. Hoboken, NJ: Wiley; 2013:192.
17. Diabetes Association of Thailand, Royal College of Physicians of Thailand, Thai Endocrine Society, Department of Medical Services, National Health Security Office. *Clinical Practice Guideline for Diabetes* 2023. Bangkok: Srimuang Printing; 2023.
18. Masuch A, Friedrich N, Roth J, Nauck M, Muller UA, Petersmann A. Preventing misdiagnosis of diabetes in the elderly: age-dependent HbA1c reference intervals derived from two population-based study cohorts. *BMC Endocr Disord* 2019;19(1):20. doi:10.1186/s12902-019-0338-7.
19. Darsini D, Hamidah H, Notobroto HB, Cahyono EA. Health risks associated with high waist circumference: A systematic review. *J Public Health Res* 2020;9(2): 1811. doi:10.4081/jphr.2020.1811.
20. Rodriguez-Gutierrez R, Mancillas-Adame LG, Rodriguez-Tamez G, Diaz Gonzalez-Colmenero A, Solis-Pacheco RC, Elizondo-Plazas AS, et al. Hypertriglyceridemia and Its Association with HbA1c Test: A Prospective In Vivo Controlled Study. *Int J Endocrinol* 2019;2019:4784313. doi:10.1155/2019/4784313.