Discrepancies between Glycated Hemoglobin and Fasting Plasma Glucose in New-onset Diabetes Mellitus

Tamrakar R,[1] Tamrakar D,[2] Katwal P[1]

[1]Department of Internal Medicine

[2]Department of Community Medicine,

Dhulikhel Hospital, Kathmandu University Hospital,

Kathmandu University School of Medical Sciences,

Dhulikhel, Kavre, Nepal.

Corresponding Author

Rajendra Tamrakar

Department of Internal Medicine,

Dhulikhel Hospital, Kathmandu University Hospital,

Kathmandu University School of Medical Sciences,

Dhulikhel, Kavre, Nepal.

E-mail: tamrakaraj@gmail.com

Citation

Tamrakar R, Tamrakar D, Katwal P. Discrepancies between Glycated Hemoglobin and Fasting Plasma Glucose in New-onset Diabetes Mellitus. *Kathmandu Univ Med J.* 2023;82(2):144-8.

ABSTRACT

Background

Fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c) are commonly used for diagnosing diabetes mellitus in Nepal. Though HbA1c criteria are convenient for diagnosis there is a discrepancy between the fasting plasma glucose and HbA1c for diagnosis.

Objective

To assess the comparability between fasting plasma glucose and glycated hemoglobin levels in the new-onset diabetes mellitus.

Method

This is a hospital-based descriptive cross-sectional study including 128 newly diagnosed diabetes mellitus conducted at Dhulikhel Hospital, Kathmandu University Hospital. New onset diabetes patients above 18 years of age who met inclusion criteria were included. The clinical characteristics and biochemical parameters were analyzed. Statistical analysis was done using student's t-test and correlation coefficient.

Result

There were 128 newly diagnosed diabetes mellitus patients included in the study among which 57.0% were males with a mean age of 49.48±11.40 years. The mean fasting plasma glucose, postprandial sugar (PPBS), and glycated hemoglobin were 205.54±88.93 mg/dL, 331.08±146.61 mg/dL, and 9.59±2.70% respectively. Diabetes was diagnosed using fasting plasma glucose, and glycated hemoglobin criteria in 84.4% and 90.6% of patients. In new-onset diabetic patients, 76.56% of patients had both elevated levels of fasting plasma glucose and glycated hemoglobin. Of the diabetic patients who had fasting plasma glucose ≥126 mg/dL, 90.7% of patients had HbA1c ≥ 6.5% whereas 1.6% of new-onset diabetes had < 126 mg/dL and glycated hemoglobin < 6.5%. There was a strong correlation between fasting plasma glucose and glycated hemoglobin ($r=0.723$; $p<0.01$).

Conclusion

Both fasting plasma glucose and glycated hemoglobin tests have to be used together for diagnosing diabetes mellitus.

KEY WORDS

Blood glucose, Diabetes mellitus*, Glycated hemoglobin*

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia due to abnormal carbohydrate, protein, and lipid metabolism.[1] The worldwide prevalence of diabetes is predicted to rise to 10.2% by 2030 and 10.9% by 2045.[2] Type 2 Diabetes Mellitus (T2DM) is a high-burden disease in Nepal with an estimated prevalence of 10%.[3]

There is a discrepancy between fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c) for diagnosing diabetes. FPG and 2-h postprandial glucose (2-h PG) are more accurate for diagnosing diabetes in whom HbA1c and glucose values are discordant.[4] In 2009, an international expert committee recommended that HbA1c be introduced into diagnostic criteria at a threshold level of ≥ 6.5% which was adopted by the American Diabetes Association (ADA) the following year.[5] In 2010, 1.9 million people aged ≥ 20 years in the United States were newly diagnosed based on either FPG or HbA1c criteria.[6] HbA1c is a better choice for monitoring and management of diabetes. Because of the imperfect correlation between HbA1c and average glucose in certain individuals, the cut-point of HbA1c for diagnosing diabetes is controversial though it has greater convenience, preanalytical stability, and less day-to-day perturbations during stress, diet, or illness.[4,7] Diabetes will remain undiagnosed if HbA1c criteria are used as the sensitivity of HbA1c to detect diabetes defined by the oral glucose tolerance test (OGTT) is < 50%. Approximately 30-40% of previously undiagnosed diabetes will be diagnosed if HbA1c ≥ 6.5% criteria are used whereas ~50% and 90% will be diagnosed with diabetes if FPG and 2-h PG criteria are used.[8] This study is aimed to assess the comparability between FPG and HbA1c levels in new-onset diabetes mellitus.

METHODS

This is a hospital-based descriptive cross-sectional study including 128 newly diagnosed diabetes mellitus, using non-probability consecutive sampling, attending the outpatient and inpatient department of Internal Medicine, Dhulikhel Hospital, Kathmandu University Hospital from April 2021 to March 2022. New onset diabetes patients above 18 years of age diagnosed with ADA criteria willing to participate in the study were included in the study to assess the comparability between FPG and HbA1c levels.[4] Patients with a history of diabetes mellitus taking antidiabetic drugs, pregnant ladies, established anemia, chronic diseases like chronic kidney disease, heart failure, psychiatric disorders, and patients taking corticosteroids were excluded from the study. Ethical approval was taken from the Institutional Review Committee of Kathmandu University School of Medical Sciences.

Information regarding the sociodemographic profile was recorded according to the proforma. A detailed clinical history and physical examination and anthropometric measurements like height, weight, and body mass index were measured. Waist circumference was measured at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest, using a stretch-resistant tape. Blood pressure was measured by standardized protocols using a sphygmomanometer. Systolic and/or diastolic blood pressure ≥ 130/85 mmHg and/or the current use of antihypertensive medication in diabetes was considered hypertension. Recent World Health Organization (WHO) guideline for the South Asian population was followed to classify their body mass index (BMI) status.[9] A blood sample was drawn after overnight fasting by trained medical personnel. FPG, HbA1c, and lipid profile along with postprandial sugar (PPBS) values were recorded. Dyslipidemia was defined by the presence of one or more abnormal serum lipid concentrations. Patients were classified as having metabolic syndrome meeting the criteria for metabolic syndrome using International Diabetes Federation (IDF) criteria.[10]

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) Version 25 software for windows. Data for categorical variables were expressed either in number or percentage (N,%). Numerical data for continuous variables were expressed in the form of mean ± standard deviation. Independent sample t-test (p values, 2-tailed) was used for statistical significance of the difference between the proportion and mean values of two or more groups of variables respectively. The correlation coefficient was used to assess the strength of the association between data variables. The tests were considered statistically significant when $p < 0.05$.

RESULTS

There were 128 newly diagnosed diabetes mellitus patients included in the study among which 57.0% were males with a mean age of 49.48 ± 11.40 years. The mean FPG, PPBS, and HbA1c were 205.54 ± 88.93 mg/dL, 331.08±146.61 mg/dL, and 9.59 ± 2.70% respectively. Diabetes was diagnosed using FPG, and HbA1c criteria in 84.4% and 90.6% of patients. The prevalence of metabolic syndrome was 72.7%. Dyslipidemia associated with hypertriglyceridemia and reduced high-density cholesterol (HDL) was present in 59.4% and 75.0% respectively. Table 2 shows the comparison of clinical characteristics of diabetics with fasting plasma glucose ≥ 126 mg/dL stratified by HbA1c < or ≥ 6.5%. Fasting plasma glucose and PPBS were significantly higher in HbA1c ≥ 6.5% group ($p < 0.01$). However, total cholesterol, HDL, low-density cholesterol (LDL), and triglycerides (TG) were not significantly different in both groups. In new-onset diabetic patients, 76.56% of patients had both elevated levels of FPG and HbA1c levels. Of the diabetic patients who had FPG ≥ 126 mg/dL, 90.7% of patients had HbA1c ≥ 6.5% whereas 1.6% of new-onset diabetes had < 126 mg/dL and HbA1C < 6.5%. Similarly, the

Table 1. Clinical characteristics of studied subjects (n=128)

Variable	Mean ±SD	n(%)
Age (in years)	49.48±11.40	
Body mass index (in kg/m²)	26.48±3.99	
Fasting plasma glucose (mg/dL)	205.54±88.93	
PPBS (mg/dL)	331.08±146.61	
HbA1c (%)	9.59±2.70	
Total cholesterol (mg/dL)	191.74±53.12	
HDL (mg/dL)	37.40±10.53	
LDL (mg/dL)	106.67±35.02	
TG (mg/dL)	223.00±188.03	
Gender, male		73(57.0%)
Smoking, yes		32(25.0%)
Alcohol consumption, yes		30(23.4%)
Hypertension, yes		47(36.7%)
FPG ≥ 126 mg/dL		108(84.4%)
PPBS ≥ 200 mg/dL		106(82.8%)
HbA1c ≥ 6.5%		116(90.6%)
Metabolic syndrome		93(72.7%)
Central obesity (Male ≥ 90 cm; Female ≥ 80 cm)		98(76.6%)
Hypertriglyceridemia		76(59.4%)
Decreased HDL		96(75.0%)

Table 2. Comparison of clinical characteristics of diabetics with FPG ≥126 mg/dL stratified by HbA1c < or ≥ 6.5%

Variable	HbA1c ≥ 6.5% (n=98)	HbA1c < 6.5% (n=10)	p-value
Age (years)	48.63±12.12	51.70±7.12	0.43
Gender, male	57 (58.2%)	7(70.0%)	0.47
Smoking, yes	27 (27.6%)	2 (20.0%)	0.61
Alcohol consumption, yes	23 (23.5%)	4 (40.0%)	0.25
Waist circumference (cm)	93.67±11.29	91.50±13.75	0.57
BMI (kg/m²)	26.67±4.21	26.09±4.73	0.68
FPG (mg/dL)	230.53±87.27	136.90±8.22	0.01
PPBS (mg/dL)	369.43±145.09	206.40±37.46	0.01
HbA1c (%)	10.46±2.47	6.13±0.37	0.01
Total cholesterol (mg/dL)	192.47±47.43	188.40±37.88	0.79
HDL (mg/dL)	37.01±9.88	39.10±14.37	0.54
LDL (mg/dL)	106.93±33.26	105.20±24.37	0.87
TG (mg/dL)	220.90±187.73	214.90±187.22	0.92

Table 3. Percentage of subjects meeting diagnostic criteria for diabetes by fasting plasma glucose and HbA1c

		Fasting plasma glucose				
		≥ 126 mg/dL		< 126 mg/dL		Total
HbA1c	≥6.5%	98	90.7%	18	90.0%	116
	<6.5%	10	9.3%	2	10.0%	12
Total		108	100%	20	100%	128

diabetic patients who had HbA1c ≥ 6.5%, 84.5% of patients had FPG ≥ 126 mg/dL. In this study, there was a strong correlation between FPG and HbA1c (r = 0.723, p < 0.01). The correlation between PPBS and HbA1c was 0.735 (p < 0.01). Figure 1. shows the scatter diagram demonstrating a relation between HbA1c and FPG in new-onset type 2 diabetic patients. The FPG and HbA1c correlated very well to a linear relationship defined as FPG (mg/dL) = -22.99 + 23.83 × HbA1c (%) (r = 0.723, p<0.01). Based on this relationship, an HbA1c of 6.5% correlated closer to an FPG of 131 mg/dL. Our findings demonstrated that FPG is a relatively good diagnostic test when compared with HbA1c.

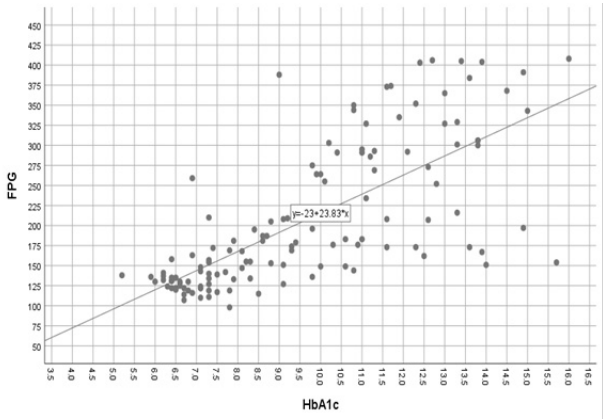

Figure 1. Scatter diagram showing the relation between FPG and HbA1c in type 2 diabetic patients. x-axis: HbA1c (%), y-axis: FPG (mg/dL)

DISCUSSION

Diabetes is associated with chronic hyperglycemia and diagnosis of diabetes mellitus requires either FPG ≥ 126 mg/dL or 2-h PG ≥ 200 mg/dL during OGTT or HbA1C ≥ 6.5% or in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, random plasma glucose ≥ 200 mg/dL. The diagnosis requires two abnormal test results from the same sample or in two separate test samples in the absence of unequivocal hyperglycemia. FPG and 2-h PG are more accurate for diagnosis if there are discrepancies between HbA1c and either glucose-based test.[4] The cut-point of HbA1c for diagnosis of diabetes is debatable though it is a reliable measure of chronic glycemia and it correlates well with the risk of long-term diabetes complications.[7]

In this study, diabetes was diagnosed in 84.4% using FPG criteria and 90.6% of patients using HbA1c criteria respectively in new-onset diabetic patients. In newly diagnosed diabetes aged 18-55 years with acute myocardial infarction, 95% of patients had elevated HbA1c ≥ 6.5% among which around 90% of patients had HbA1c between 6.5-8.0%.[11] The Chinese younger newly diagnosed T2DM aged less than 65 years had HbA1c ≥ 6.5% in 72% of patients while the older newly diagnosed T2DM aged ≥ 65 years had HbA1c ≥ 6.5% in 69% of patients with 76% of newly diagnosed T2DM having elevated HbA1c ≥ 6.5%.[12] The average HbA1c and FPG at diagnosis were 9.59 ± 2.70% and 205.54±88.93 mg/dL respectively which were higher

than in the study done by Fang et al. however, the presence of hypertriglyceridemia was comparable.[12] In other studies, done in Nepal, the mean HbA1c among patients with new onset diabetes was 10.20% and 10.43% respectively.[13,14] HbA1c is a measure of chronic hyperglycemia, the higher HbA1c at diagnosis states that the diabetes is diagnosed later in the Nepalese population. Criteria for screening for diabetes or prediabetes in asymptomatic adults have to be followed so that diabetes is diagnosed earlier and proper interventions could be taken to ameliorate the complications.[4] 2-h PG detects more undiagnosed diabetes (90%) than HbA1c which detects only 30% of undiagnosed diabetes defined by any of the three criteria to diagnose diabetes. Furthermore, around 19% of undiagnosed diabetes was detected by using both FPG and 2-h PG glucose but not by HbA1c.[15] The sensitivity of HbA1c ≥ 6.5% to diagnose diabetes was only 39%, i.e., 61% of newly diagnosed subjects had HbA1c < 6.5% according to the Finnish Diabetes Prevention Study.[8] Using the cut-off value of HbA1c ≥ 6.0% the sensitivity and specificity to diagnose diabetes are 69.8% and 91.9%, respectively.[6]

The comparison of clinical characteristics of diabetics with fasting plasma glucose ≥ 126 mg/dL stratified by HbA1c < or ≥ 6.5% in this study showed FPG and PPBS to be significantly higher in the HbA1c ≥ 6.5% group. There was the presence of dyslipidemia with reduced HDL cholesterol and hypertriglyceridemia in both groups. However, total cholesterol, HDL, LDL, and TG were not significantly different in both groups. The significantly high level of FPG, postprandial glucose, and HbA1c in diabetic patients with HbA1c ≥ 6.5% than in patients with HbA1c<6.5% is similar to Karnchanasorn et al. however, the FPG, PPBS, and HbA1c were higher in our newly diagnosed diabetic population which reflects the higher FPG and PPBS most likely contributed by eating patterns leading to high HbA1c.[6] Hypertriglyceridemia, low HDL cholesterol, and increased concentration of small dense cholesterol are typical of diabetic dyslipidemia which increases the risk for coronary heart disease.[16] The increased free fatty acid flux secondary to insulin resistance is associated with diabetic dyslipidemia. Hyperglycemia impairs the removal of triglyceride-rich lipoproteins eventually leading to the accumulation of triglycerides and abnormality in HDL and LDL cholesterol.[16,17]

In new-onset diabetic patients, 76.56% of patients had both elevated levels of FPG and HbA1c levels whereas 1.6% of new-onset diabetes doesn't meet the diagnostic cut-off for FPG and HbA1c. Of the diabetic patients who had FPG ≥ 126 mg/dL, 90.7% of patients had HbA1c ≥ 6.5%. Similarly, the diabetic patients who had HbA1c ≥ 6.5%, 84.5% of patients had FPG ≥ 126 mg/dL. The use of both FPG and HbA1c increases the diagnostic yield more than using either test alone for timely diagnosis and metabolic control. HbA1c provides an individual's average blood glucose levels of the previous two to three months which parallels the predicted half-life of red blood cells. Though measuring glycated hemoglobin has greater convenience, greater preanalytical stability, and less day-to-day perturbations during stress, diet, or illness; the lower sensitivity of HbA1c at designated cut point, high cost and the imperfect correlation between HbA1c and average blood glucose in certain individuals have been its limitations.[4,7] The diagnostic agreement in the clinical setting revealed the current HbA1c ≥ 6.5% is less likely to detect diabetes than those defined by FPG and 2h-PG. HbA1c ≥ 6.5% detects less than 50% of diabetic patients defined by FPG and less than 30% of diabetic patients defined by 2h-PG. When the diagnosis of diabetes is in doubt by HbA1c, FPG, and/or 2h-PG should be obtained.[6] The relation between FPG and HbA1c is strong ($r=0.723$; $p < 0.01$) as is the correlation between PPBS and HbA1c ($r=0.735$; $p < 0.01$) in new-onset type 2 diabetes indicating that both FPG and PPBS had a similar contribution to the HbA1c in new-onset diabetes. The correlation between FPG and HbA1c resembles the other study.[6] In a meta-analysis, where eleven eligible studies were evaluated for the correlations of fasting and postprandial glucose to glycated hemoglobin, revealed postprandial glucose had a stronger correlation with HbA1c ($r=0.68$) than FPG ($r=0.61$), the reduction in postprandial glucose would have better glycemic control.[18] A cross-sectional study conducted in Kathmandu showed that postprandial blood glucose had a better correlation with HbA1c than the fasting plasma glucose revealing postprandial glucose contributed to the overall glycemic control than HbA1c.[19]

CONCLUSION

The diagnostic yield for diabetes is high if FPG diagnostic criteria is used alone than HbA1c alone as FPG ≥ 126 mg/dL will comprise more diabetic patients with HbA1c cut-off point ≥ 6.5%. As FPG is easily available and cheaper than HbA1c, this test alone can be considered where the HbA1c test is not available. However, using both FPG and HbA1c together will diagnose additional diabetes cases than using any diagnostic test alone so that active intervention could be undertaken to lessen the chronic complications due to hyperglycemia.

REFERENCES

1. Kharroubi AT, Darwish HM. Diabetes mellitus: The epidemic of the century. *World J Diabetes*. 2015;6(6):850-867.
2. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th ed. *Diabetes Res Clin Pract*. 2019;157:107843.
3. Shrestha DB, Budhathoki P, Sedhai YR, Marahatta A, Lamichhane S, Nepal S, et al. Type 2 Diabetes Mellitus in Nepal from 2000 to 2020: A systematic review and meta-analysis. *F1000Res.* 2021;10:543.
4. American Diabetes Association Professional Practice Committee. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2022. *Diabetes Care.* 2022;45(Suppl 1):S17-S38.
5. Florkowski C. HbA1c as a Diagnostic Test for Diabetes Mellitus - Reviewing the Evidence. *Clin Biochem Rev*. 2013;34(2):75-83.
6. Karnchanasorn R, Huang J, Ou HY, Feng, W, Chuang LM, Chiu KC, et al. Comparison of the Current Diagnostic Criterion of HbA1c with Fasting and 2-Hour Plasma Glucose Concentration. *J Diabetes Res.* 2016;2016:6195494.
7. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomark Insights*. 2016;11:95-104.
8. Bonora E, Tuomilehto J. The pros and cons of diagnosing diabetes with A1C. *Diabetes Care*. 2011;34 Suppl 2(Suppl 2):S184-S190.
9. World Health Organization. Regional Office for the Western, P., The Asia-Pacific perspective: redefining obesity and its treatment. 2000: Sydney: Health Communications Australia.
10. Kaur J. A comprehensive review on metabolic syndrome [retracted in Cardiol Res Pract. 2019 Jan 31;2019:4301528]. *Cardiol Res Pract*. 2014;2014:943162.
11. Ding Q, Spatz ES, Lipska KJ, Lin H, Spertus JA, Dreyer RP, et al. Newly diagnosed diabetes and outcomes after acute myocardial infarction in young adults. *Heart*. 2021;107(8):657-666.
12. Lv F, Cai X, Hu D, Pan C, Zhang D, Xu J, et al. Characteristics of Newly Diagnosed Type 2 Diabetes in Chinese Older Adults: A National Prospective Cohort Study. *J Diabetes Res*. 2019;2019:5631620.
13. KC A, Kansakar A, Kansakar AR, Poudel A. Prevalence of complications in newly diagnosed Diabetes Mellitus visiting Nepal Medical College & Teaching Hospital. *Nepal Med Coll J.* 2018; 20(1-3): 78-82.
14. Tamrakar R, Shrestha A, Tamrakar D. Prevalence of Metabolic Syndrome in Newly Diagnosed Type 2 Diabetes Mellitus. *Kathmandu Univ Med J (KUMJ).* 2019;17(68):273-8.
15. Cowie CC, Rust KF, Byrd-Holt DD, Gregg EW, Ford ES, Geiss LS, et al. Prevalence of diabetes and high risk for diabetes using A1C criteria in the U.S. population in 1988-2006. *Diabetes Care*. 2010;33(3):562-568.
16. Mooradian AD. Dyslipidemia in type 2 diabetes mellitus. *Nat Clin Pract Endocrinol Metab.* 2009;5(3):150-9.
17. Kreisberg RA. Diabetic dyslipidemia. *Am J Cardiol*. 1998;82(12A):67U-86U.
18. Ketema EB, Kibret KT. Correlation of fasting and postprandial plasma glucose with HbA1c in assessing glycemic control; systematic review and meta-analysis. *Arch Public Health*. 2015;73:43.
19. Shrestha L, Jha B, Yadav B, Sharma S. Correlation between fasting blood glucose, postprandial blood glucose and glycated hemoglobin in non-insulin treated type 2 diabetic subjects. *Sunsari Tech Coll J.* [Internet]. 2013 Sep. 16 [cited 2022 Dec. 2];1(1):18-21