

Glycated Hemoglobin: Better Diagnostic Parameter than Fasting Plasma Glucose Levels: A Comparative study in Patients undergoing Dental Surgery.

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Abstract: HbA_{1c} expressed as the percentage of adult haemoglobin that is glycated, is the most widely used measure of glycemic status. Achieving near-normal HbA_{1c} levels has been shown to reduce long-term complications of diabetes mellitus and the HbA_{1c} assay is recommended to determine whether treatment is adequate and to guide adjustments. To compare fasting plasma glucose (FPG) and glycated hemoglobin (HbA_{1c}) were compared in identifying type 2 diabetes mellitus patients. One hundred (100) participants were included in this prospective study. Diabetes was defined as an FPG level ≥ 126 mg/dl or an HbA_{1c} level $\geq 6.5\%$. Data was compiled and analyzed from the baseline and second examination conducted at 6 months. The screening model using FPG ≥ 126 mg/dl had sensitivity of 62.29% while that of $HbA_{1c} \geq 6.5\%$ was 95.08% whereas the specificity were 89.74% and 94.87% respectively for detecting undiagnosed diabetes. **Conclusion:** FPG and HbA_{1c} criteria do not identify identical groups of individual from a population-based sample as having diabetes. Using HbA_{1c} alone to conduct an initial diabetes screening in undiagnosed participants detects more cases of prevalent diabetes than FPG alone.

Keywords: Diabetes mellitus, fasting plasma glucose, glycated haemoglobin.

INTRODUCTION

Diabetes mellitus has emerged as an important public health and economic problem worldwide¹. One third of people with diabetes mellitus do not know whether they have the disease and the average lag between onset and diagnosis of the disease is seven years². The World Health Organization (WHO) estimates that worldwide there are currently 220 million people living with diabetes³. The greatest increase in prevalence is however, expected in developing countries of Asia and Africa, where most of the patients will likely be found by the year 2030⁴.

Diabetes is becoming an important health related problem in India. In 2010, 45.5 million individuals had diabetes. Of these, 14.7 million and 30.5 million were found in rural and urban areas, respectively. By 2020, the number of prevalent diabetes cases will increase to 69.7 million. By the end of 2011 and 2020, data-monitor estimates that the total prevalent cases of type 2 diabetes mellitus will increase to 47.2 and 69.7 million, respectively⁵. In India the prevalence of this disease is 2.4% in rural population and 11.6% in urban population⁴. More efficient approaches to diagnose diabetes mellitus at an early stage need to be developed to improve health care for patients with diabetes mellitus.

The diagnosis of diabetes is usually delayed in a number of individuals due to unsatisfactory, unreliability and inconvenience of the currently available diagnostic methods. Clinical as well as economic benefits of an early diagnosis of diabetes are generally acknowledged. However, it is estimated that almost 30% of individuals with diabetes mellitus are not aware of this disease, and moreover, they already have long-term complications of chronic hyperglycemia developed before actual diagnosis. That is why an International Expert Committee recommended the use of glycated hemoglobin (HbA_{1c}) testing in the diagnosing of this deleterious disease⁵. HbA_{1c} has significant advantages over fasting plasma glucose in the form of low variability from day to day. Further, it has greater stability and the patient is not required to fast before the test is performed⁶.

According to a study by researchers at the Johns Hopkins Bloomberg School of Public Health, HbA_{1c} levels accurately predict future diabetes, and it better predicts mortality and morbidity due to stroke, heart disease etc⁷. An HbA_{1c} threshold of 6.5% was proposed for the diagnosis of diabetes on the basis of the data from the US National Health and Nutrition Examination Survey⁸.

MATERIALS AND METHODS

In this prospective cross-sectional study, a total of 100 Indian men and women attending Dental OPD, aged 34-68 years, from November 2010 to April 2011 was conducted in the department of Biochemistry at Maharishi Markandeshwar Institute of Medical Sciences & Research, Mullana after providing written informed consent. Briefly, each examination included a personal interview and a physical examination. Diabetes status was defined by American Diabetes Association (ADA) 2010 criteria. Obesity status was defined as obese if BMI was ≥ 30 kg/m², overweight if BMI was 25-29.9 kg/m², and normal if BMI was 19-24.9 kg/m².⁹ According to Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) criteria, hypertension (HTN) was defined as SBP/DBP $\geq 140/90$ mmHg or on antihypertensive medications, normal if SBP < 120 mmHg and DBP < 80 mmHg, and pre-hypertension (Pre-HTN) otherwise¹⁰. The samples were analysed for fasting plasma glucose by the glucose oxidase-peroxidase (GOD-POD) method and glycated hemoglobin by ion exchange resin method^{11,12}. The internal control sera of two different levels were used to calibrate the instruments. Data collected at the baseline and second examination for those participants who had HbA_{1c} and FPG measured and did not receive insulin treatment or an oral agent for diabetes, were not anaemic, nor on renal dialysis, and did not have a kidney transplant were used to compare the performances of HbA_{1c} and FPG in identifying diabetes in undiagnosed participants.

Statistical Analysis

The data obtained was compiled and analyzed using SPSS 11.5 for Windows version. Means were calculated and Student t-test was applied to find out significance level. Statistical significance was defined as two-tailed $p < 0.05$ for all tests unless otherwise specified. The best predictive cut-off values for FPG and HbA_{1c} for detecting new patients with diabetes were identified using the optimal sensitivity and specificity values.

RESULTS

Out of 100 subjects, 61 proved to be having diabetes mellitus. If current criterion of FPG (≥ 126 mg/dL) for diabetes screening was used, a good proportion of diabetic subjects remained unidentified.

Table 1 and 2 demonstrates the demographic profile of 100 subjects under

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study. There was no statistically significant difference between the two groups (visits) as far as the demographic variables were concerned except for fasting plasma glucose at second visit ($P=0.005$). Figure 1 shows the receiver operating curve (ROC) plot representing the sensitivity and specificity of HbA_{1c} and FPG in detecting undiagnosed diabetes. The optimal cut-off points of HbA_{1c} and FPG values for diagnosis of diabetes were $\geq 6.5\%$ (AUC 0.991, sensitivity 95.08 % and specificity 94.87%; positive predictive value 96%, negative predictive value 92.50%) and ≥ 126 mg/dL (AUC 0.909, sensitivity 62.29 % and specificity 89.74%; Positive predictive value 90.47%, Negative predictive value 60.34%) respectively. Table 3 shows the weighted sensitivity and specificity of model incorporating combinations of criteria for FPG and HbA_{1c} for detecting undiagnosed diabetes.

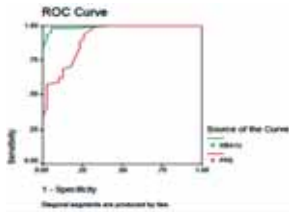


FIGURE 1: Receiver-operating characteristic curves for cut-off values of glycated hemoglobin (HbA_{1c}) and fasting plasma glucose (FPG) to diagnose diabetes.

Table 1: Demographic profile of the study groups.

Demographic Characteristics	First visit (mean±SD)	Second visit (mean±SD)	P-value	
Age	51.66±9.00	51.66±9.00	1.00	
Sex (M/F)	50/50	50/50	1.00	
Hypertension (n/100)	46/100	50/100	0.693	
BMI	20.76±2.29	21.31±2.17	0.23	
Lipid profile	LDL	132.36±34.63	131.30±34.35	0.88
	HDL	36.54±9.79	39.10±9.50	0.188
	TG	179.94±63.71	176.92±61.73	0.81

Table 2: depicting Mean and standard deviation values of FPG and HbA_{1c} at first and subsequent second visit.

		First visit (mean±SD)	Second visit (mean±SD)	P-value
Fasting Plasma Glucose	Normal	93.63±18.0	82.50±17.32	>0.05
	Raised	109±18.96	139.27±11.42	<0.005
HbA _{1c}	Normal	4.94±1.21	4.54±0.55	>0.05
	Raised	7.74±1.21	7.77±0.99	>0.05

Table 3: Diagnostic indices of criteria using fasting plasma glucose (FPG) and glycated hemoglobin (HbA_{1c}) for detecting undiagnosed diabetes.

Criterion	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
FPG ≥ 126 mg/dL	62.29	89.74	90.47	60.34
HbA _{1c} ($\geq 6.5\%$)	95.08	94.87	96	92.50

Mean (95% confidence interval).

Table 4: Data depicting number of diabetic patients with raised FPG and HbA_{1c} during their 1st and 2nd visits.

		Fasting plasma glucose	HbA _{1c}	P-value
Diabetes Mellitus (n=61)	1 st visit	22	61	< 0.005
	2 nd visit	58	59	□ 0.05

DISCUSSION

We found that using HbA_{1c} alone in initial diabetes screening among undiagnosed adults in a population-based sample identified more cases of prevalent diabetes than using FPG alone. In general, HbA_{1c} has detected higher prevalence of diabetes than glucose criteria in United States and other populations, especially in undiagnosed participants, which is consistent with our findings. The discordances between diabetes identified by HbA_{1c} and FPG among undiagnosed participants may be caused in part by the fact that HbA_{1c} level reflects an integrated measure of glycemia

over a 2-3 month period, whereas FPG reflects the influence of hepatic glucose output on the day of the visit¹. We found that in the initial diabetes screening, among undiagnosed participants at the baseline examination FPG ≥ 126 mg/dL identified less cases of diabetes than HbA_{1c} $\geq 6.5\%$, but in a successive diabetes screening 6 months later, among undiagnosed participants the percentages were nearly equal (Table 4). Two of the patients who were missed to be having diabetes by HbA_{1c} criterion on second visit were found to be anemic explaining the reason for normal HbA_{1c} in them. Both of them were proven out to diabetic by FPG criterion. The difference between the initial and successive diabetes screenings may be because at the baseline examination, those newly diagnosed participants might have had unrecognized diabetes for many years, while those newly diagnosed at the successive examination might have had unrecognized diabetes for at most 6 months. This supports the contention that HbA_{1c} $\geq 6.5\%$ represents sustained daily hyperglycemia sufficient to meaningfully influence glycation, whereas FPG ≥ 126 mg/dL may be a transient phenomenon that happens occasionally in many people. Our data show that a large number of people at risk can be identified using both HbA_{1c} and FPG. A cost-effective diabetes screening procedure could be to: 1) measure HbA_{1c} for all participants and 2) further measure FPG only for those participants with HbA_{1c} $\geq 6.5\%$, since our data show that this would result in the identification of most of the remainder of those who would have diabetes by FPG criterion. The strength of the study includes population-based sampling and systematic measures at two examinations.

CONCLUSION

The FPG and HbA_{1c} criteria do not identify identical groups of individual from a population-based sample as having diabetes. Using HbA_{1c} alone to conduct an initial diabetes screening in undiagnosed participants detects more cases of prevalent diabetes than FPG alone. Hence, the use of glycated haemoglobin should be encouraged on a wider scale for diagnosing diabetes mellitus at an early stage.

COMPETING INTERESTS

The authors declare that there were no competing interests associated with this study.

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