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Original Article

Diagnostic Efficacy of HbA1c in Diagnosis of Diabetes Mellitus in a Bangladesh Population

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Abstract:

American Diabetic Association (ADA) affirms HbA1c with cut off value of 6.5% as a diagnostic criteria of diabetes mellitus. World Health Organization (WHO) also supports but recommended that a value <6.5% does not exclude diabetes which is diagnosed by glucose test. The aim of this study was to evaluate the diagnostic efficacy of HbA1c in terms of sensitivity, specificity, positive and negative predictive value and accuracy in a selected group of Bangladeshi subjects. This cross-sectional study included 761 adult Bangladeshi subjects of both sex attending the outdoor in a tertiary healthcare center during the period of September 2009 to September 2010. Fasting, postprandial (2 hours after glucose load) plasma glucose and HbA1c were measured. Diabetes is defined according to HbA1c and plasma glucose. Sensitivity, specificity, positive and negative predictive value of HbA1c were 90.00% (CI 86.48-92.86%), 76.21% (CI 71.68-80.35%), 78.17% (CI 73.94-82.00%) and 88.96% (CI 85.10-92.10%) respectively. Accuracy was 82.92% with odds ratio (OR) 28.84 (CI 19.10-43.54%); p < 0.001. Though HbA1c revealed remarkable diagnostic efficacy and ease of performance, still it can not over rule the role of plasma glucose in diagnosis of diabetes mellitus.

Key words: HbA1c, Sensitivity, specificity, positive predictive value, negative predictive value.

Introduction:

Glycosylated haemoglobin (HbA1c) is a term used to describe a series of stable minor haemoglobin components formed slowly and nonenzymatically from haemoglobin and glucose. HbA1c most accurately reflects the previous 2-3 months of glycaemic control, does not require fasting, has less day-to-day biologic variability, and is a well-accepted marker of risk of long-term microvascular complications.[1,2]

In 1997, the first American Diabetic Association (ADA) Expert Committee on the Diagnosis and Classification of Diabetes Mellitus suggested the diagnostic cut point of either 126 mg/dl (7.0 mmol/l) for fasting plasma glucose (FPG) and 2 hour post glucose (2hPG) value of 200 mg/dl (11.1 mmol/l) independently to define diabetes. The FPG level is easy to obtain and is suggested as the single test to use for diabetes screening. However, there are reports showing a lack of concordance between the FPG and the 2hPG criteria. Such discrepancies reduce the efficacy of using FPG alone in diabetes screening. It is difficult for physicians and patients to use the oral glucose tolerance test (OGTT) because of its drawbacks, especially for those patients already having an FPG <7.0 mmol/l. It is also impractical to conduct the OGTT for everyone in a diabetes screening. Therefore, an additional, simple, cost-effective, efficient, and tolerable diagnostic process for detecting these cases of diabetes would be highly desirable for diabetes screening.[3]

In a recent report, after an extensive review of both established and emerging epidemiological evidence, an International Expert Committee recommended the use of the HbA1c test to diagnose diabetes with a threshold of ?6.5%, and ADA affirms this decision.[4] WHO also recommended HbA1c =6.5% as a cut off value to diagnose diabetes but a value <6.5% does not exclude diabetes which is diagnosed by glucose test. So it is obvious that diagnosis of diabetes by HbA1c alone is not the ultimate and confirmation needs measurement of plasma glucose. Previous diagnostic studies of HbA1c have relied exclusively on a single elevated fasting or 2-hour glucose values as gold standards.[5]

So aim of our study is to evaluate the efficacy of HbA1c as a diagnostic tool for diagnosis of diabetes in a selected Bangladeshi population in terms of sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

Method:

This cross sectional study was undertaken in the department of Biochemistry and Cell Biology, Bangladesh Institute of Health Science, Dhaka, Bangladesh during the period of September 2009 to September 2010. A total 761 adult subjects of both sex were included irrespective of any confounder purposively. Fasting and two hours postprandial (after oral glucose load) plasma glucose concentrations were measured by standard method (Hexokinase method) using kits manufactured by Siemens Health Care Ltd. by Dimension RxL automated chemistry analyzer. HbA1c was measured by cation exchange high pressure liquid chromatography (using D-10TM BioRad, USA Haemoglobin Assay System). Subjects were categorized into two groups taking the cut off value of HbA1c 6.5%. Subjects were also categorized into diabetic and nondiabetic (including prediabetics) on the basis of plasma glucose level. Fatsing

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=7.0mmol/L and postprandial >11.1 mmol/L were the cut off values. Data were analyzed using relevant statistical formula using SPSS 12.0 for Windows and Graph pad prism software. Sensitivity [{True positive / (True positive + False negative)} x 100], specificity [{True negative / (False positive + True negative)} x 100], positive predictive value [{True positive / (True positive + False positive)} x 100], negative predictive value [{True negative / (True negative + False negative)} x 100], accuracy [{(True positive +True negative) / Total subjects} x 100] and odds ratio (OR) were determined along with confidence interval (CI) at 95% confidence limit.

Results:

Mean ± SD age of the study subjects was 43.56 ± 10.92 years with range of 25-70 years. Out of 761 subjects 312 (40.99%) were male and 449 (59.01%) were female. Table 1 shows the distribution of the subjects according to HbA1C value and plasma glucose level.

Table 1: Distribution of the subjects according to HbA1c value and plasma glucose level:

Grouping on the basis of HbA1C(%)	Grouping on the basis of Diabetic	Plasma glucose Non diabetic	Total
6.5%	333	93	426
<6.5%	37	298	335
Total	370	391	761

Sensitivity, specificity, positive predictive value and negative predictive value were 90.00%, 76.21%, 78.17% and 88.96% respectively and shown in table 2. Accuracy was 82.92% with odds ratio (OR) 28.84 (CI 19.10 - 43.54%); p < 0.001.

Table 2: Sensitivity, specificity, positive predictive value and negative predictive value of HbAIC in diagnosis of diabetes:

Diagnostic parameters	Value (%)	CI (at 95% confidence limit)
Sensitivity	90.00%	86.48 – 92.86%
Specificity	76.21%	71.68 – 80.35%
Positive predictive value	78.17%	73.94 – 82.00%
Negative predictive value	88.96%	85.10 – 92.10%

Discussion:

Though the International Expert Committee suggested 6.5% as the cut off value of HbA1c, different countries have set different cut off values of their own to improve its diagnostic efficacy.[6] Interestingly some researchers got almost similar findings taking different set values whereas some others reached to widely different conclusions even after taking same cut off value. In recent studies done in China and Abu Dhabi the set points were 6.3% and 6.4% respectively and they got sensitivity and specificity of 63%, 96% and 72%, 84% respectively.[7,8] Taking 6.5% as the cut off value Sonia et al. found sensitivity and specificity of 83.3% and 88.0% which are in line with our findings and that of Rohlfing et al. were 42.8% and 99.6% respectively which differs from ours.[9,10] In a recent study by Saiedullah et al. done on Bangladeshi population, notable inequity in diagnosis of DM by plasma glucose and HbA1c was found taking 6.5% as the cut off value.[11] It is of no doubt that HbA1c is informative & has no diurnal or dietary prerequisite to perform and in some cases it is helpful to assess the glycaemic status of an irregular patient or a patient without previous records. But taking all the facts and study findings in consideration HbA1c seems not to be sufficient enough to be the sole diagnostic parameter with a cut off value of 6.5% in our population. Though we got remarkable sensitivity, specificity, positive and negative predictive value and accuracy of HbA1c over plasma glucose taking 6.5% as cut off value but further studies should be done by increasing the set value along with large population size to get more reliable results. As once diabetic is a diabetic forever, so it demands great caution and authenticity.

References:

1. Goldstein DE, Little RR, Lorenz RA, et al. Tests of Glycemia in Diabetes. Diabetes Care 2004;27(7):1761-1773.
2. Cheng P, Neugaard B, Foulis P, Conlin PR. Hemoglobin A1c as a Predictor of Incident Diabetes. Diabetes Care 2011;34(2):610-615.
3. Wang W, Lee ET, Fabsitz R, Welty TK, HowardBV. Using HbA1c to Improve Efficacy of the American Diabetes Association Fasting Plasma Glucose Criterion in Screening for New Type 2 Diabetes in American Indians: The Strong Heart Study. Diabetes Care 2002;25 (8):1365-1370.
4. Position Statement. American Diabetes Association. Standards of Medical Care in Diabetes - 2010. Diabetes Care 2010;33:S11-S61.
5. Selvin E, Steffes MW, Gregg E, Brancati FL, Coresh J. Performance of A1C for the Classification and Prediction of Diabetes. Diabetes Care 2011;34(1):84-89.
6. International Expert Committee Report on the role of the a1c assay in the diagnosis of diabetes. Diabetes Care 2009;32:1327-1334.
7. Bao Y, Ma X, Li H, et al. Glycated haemoglobin A1c for diagnosing diabetes in Chinese population: cross sectional epidemiological survey. BMJ 2010;340.
8. Hajat C, Harrison O, Siksek ZA. Diagnostic Testing for Diabetes Using HbA1c in the Abu Dhabi Population Weqaya: the Abu Dhabi Cardiovascular Screening Program. Diabetes Care 2011;34(11):2400-2402.
9. Sonia SA, Razak F, Vuksan V, et al. Diagnostic Strategies to Detect Glucose Intolerance in a Multiethnic Population. Diabetes Care 2003;26(2):290-296.
10. Rohlfing CL, Little RR, Wiedmeyer HM, et al. Use of