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**Research Article**

# Determine the Diagnostic Accuracy of Hba1c for Detection of Diabetes Mellitus by Taking Fasting Blood Sugar as Gold Standard

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## ABSTRACT

HbA1c is now formally endorsed in many countries as a diagnostic test for (type 2) diabetes as well as for monitoring, although some debate still continues regarding its applicability for diagnosis.

**OBJECTIVE:** The objective of the study was to:Determine the diagnostic accuracy of HbA1C for detection of diabetes mellitus by taking fasting blood sugar as gold standard.

**STUDY DESIGN:** Cross Sectional Study (Validation)

**SETTING:** Medical department, Allied Hospital, Faisalabad

**DURATION OF STUDY:** 6 Months Duration after approval of synopsis From: 25-02-2015 to 25-08-2015

**METHODOLOGY:** A total of 145 cases with more than 40 years of age of either gender were enrolled in the study. Informed consent was taken from each participant of the study from medical department, Allied Hospital, Faisalabad. Information was collected by trainee researcher and comprised age, Gender, address and contact number, HbA1C and Fasting Blood Sugar. HbA1C and Fasting blood sugar was measured by drawing 3cc blood from a peripheral vein after antiseptic measures and sent to pathology laboratory, Allied Hospital, Faisalabad where it was reported by Pathologist. All the information was collected on Performa by Principal Investigator.

**RESULTS:** In our study, 71.72%(n=104) were between 40-60 years while 28.28%(n=41) had >60 years of age, mean±sd was calculated as 56.75±6.45 years, 52.41%(n=76) were male and 47.59%(n=69) were females, frequency of diabetes mellitus on gold standard was recorded as 26.21%(n=38) while 73.79%(n=107) had no findings of the morbidity. Diagnostic accuracy of HbA1C for detection of diabetes mellitus by taking fasting blood sugar as gold standard was calculated for sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate as 78.95%, 83.17%, 62.15%, 91.75% and 82.07% respectively.

**CONCLUSION:** We concluded that the diagnostic accuracy of HbA1C at cutoff point more than 6.15% for detection of diabetes mellitus by taking fasting blood sugar as gold standard is high and this modality can be used in our population.

**KEYWORDS:** Diabetes mellitus, diagnosis, HbA1c, diagnostic accuracy

## INTRODUCTION

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the β-cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action.[1]

There are two different types of diabetes mellitus. In type 1 diabetes mellitus, the problem is that the pancreas (an organ in the abdomen) does not make enough insulin. In type 2 diabetes mellitus, the pancreas does not make enough insulin (Fig. 1), the body becomes resistant to normal or even high levels of insulin, or both.[2,3]

Diabetes is among the most common chronic illnesses worldwide, with Type 2 diabetes mellitus accounting for approximately 90% of all cases.[4] Over the past three decades, the number of people with diabetes mellitus has more than doubled globally, making it one of the most important public health challenges to all nations.[5] Rate of Diabetes are increasing world wide the international diabetes federation predicts that number of people with diabetes will case from 266 million in 2011 to 552 million by 2030.[6,7] The prevalence of diabetes has been estimated around 24% in those aged over 40.[8] Diabetes mellitus is an ever increasing epidemic that is adding to so many chronic diseases like Cardiovascular, Cerebrovascular, End Stage Kidney Disease and Retinopathies.[9]

The importance of early diagnosis of diabetes mellitus cannot be more over emphasized as it is imperative for early treatment and prevention of ghastly complications which are part and parcel of this deadly disease. Diagnosis of Diabetes Mellitus is established by Fasting and random blood sugars of $\geq$126mg/dl and $\geq$200mg/dl respectively. These are also used as screening tests. In order to detect diabetics, fasting blood glucose (FBS) is suggested as the best and the most common test with the cutoff point $\geq$126 mg/dl.[10] However, there are some issues about using FBS such as keeping the clients fast for about 8 hours and not being applicable in the afternoon.

HbA1C is a commonly used investigation in assessing control of diabetes mellitus over previous 2 to 3 months for long term complcations.[11]Recently its role has been suggested in diagnosis and screening of diabetes mellitus also but it has been argued that due to problems in standardization and variations in styles of HbA1c test, it is not recommended as a routine test for screening of diabetes.

The best cutoff point for defining high HbA1c is another important issue. It seems that in different settings such as screening, diagnosis and prediction of progression of diabetes we need to define different cut off points.

The 2010 American Diabetes Association (ADA) standards of care for diabetes, based largely on the opinion of an international expert committee, added hemoglobin A1c (HbA1c) as diagnostic criteria for diabetes ($\geq$6.5%) and prediabetes (5.7–6.4%).[12]

In one study by G Zahra et al, it was found that the sensitivity, specificity, positive predictive value and negative predictive value of HbA1c in the prediction of FBS>126 mg/dl were 85%, 79%, 38%, and 97%, respectively.[13]

The Aim of this study is to explore the role of HbA1C in diagnosis of diabetes mellitus as compared to fasting blood sugar and to establish an optimum cutoff point for HbA1C as a screening test for separation of diabetics and non-diabetics was explored.

## OBJECTIVE

The objective of this study was to:

- Determine the diagnostic accuracy of HbA1C for detection of diabetes mellitus by taking fasting blood sugar as gold standard.

## MATERIAL AND METHODS

### STUDY DESIGN:

- Cross Sectional Study (Validation)

### SETTING:

- Medical department, Allied Hospital, Faisalabad

**DURATION OF STUDY:**

- 6 Months Duration after approval of synopsis From: 25-02-2015 to 25-08-2015

**SAMPLE SIZE:**

- By using WHO sample size calculator for sensitivity

Sensitivity = 85% [8]
Specificity = 79%[8]
Prevalence = 24% [8]
Precision for sensitivity = 10%
Precision for specificity = 10%
Confidence Level = 95%
Sample size = 145

**SAMPLING TECHNIQUE:**

- Non-Probability Consecutive Sampling

**SAMPLE SELECTION:**

**Inclusion Criteria:**

- More than 40 years of Age
- Male and Female Gender
- People with complaint of polyuria (passing urine more than 8 times per day)

**Exclusion Criteria:**

- Already Diagnosed cases of type I and type2 diabetes mellitus
- Who have undergone screening of diabetes mellitus within past 1 year

**DATA COLLECTION PROCEDURE:**

Informed consent was taken from each participant of the study. Persons fulfilling inclusion criteria were enrolled from medical department, Allied Hospital, Faisalabad. Information was collected by trainee researcher and comprised age, Gender, address and contact number, HbA1C and Fasting Blood Sugar. HbA1C and Fasting blood sugar was measured by drawing 3cc blood from a peripheral vein after antiseptic measures and sent to pathology laboratory, Allied Hospital, Faisalabad where it was reported by Pathologist. All the information was collected on Performa by Principal Investigator.

**DATA ANALYSIS PROCEDURE:**

The collected data was entered into SPSS version 16 and analyzed accordingly. Mean and standard deviation was calculated for the quantitative variables like age, HbA1C and Fasting Blood Sugar. Frequency and percentages were calculated for qualitative variables like Gender and true positives. Sensitivity, specificity, Positive predictive value and negative predictive value was calculated by constructing 2*2 table as given under:

| HbA1C >6.15% | Fasting Blood sugar ≥126mg/dl | Fasting Blood Sugar <126mg/dl |
|---|---|---|
| Positive test | True positive(a) | False positive(b) |
| Negative test | False negative(c) | True negative(d) |

- Sensitivity (%) = [a/(a+c)] * 100
- Specificity (%) = [d/(b+d)]* 100
- Positive predictive value =a/(a+b)
- Negative Predictive value = d/(c+d)
- Diagnostic accuracy = true positive + true negative/ true positive + false positive + true negative + false negative * 100

**RESULTS**

A total 145 cases were fulfilling the inclusion/exclusion criteria were enrolled to determine the diagnostic accuracy of HbA1C for detection of diabetes mellitus by taking fasting blood sugar as gold standard.

Age distribution of the patients was done, showing that 71.72%(n=104) were between 40-60 years while 28.28%(n=41) had >60 years of age, mean±sd was calculated as 56.75±6.45 years. (Table No. 1)

Patients were distributed according to gender showing that 52.41%(n=76) were male and 47.59%(n=69) were females. (Table No. 2)

Frequency of diabetes mellitus on gold standard was recorded as 26.21%(n=38) while 73.79%(n=107) had no findings of the morbidity. (Table No. 3)

Mean fasting sugar level was recorded as 115.54±18.02 mg/dl. (Table No. 4)

Mean HbA1C level was calculated as 6.98±2.45%. (Table No. 5)

Diagnostic accuracy of HbA1C for detection of diabetes mellitus by taking fasting blood sugar as gold standard was calculated for sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate as 78.95%, 83.17%, 62.15%, 91.75% and 82.07% respectively. (Table No. 7)

**TABLE No. 1** AGE DISTRIBUTION (n=145)

| Age(in years) | No. of patients | % |
|---|---|---|
| 40-60 | 104 | 71.72 |
| >60 | 41 | 28.28 |
| **Total** | **145** | **100** |
| **mean±sd** | **56.75±6.45** | |

**TABLE No. 2** GENDER DISTRIBUTION (n=145)

| Gender | No. of patients | % |
|---|---|---|
| Male | 76 | 52.41 |
| Female | 69 | 47.59 |
| **Total** | **145** | **100** |

**TABLE No. 3** FREQUENCY OF DIABETES MELLITUS ON GOLD STANDARD (n=145)

| Diabetes mellitus | No. of patients | % |
|---|---|---|
| Yes | 38 | 26.21 |
| No | 107 | 73.79 |
| **Total** | **145** | **100** |

**TABLE No. 4** MEAN FASTING SUGAR LEVEL (n=145)

| Sugar level(mg/dl) | Mean | SD |
|---|---|---|
| | 115.54 | 18.02 |

**TABLE No. 5** MEAN HbA1C LEVEL (n=145)

| HbA1C | Mean | SD |
|---|---|---|
| | 6.98 | 2.45 |

**TABLE No. 6** DIAGNOSTIC ACCURACY OF HBA1C FOR DETECTION OF DIABETES MELLITUS BY TAKING FASTING BLOOD SUGAR AS GOLD STANDARD (n=145)

| HbA1C >6.15% | Fasting Blood Sugar | | Total |
|---|---|---|---|
| | Fasting Blood Sugar ≥126mg/dl | Fasting Blood sugar <126mg/dl | |
| Positive | 30(a) | 18(b) | 48 |
| Negative | 8(c) | 89(d) | 97 |
| **Total** | **38** | **107** | **145** |

Sensitivity = a / (a + c) x 100 =78.95%

Specificity = d / (d + b) x 100 = 83.17%

Positive predictive value = a / (a + b) x 100 =62.5%

Negative predictive value = d / (d + c) x 100 =91.75%

Accuracy rate = a + d / (a + d + b + c) x 100 = 82.07%

## DISCUSSION

HbA1c is now formally endorsed in many countries as a diagnostic test for (type 2) diabetes as well as for monitoring, although some debate still continues regarding its applicability for diagnosis. We planned this study to explore the role of HbA1C in diagnosis of diabetes mellitus as compared to fasting blood sugar and to establish an optimum cutoff point for HbA1C as a screening test for separation of diabetics and non-diabetics was explored.

Our findings regarding frequency of diabetes mellitus is in agreement with a study by haghdoost AA and others[8] who estimated around 24% in those aged over 40.

Diagnostic accuracy recorded in our study is in agreement with one study by G Zahra et al, where it was found that the sensitivity, specificity, positive

predictive value and negative predictive value of HbA1c in the prediction of FBS>126 mg/dl were 85%, 79%, 38%, and 97%, respectively.[13]

A recent analysis by Yu EY and others[14] reveal that HbA1c ≥ 6.5% has been recommended as a diagnostic criterion for the detection of diabetes mellitus (DM) since 2010 because of its convenience, stability and significant correlation with diabetic complications. Nevertheless, the accuracy of HbA1c compared to glucose-based diagnostic criteria varies among subjects of different ethnicity and risk profile.

In their study,[14] among the 1128 subjects (mean age 64.2±8.9 year, 48.8% male), 229 (20.3%) were diagnosed to have DM by OGTT. The sensitivity and specificity of HbA1c ≥6.5% were 33.2% and 93.5%, respectively, for predicting DM diagnosed by OGTT. The area under the ROC curve was 0.770, indicating HbA1c had fair discriminatory power.

Bennett CM and others[15] assessed the validity of glycated haemoglobin A(1c) (HbA(1c)) as a screening tool for early detection of Type 2 diabetes and recorded that at certain cut-off points, HbA(1c) has slightly lower sensitivity than fasting plasma glucose (FPG) in detecting diabetes, but slightly higher specificity.[16,17] For HbA(1c) at a Diabetes Control and Complications Trial and UK Prospective Diabetes Study comparable cut-off point of > or = 6.1%, the sensitivity ranged from 78 to 81% and specificity 79 to 84%. For FPG at a cut-off point of > or = 6.1 mmol/l, the sensitivity ranged from 48 to 64% and specificity from 94 to 98%. Both HbA(1c) and FPG have low sensitivity for the detection of impaired glucose tolerance (around 50%). They concluded that HbA(1c) and FPG are equally effective screening tools for the detection of Type 2 diabetes. The HbA(1c) cut-off point of > 6.1% was the recommended optimum cut-off point for HbA(1c) in most reviewed studies. Previous studies have aslo demonstrated that HbA(1c) has less intra-individual variation and better predicts both micro- and macrovascular complications.

Shibata K and others[18] compared the sensitivity, specificity, and total accuracy of an HbA1c of > or =6.5% in the detection of hyperglycemia (PPHG) relative to those of a fasting blood glucose (FBG) of > or =7.0 mmol/L and concluded that although the HbA1c test was marginally more specific but less sensitive than the FBG test, at the given cutoff points the accuracies of two tests were equivalent but this study was conducted in 2001 to 2002.

The ADA endorsed $HbA_{1c}$ as a diagnostic test for diabetes at a cut-off of ≥48 mmol/mol (≥6.5%) with the provision that this be measured in a laboratory using a NGSP-certified assay aligned to the DCCT study, and that in the absence of unequivocal hyperglycaemia the test should be repeated.[19] Individuals with an $HbA_{1c}$ of 39–46 mmol/mol (5.7–6.4%) are considered to be at 'increased risk' for diabetes as well as cardiovascular disease, and should be counselled about effective strategies, such as weight loss and physical activity, to lower their risks.[19]

In formulating the WHO recommendations, a process of consultation included experts in diabetology, biochemistry, immunology, genetics, epidemiology and public health. The main question to be answered for the update was agreed upon by the expert group: how does $HbA_{1c}$ perform in the diagnosis of type 2 diabetes based on the detection and prediction of microvascular complications? Applying the principles of Evidence Based Medicine, a search for existing systematic reviews in Embase did not identify any such review. Therefore, a systematic review to answer this question was conducted by the Boden Institute of Obesity, Nutrition and Exercise, The University of Sydney, Australia. The recommendation was drafted by the expert group following the GRADE methodology, and the process outlined in the WHO Handbook for Guideline Development. All the experts agreed on the recommendation.

In New Zealand, $HbA_{1c}$ as a diagnostic test was formally endorsed by the New Zealand Society for the Study of Diabetes (NZSSD) from 3 October 2011.[20] This recommendation was coordinated with the adoption of exclusively molar units for reporting $HbA_{1c}$ (following a two year period of dual reporting, like the United Kingdom), with the diagnostic cut-off rounded up to ≥50 mmol/mol

(≥6.7%), and with repeat testing on a second occasion in asymptomatic individuals. Individuals with $HbA_{1c}$ in the range 41–49 mmol/L are categorised as having 'dysglycaemia' or abnormal glucose tolerance, with the recommendation for re-testing in 6–12 months and also implementation of cardio-vascular risk management. Part of the NZSSD rationale for rounding of $HbA_{1c}$ was to make the molar units more memorable, although in addition, to maximise the specificity for the diagnosis of diabetes.[20] It may be argued that sensitivity is being compromised by adoption of $HbA_{1c}$ as a diagnostic test, and especially at a still higher level, and that cases of diabetes will be missed. NZSSD would contend, however, that individuals with $HbA_{1c}$ close to the cut-off (41–49 mmol/mol) will be re-tested in 6–12 months and will enter a lifestyle programme where cardiovascular risk factors will be appropriately addressed so they are not really being 'missed'. In addition, although glucose-based criteria remain valid, the NZSSD recommendations strongly favour $HbA_{1c}$ as the diagnostic test in preference to OGTT testing.[20]

Keeping in view all above discussion and results of our study, we are of the view that HbA1C for detection of diabetes mellitus is a reliable and useful modality and suitable in our population.

## CONCLUSION

- We concluded that the diagnostic accuracy of HbA1C at cutoff point more than 6.15% for detection of diabetes mellitus by taking fasting blood sugar as gold standard is high and this modality can be used in our population. Although the current cost of HbA(1c) is higher than FPG, the additional benefits in predicting costly preventable clinical complications may make this a cost-effective choice.

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