Research Article

Cross-sectional study of glycosylated haemoglobin in type 2 diabetes mellitus patients of South Indian origin

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ABSTRACT

Background: Prevalence of Type 2 Diabetes Mellitus in Indian population is on rise and is leading to significant morbidity and mortality. The revised ADA guidelines since 2010 have suggested glycated haemoglobin (HbA1c) as a diagnostic test for Type 2 diabetes. HbA1c level is having geographic and ethnic variability independent of glycaemic status and this has not been extensively studied in many regions.
Objective: To study the characteristics of HbA1C in the South Indian population and to determine the cut off value for HbA1C in diagnosing Diabetes in them.
Methods: This is a hospital based observational study conducted at a Tertiary care centre in North Kerala. Patients with age ≥30yrs with Fasting Plasma Glucose (FPG) ≥ 100 or Random Plasma Glucose (RPG) ≥ 200 with symptoms of hyperglycaemia with no previous history of anti diabetic treatment were selected for the study. A preset questionnaire was used to collect the data which was later analysed using relevant statistical techniques.
Results: Out of the consecutive diabetic patients attending medicine OPD 99 newly detected diabetics/prediabetics who were not under any anti diabetic medications were studied. New onset diabetes/prediabetes patients showed a mean HbA1c of 8.26(SD=2.31). There was no significant correlation of HbA1c values with age, sex and duration of diabetes in the study population. The HbA1c values also had no significant correlation with systolic blood pressure, total cholesterol values or triglyceride levels. However it was significantly related to Fasting plasma glucose, Post prandial plasma glucose and serum LDL cholesterol values. In newly detected diabetic patients (with FPG≥126 taken as gold standard) ROC analysis determined a HbA1c cut off at 6.45% (AUC=0.76, sensitivity=79%, specificity=60%).
Conclusion: The study provides a reliable cutoff of glycated haemoglobin (6.45%) among South Indian population which is in accordance with the ADA recommendations.

Keywords: Diabetes, HbA1c, Cut off, South Indian population, Fasting plasma glucose

INTRODUCTION

Type 2 Diabetes Mellitus is one of the leading causes of the morbidity and mortality worldwide. There is an estimated 382 million people with diabetes worldwide in the year 2013 out of which 65.1 million are from India.[1]

American Diabetes Association guidelines of 2010 have incorporated HbA1c as a diagnostic criterion for Diabetes Mellitus.[2] Glycated haemoglobin is formed by post translational, non enzymatic, substrate concentration dependent irreversible process and HbA1c is the sub fraction of glycated normal Haemoglobin. Several factors like hemoglobinopathies, renal failure, use of different drugs and even laboratory error will influence the accuracy of HbA1c.[3]

Evidence suggests that HbA1c has geographic and ethnic variability independent of glycaemic status.[2] This may be

related to genetic differences in the concentration of haemoglobin (Hb), the rates of glycation and the lifespan or amount of red blood cell etc. So it is essential to find out the variability of HbA1c in South Indian population and to ascertain its suitable cut off point for diagnosing Diabetes. Our study intended to study the characteristics of HbA1c values in South Indian population and to find out a cut off for diagnosing diabetes against the previous gold standard criteria.

METHODS

This is a hospital based observational study conducted in Department of Medicine at a Tertiary Care Centre in North Kerala. Consecutive patients aged more than 30 years attending medicine OPD over a period of 1 year who had Fasting Plasma Glucose (FPG) ≥ 100 or those who give history suggestive of Hyperglycaemia with Random Plasma Glucose (RPG) ≥ 200 with no previous anti diabetic treatment history were selected for the study.

Those patients having anaemia, critical illnesses including heart failure, end stage renal disease, chronic liver disease, malignancies etc were excluded. The need for study was explained to the patients and their informed written consent was taken. Clearance from the Institutional research committee and Institutional ethical committee were obtained beforehand.

Data from the study population were collected by a pretested and validated proforma which included detailed history, physical examination and relevant investigations. In the study group newly detected diabetics (FBS≥126) or pre-diabetic patients (FBS100-125) with no previous treatment history were taken and data were collected from them. The descriptive data were analysed using, percentages, mean and standard deviation of individual variables. The correlation of individual variables with glycosylated haemoglobin (HbA1c) values were analysed using Pearson correlation coefficient.

A cut off for diagnosing diabetes by means of glycosylated haemoglobin with maximum sensitivity and specificity in the study population was determined using Receiver operating characteristics curve (ROC curve) considering fasting blood glucose ≥126 as the gold standard diagnostic criteria. All statistical calculations were done using PSPP open source statistical software.

RESULTS

Total of 278 consecutive diabetic patients attending the medicine out patient department during the study period 99 patients were newly diagnosed diabetic/ prediabetic patients with no previous anti diabetic treatment history. Average age of the study population was 53.59 yrs Study population consists of 61.6% males compared to 38.4% females. The most common symptoms among patients

were Fatigue (54%), Polyuria (42.8%) and Polydipsia (39.9%). Mean HbA1c values of the study population was 8.26.

Table 1: Baseline characteristic variables in the study group.

| Variables	Mean	Standard Deviation
Age	53.59	15.28
BMI	25.57	11.51
Systolic BP	136.24	22.28
Diastolic BP	83.04	10.99
FBS	196.24	86.59
HbA1c	8.26	2.32
S Cholesterol	212.24	45.80
S LDL	136.68	38.35

The data was analysed for correlation between various patient variables and HbA1c values. There was no significant correlation between age and HbA1C considering the total study population (p=0.07). Other patient characteristics like sex of the patient (p=0.781), duration of diabetes (p=0.278) and body mass index (p=0.41) were also not significantly correlated with HbA1c values.

Out of the biochemical parameters the fasting blood sugars (p<0.001), post prandial blood sugars (p<0.001) and random blood sugar values (p<0.001) were all showing significant correlation with HbA1c. Whereas serum LDL (p=0.022) levels showed significant correlation with HbA1c, total cholesterol (p=0.062)and serum Triglycerides(p=0.155) were not significantly related to HbA1c values.

ROC curve plotted of HbA1c in relation to FBS showed area under the curve to be 0.76 and a cut off values of HbA1c ≥ 6.45% shows the maximum sensitivity(79%) with good specificity(60%) for diagnosis of diabetes taking FBS ≥126 as the gold standard test for the diagnosis.

Table 2: Data showing coordinates of ROC curve.

HbA1c	Sensitivity	Specificity
5.95	0.93	0.33
6.10	0.83	0.40
6.30	0.79	0.47
6.45	0.79	0.60
6.55	0.77	0.60
6.85	0.70	0.60
6.95	0.70	0.67
7.10	0.66	0.67
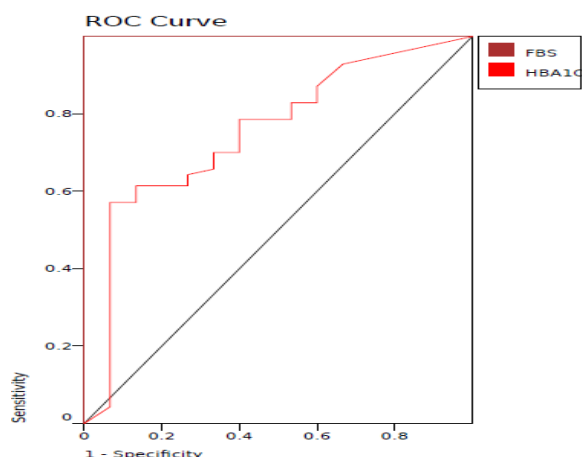
Diagram 1: ROC Curve for HbA1c against FBS.

DISCUSSIONS

Several studies have shown that glycated haemoglobin is as sensitive as fasting plasma glucose in screening of diabetes and it is also a good predictor of the microvascular complications in diabetes.[4,5,6,7] According to ADA criteria an HbA1c cut off value of 6.5 is diagnostic of diabetes mellitus. Many previous studies have shown that HbA1c have geographic and ethnic variations. Studies conducted at different places around the globe have suggested variability in optimal cut off values in different populations and also different sensitivity and specificity for the same HbA1c values.

Western studies published from various countries like *Wiener K, Jesudason DR, Silverman RA* etc have suggested HbA1c cut off value between 6.0 to 6.2%.[8,9,10,11] Major Asian studies of *Ma H, Wan Nazaimoon WM, Hu Y, Bhowmik B* etc suggested a range of 6.0 to 6.3% as the reliable value for HbA1c among Asian populations.[12,13,14,15,16] West Asian and Arab studies of *Akram T and Hajat C* on the other hand suggested a higher level of 6.3 to 6.4%[17,18]. Whereas previous Indian studies by *Nair M* and *Ramachandran A* reported a much lower cut off level of 5.8% and 6.05% respectively.[19,20]

Our study among the South Indian population suggested HbA1c ≥6.45% with a sensitivity of 79% and specificity of 60% as the most reliable cut off value for this population. This is in very much accordance with the current ADA recommendation of 6.5%. Lower cut off values in the previous Indian studies may be indicative of the ethnic diversity of Indian population and points to the need for more regional studies in the subject. Even though a community based study with a larger sample size may be needed to further validate our findings, this study shows that the current ADA recommendation for diagnosis of diabetes mellitus with HbA1c ≥ 6.5% can be equally applied in the South Indian population with fair degree of accuracy.

Our study also showed that HbA1c has no significant correlation with patient characteristics like age, sex, body mass index and duration of diabetes. It is significantly correlated to the fasting, post prandial and random glucose levels which reconfirm the fact that HbA1c represents the average glycaemic status of the patients. It is also found to be having significant correlation with metabolic parameters like serum LDL level but did not show much correlation with rest of the lipid parameters.

CONCLUSION

This study concluded that HbA1c is a reliable indicator of the glycaemic status of an individual. Its value is not dependent on patient characteristics like age, sex, body mass index etc and duration of the disease. The study derives an HbA1c cut off of 6.45% as the most appropriate value in diagnosing new diabetic patients in the South Indian population which is in accordance with the current ADA recommendation.

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