WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.045
Volume 3, Issue 9, 494-503. Research Article ISSN 2277– 7105

VALUE OF ASSESSING POST PRANDIAL AND FASTING PLASMA GLUCOSE AS A SURROGATE FOR GLYCATED HEMOGLOBIN IN DIABETIC GLYCEMIC CONTROL

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Article Received on
24 August 2014,

Revised on 17 Sept 2014,
Accepted on 12 Oct 2014

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ABSTRACT

Background: Control of plasma glucose could prevent the progression of most of the complications of diabetes mellitus and glycated hemoglobin is the most important criterion in controlling these complications. But its non-availability in grass root level of health sector and high cost, post-prandial and fasting blood glucose estimation have came into the field particularly in developing countries to assess glycemic control. **Aim:** To assess the better surrogate parameter fasing or post-prandial blood glucose for glycated haemoglobin that help in detecting the glycemic control status of diabetic patients. **Methods:** In the study One 120 diabetic patients attending an out-patient medical clinic were selected after simple random method. The study population was divided into three groups based on the HbA1c values i.e. Group 1 (HbA1c<7%-good control), Group 2 (HbA1c 7-9%-fairly controlled), Group 3 (HbA1c >9%-Poorly controlled). Glycated haemoglobin and blood glucose estimations in all patients were carried out in the fasting state (at least after 8 hours of fasting) as well as postprandial state (two hours after lunch) on the same day. **Result:** The mean glycated haemoglobin in three groups were 121.29 ± 28.91mg/dl and 165.61 ± 34.51mg/dl for group I, 154.78 ± 12.83 mg/dl and 206.92 ± 46.95 mg/dl for group II and for group III 179.38 ± 26.02 mg/dl and 179.38 ± 26.02 mg/dl respectively and the difference was statistically significant ($p < 0.001$). Regression analysis has pointed that PPBS is more significantly correlated with HbA_{1C} than FBS. PPBS showed better sensitivity (92.5% vs. 85%), specificity (90% vs. 81%), positive predictive value (95% vs. 89%),

negative predictive value (86% vs. 74%) and accuracy (92% vs. 83%) than Fasting glucose. **Conclusion:** HbA1c remains the gold standard in assessment of glycemic control with availability of standardized methods. However in resource poor settings & in conditions with limitations for using HbA1c, PPBS can be used to monitor the glycemic control of diabetes.

KEY WORDS: Glycated hemoglobin, glycemic control, fasting glucose, post-prandial glucose.

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. [1] The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. [2] Glycemic control is an important aspect in managing diabetes in order to prevent acute or chronic complications of diabetes mellitus. Control of blood glucose in patients with diabetes can be assessed by several methods. These include assessment of glycosylated hemoglobin (HBA1C), fasting blood sugar (FBS), and postprandial blood sugar (PPBS). [3] The gold standard for assessment of glycaemic control at follow up is the glycosylated haemoglobin level. [4] But it is relatively costlier and it is not available in primary as well as secondary health sector level. So this test is beyond the reach to most patients attending clinics at this trier of health delivery. So, the present study was conducted in diabetic patients to investigate that overall efficiency of FBS or PPBS to assess glycemic control in the absence of the ideal standard test for treatment follow up.

2. MATERIALS AND METHODS

2.1 Study Area

This descriptive and cross-sectional study was conducted in the Department of Biochemistry of Burdwan Medical College, Burdwan, West Bengal, India, with the collaboration of Diabetic clinic in the Department of Medicine. All participants were recruited from the same geographical area of the northern and southern areas of the Burdwan district.

2.2 Selection of Participants

A total of 120 individuals were selected, from 917 diabetic patients irrespective of type of diabetes residing in the study area, by simple random sampling between February 2011 and May 2014. Informed consent was obtained from individuals after details of the procedure

were explained to them. Information regarding age, gender, Body mass index (BMI), type and duration of intake of hypoglycaemic agents, self-reported dietary and drug compliance were gathered. All the study population was strictly followed the Diabetic diet [5] and none of them were affected by any infection nor taken any medication that affects the glycemic status of the subject atleast 6 months. Patients having any concomitant infection and suspicious or diagnosis of other disease than diabetes mellitus were not included in the study. The study population was divided into three groups based on the HbA1c values i.e. Group I (n = 40) - HbA1c <7%-good control, Group II (n = 39) - HbA1c 7-9%,-fairly controlled, Group III (n = 41) HbA1c >9%-Poorly controlled.

2.3 Collection of Samples

Peripheral venous blood was drawn from all participants and the samples were divided into two aliquots. The first one was collected in oxalate and fluoride vial for obtaining plasma for fasting glucose estimation (at least eight hours of fasting) as well as in the postprandial state two hours after lunch) on the same day, second one in EDTA containing vial for HbA1C assays.

2.4 Estimation of Plasma Glucose Level

It was estimated by glucose oxidase-peroxidase enzymatic method using span diagnostic kit as per the manufacturer's instructions [6] by completely automated clinical chemistry analyzers – ERBA XL-600 after usual daily calibration and ensuring quality performance before starting analysis and the samples were analyzed along with the other routine samples. Intraassay CV% was 1.2% and interassay CV% was 2.1%.

Qualitative detection of glucose in urine was accomplished by Benedict's test. Acceptable control level of blood glucose were defined as FBS value equal or less than 110 mg/dL and PPBS value equal or less than 126 mg/dL. (Harrison)

2.5 Estimation of HBA_{1C}

Using commercially available Hemoglobin A_{1C} kit supplied by Siemens Company did Hemoglobin A1C test. It implies the principle of turbidimetric inhibition immunoassay (TINIA). [8, 9] This company also supplied total Hb kit for estimation total Hb by alkaline hematin method.

2.6 Anthropometric Measurements

Weight and height measurements were obtained, usingstandardized technique. [10] BMI was calculated as the weight in kilograms divided by the square of height in meters.

2.7 Statistical Analysis

The data for biochemical analysis was subjected to standard statistical analysis using the Statistical Package for Social Science (SPSS) 11.5 software for windows.

3. RESULT

3.1 Personal Profile and Clinical Details of Population under the Study

The personal profiles and clinical parameters of all the subjects under study are shown in Table 1.

Table 1: Baseline Characteristics of the Study Population.

Characteristics	Value	p value
n	120	
Age (Years)	51± 12.2	
Sex Male Female	 56 (46.7) 64 (53.3)	0.14
BMI	25.9 ± 5.1	
Types of DM 1 2	 58 (48.3) 62 (51.7)	0.22
Duration of diabetic treatment in years †	6.5 (2-25)	
Treatment modality Diet and life-style **management only** Sulfonylurea only Metformin only Sulfonylurea + Metformin Insulin	 21 (17.5) 20 (16.7) 28 (23.3) 27 (22.5) 24 (20)	0.08

Data are expressed as numbers (group percentages in parentheses) for categorical variables and mean values ± SD for continuous variables. When variables were not normally distributed, median values (Q1-Q3 IQR in parentheses) are given instead (indicated by †); IQR means Interquartile range.

Abbreviations

BMI, Body Mass Index; DM, Diabetes Mellitus.

3.2 Comparison of Mean Fasting and Post Prandial Blood Glucose Levels Among the Study Groups.

The mean fasting plasma glucose and PPBS level in all three groups were 121.29 ± 28.91mg/dl and 165.61 ± 34.51mg/dl for group I, 154.78 ± 12.83 mg/dl and 206.92 ± 46.95 mg/dl for group II and for group III 179.38 ± 26.02 mg/dl and 179.38 ± 26.02 mg/dl respectively and the difference was statistically significant ($p<0.001$) as shown in the Table 2.

Table 2: Mean Fasting And Post Prandial Blood Glucose Levels Among The Study Groups.

Parameters	Group I (n =40)	Group II (n = 39)	Group III (n = 41)
Mean FBS (mg/dl)	121.29 ± 28.91	154.78 ± 12.83*	179.38 ± 26.0179.38 ± 26.02 2*
Mean PPBS (mg/dl)	165.61 ± 34.51	206.92 ± 46.95*	234.98 ± 43.12*

Value are mean ± SD; n = number of cases;* indicates $p < 0.05$ (Statistically significant)

3.3 Correlation of HbA_{1C} with PPBS and FBS

Regression analysis is performed to evaluate which method blood glucose estimation shows best correlate with HbA_{1C} parameter. Over the HbA_{1C}, the PPBS shows a higher r value (r = 0.859, p 0.028) and FBS a lower r value (r = 0.838, p 0.041) of blood glucose estimation. That signifies that PPBS is more significantly correlated with HbA_{1C} than FBS as shown in Table 3.

Table 3: Pearson's Correlation of HbA_{1C} with PPBS and FBS

Category	r value	Significance
HbA_{1C} vs PPBS	0.859	0.028
HbA_{1C} vs FBS	0.838	0.041

3.4 Detection of Performance of FBS and PPBS

To find out the validity of PPBS as an alternative to HbA_{1C} over FBS in detection of diabetic control status it was observed that the sensitivity of elevated PPBS in detecting the controlled status of the patients was 87% with a specificity of 72%. The positive predictive value of elevated PPBS was 87% and the negative predictive value of normal PPBS was 72% (Table 4 and Figure 1).

The sensitivity of elevated FBS in detecting the controlled status of the patients was 76% with a specificity of 63%. The positive predictive value of elevated PPBS was 78% and the negative predictive value of normal PPBS was 56% (Table 4 and Figure 1).

Table 4: Validity of Ppbs as an Alternative to Hba_{1c} over Fbs in Detection of Diabetic Good Control Status.

Mode of blood glucose estimation	Sensitivity (%)	Specificity (%)	PPV (%)	NPV(%)	Accuracy (%)
PPBS	92.5	90	95	86	92
FBS	85	81	89	74	83

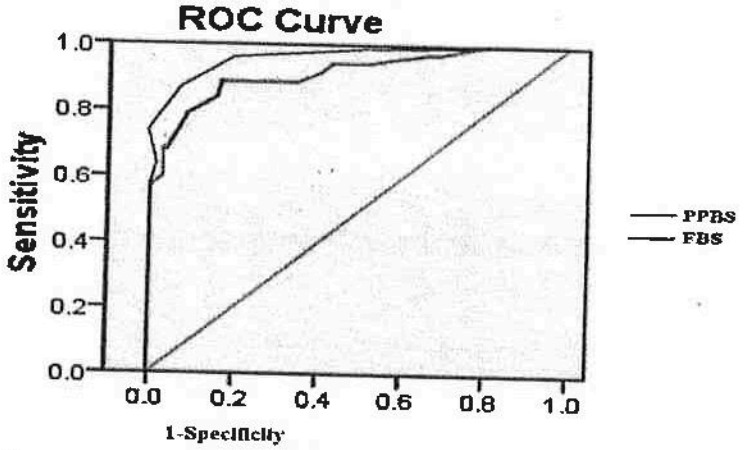

Figure 1: Receiver Operative Characteristic (ROC) Curves of Two Modes of Blood Glucose Estimation.

The area under the curve (AUC) of ROC curve of PPBS is more than FBS as shown in **Table 3** and **Figure 1** that is also proves PPBS is the better alternative than FBS.

Table 3: Area under the Roc Curve and Ci between the Different Modes of Blood Glucose Estimation.

Category	Area under the ROC curve	CI
PPBS	0.933	86.1% - 99.2%
FBS	0.897	85.7% - 97.8%

4. DISCUSSION

Diabetes is a common non-communicable disease. In developing countries like India, posing a huge economic burden on the family and nation as a whole. .Diabetes mellitus is a chronic illness that requires continuing medical care, patient education, and support to prevent acute complications and to reduce the risk of long-term complications. Control of blood glucose in patients with diabetes can be assessed by several methods. These include assessment of glycated hemoglobin (HBA1c), fasting blood sugar (FBS), and postprandial blood sugar (PPBS). The gold standard for assessment of glycaemic control at follow up is the glycated haemoglobin level. [11] High concentrations of glucose can increase the glycation of common

proteins such as HbA1c, formed through the non-enzymatic attachment of glucose to haemoglobin, which is commonly considered to reflect the integrated mean glucose level over the previous 8–12 weeks, the time period being dictated by the 120-day lifespan of the erythrocyte.[12] The concentration of HbA1c predicts diabetes complications because it reflects more harmful glycation sequelae of diabetes, such as retinopathy and nephropathy, which are understood to be due to harmful advanced glycation end products. [13-15] Moreover, HbA1c is undoubtedly a user friendly and stable test with very minimal biological variability and which is not affected by factors which otherwise has considerable impact on glucose measurement. [1, 6, 16] So the compliance of diabetic subjects is increased which is an important and welcome feature in diabetic management for patient as well as the treating physicians. But despite its good compliance, a large number of medical conditions are associated with alterations in the HbA1c values. Hematological conditions such as the presence of hemoglobin variants, iron deficiency, and hemolytic anemia, the presence of carbamylated hemoglobin in uremia, a variety of systemic conditions, including certain forms of dyslipidemia, malignancies, and liver cirrhosis, various medications, and finally, pregnancy are among the factors that influence the HbA1c measurement. [17, 18] So, the present study was performed to relate PPBS and FBS with HbA_{1C} to search a better alternative of HbA_{1C} in developing countries like India where relatively costlier test HbA1C is the beyond the reach of most patients attending clinics at state hospitals.

It was found that PPBS is more significantly correlated with HbA_{1C} than FBS. Numerous factors like stress, acute illness, medication, venous stasis, posture, sample handling, food ingestion, prolonged fasting and exercise can alter fasting plasma glucose [19] not the PPBS. Very recent studies have also shown that PPBS predicts cardiovascular complications in diabetic subjects.[20-23] Another study observed that with the focus on FBS did not show signifdicant reduction in macrovascular but with PPBS monitoring, there was better reduction of macrovascul;ar complications. [24-26]

From the data, sensitivity, specificity and positive predictive value was also calculated, to predict good control of diabetes (HbA1c<7%) was considered as per American Diabetic association (ADA) guidelines. PPBS showed better performance than Fasting glucose, in detection of better glycemic control status. Result of the study indicate that PPBS level increased in all three groups and has a strong relationship with the rising of HbA_{1C}

5. CONCLUSION

Our results indicate that PPBS level increased in all three groups and has a strong relationship with the rising of HbA_{1C} level. Increasing of HbA_{1C} has shown more dependency with PPBS as compared to with FBS level. So the PPBS is the better alternative to HbA_{1C} than FBS in developing countries to reduce the microvascular as well as macrovacular complications and thus overall mortality in diabetes mellitus.

6. ACKNOWLEDGEMENT

Authors are thankful to Dr. Keya Pal, Dr. Supreeti Biswas and Dr. Shikha Banerjee and Dr.G.D.Mitra of Burdwan Medical College and Hospital for constant support & inspiration.

7. Declaration of Conflict of Interest

We, the authors, are declaring that we do not have any conflict of interest regarding this study.

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