

# A Comparative Study of Correlation of Random, Fasting and Postprandial Blood Glucose with Glycated Haemoglobin - A Multicentre Study

B G Vittal<sup>1</sup>, Mahantesh Patil<sup>2</sup>, D Abhijith<sup>3</sup>

## ABSTRACT

**Background:** Blood glucose estimation has been the mainstay of diabetes diagnosis, monitoring and treatment over years until the emergence of Glycated haemoglobin (HbA1c), a new benchmark. However, the cost has prevented the use of HbA1c in small laboratory settings. Data from previous studies yielded ambiguous results about the correlation of HbA1c with blood sugars. **Objective:** To check for correlation between HbA1c with fasting blood sugar (FBS), postprandial blood sugar (PPBS) and random blood sugar (RBS) and to assess usefulness of blood glucose in monitoring the glycemic control in diabetic patients. **Methodology:** Retrospective one-year data of diabetic patients who were investigated for HbA1c, FBS, PPBS and RBS was obtained. Data was analysed to find correlation between HbA1c and blood sugars. Pearson's Correlation coefficient was also used to find correlation of different decision limits of blood sugars with HbA1c. **Results:** Significant correlation was observed between RBS, FBS and PPBS and HbA1c with Pearson's Correlation coefficients (r) 0.7005, 0.6903 and 0.6881. Blood glucose levels in diabetic range correlated better than non-diabetic glucose levels with HbA1c. **Conclusion:** FBS, PPBS and RBS do not have higher clinical utility over each other in predicting long-term glycemic control. Blood glucose levels higher than clinical decision limits have a high-reliability index of predicting poor long-term glycemic control. **KEY WORDS:** Blood glucose, Diabetes, Glycemic control, HbA1c.

## Introduction

Glycaemic control is the cornerstone in the management of diabetes mellitus, and good glycaemic control reduces morbidity and mortality of the diseases.<sup>[1,2]</sup> Hyperglycaemia in diabetic patients is associated with damage, dysfunction, and failure of kidneys, nerves, heart, eyes and vasculature.<sup>[3]</sup> Landmark randomized clinical trials and observational studies on diabetic patients have inferred that achieving strict glycemic control significantly decreases the microvascular and macrovascular

complications of the disease.<sup>[4,5]</sup> glycaemic control of diabetics can be assessed by measurement of glycated haemoglobin (HbA1c), fasting plasma glucose (FPG), and postprandial plasma glucose (PPG).

Glycated Hb (HbA1c) is the percentage of total haemoglobin that is nonenzymatically attached to glucose. It reflects the glycemic control in the previous 2–3 months. HbA1c is an indicator for overall glucose exposure integrating both fasting and postprandial hyperglycemia even though their relative contribution is undefined.<sup>[6,7]</sup>

Although a very useful investigation, due to its high cost, the availability of HbA1c test is very limited in resource-poor settings. Due to the non-availability of HbA1c test and high prevalence of diabetic problems, post-prandial and fasting plasma glucose estimation are used in developing countries for assessment of glycemic control.<sup>[8]</sup>

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<sup>1</sup>Professor and HOD, Department of Biochemistry, Hassan Institute of Medical Sciences, Hassan, Karnataka, India,

<sup>2</sup>Associate Professor, Department of Biochemistry, Mysore Medical College & Research Institute, Mysore, Karnataka, India, <sup>3</sup>Senior Resident, Department of Biochemistry, JSS Medical College, Mysore, Karnataka, India

**Address for correspondence:**

B G Vittal, Professor and HOD, Department of Biochemistry, Hassan Institute of Medical Sciences, Hassan, Karnataka, India. E-mail: [vittal.bg@gmail.com](mailto:vittal.bg@gmail.com)

An acceptable correlation between HbA1c levels and FPG and PPG levels has been shown in many studies.<sup>[9,10]</sup> Many studies have observed the correlation of HbA1c with FBS,<sup>[11-13]</sup> while others have observed a better correlation with PPBS.<sup>[7,8,14-18]</sup> However, there is no consensus regarding whether FPG or PPG is a better predictor of glycemic control if HbA1c is not available. Data from studies correlating random blood glucose (RBS) adds to the ambiguities.

Most of the studies have the limitation of a smaller sample size causing less generalizability of their results to the population. Nevertheless, for health care providers and patients, knowledge of the relationship of random, fasting and postprandial plasma glucose measurements with HbA1c is necessary for setting plasma glucose goals to achieve specific HbA1c targets.

The study intends to know the correlation of fasting and postprandial plasma glucose with HbA1c in a larger population that in turn would help to identify the better surrogate glycaemic marker for achieving target HbA1c level and for early detection of glycaemic control status.

## Methodology

### Source of data

A retrospective cross-sectional study was conducted from data obtained from two tertiary care centres of Karnataka, India. Hassan Institute of Medical Sciences, Hassan (HIMS, Hassan) and Mysore Medical College and Research Institute, Mysore (MMCRI, Mysore) were the study centres. Institution Ethics Committee permission was obtained before the start of the study.

### Sample size

Sample size was calculated by using formula  $n = Z^2 \times PQ / d^2$ , where  $Z = 3.891$  at 99.99% confidence,  $p$  = Prevalence and  $q = 1-p$  and  $d$  = allowable error. (sample size of 491 was calculated by keeping 8.9% prevalence of diabetes mellitus and allowable error of 5%) (19). One year data which was well above the statistically required sample size was considered for our study.

**Inclusion Criteria:** Data of type 2 diabetic subjects with HbA1C, fasting blood sugar (FBS), postprandial blood sugar (PPBS), or RBS with the age group of 30-99 years.

**Exclusion Criteria:** Data of subjects with other comorbid conditions that would alter blood glucose levels like thyroid disorders were excluded.

**Study duration:** Three months for data compilation and analysis.

**Study design:** A retrospective cross-sectional study

## Study procedure

Retrospective one-year data (from April 2019 to March 2020) of subjects who were investigated for Glycated haemoglobin (HbA1c) was obtained. Their laboratory investigation data on fasting serum glucose, postprandial serum glucose and random serum glucose was obtained. Their clinical data on diabetic status was also obtained from records. The patient data which met the inclusion criteria was included and data of patients that met exclusion criteria was excluded. From the laboratory records, it was ensured that standard internal and external quality control practices were in place during the entire period of the study. Both study centres used similar laboratory methods to ensure uniformity. Fasting, postprandial and random blood glucose was estimated in serum using hexokinase method. HbA1c was estimated using enzymatic method traceable to NGSP. At HIMS, Hassan tests were performed using Abbott Architect ci4100 integrated analyser and at MMCRI, Mysore tests were performed by Roche Cobas 6000 analyser with their reagents.

**Statistical methods:** All subjects' demographic data were obtained and tabulated in MS Excel spreadsheet. Their FBS, PPBS, RBS and HbA1c values were tabulated. Data was analysed using Graphpad prism v-9 statistical software. Pearson's correlation coefficient was used to calculate the correlation between HbA1c and FBS, PPBS, or RBS. Pearson's Correlation coefficient was also used to find correlation of different decision limits of FBS and PPBS with HbA1c.

## Results

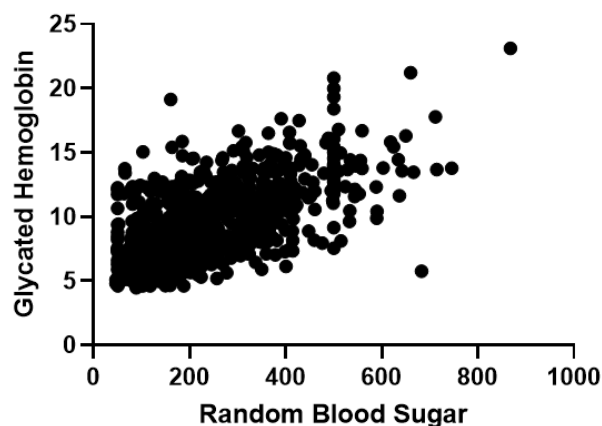
Data of 6514 diabetic subjects who had undergone HbA1c investigation and met inclusion and exclusion criteria was obtained. Out of these subjects 1750 patients were investigated with FBS, 1582 patients were investigated with PPBS, and 1149 patients were investigated with RBS investigations. Age and sex distribution are illustrated in Table 1.

**Table 1: Age and Sex distribution of study population**

Age group in years	FBS		PPBS		RBS	
	Male	Female	Male	Female	Male	Female
30-39	115	107	105	101	71	65
40-49	219	214	197	184	145	128
50-59	224	207	212	182	150	123
60-69	227	190	201	177	158	135
70-79	109	76	105	64	79	61
80-89	35	20	36	12	17	14
90 and above	5	2	4	2	3	0
Total	934	816	860	722	623	526

A positive and significant correlation was observed between RBS values and HbA1c values of 1149 patients. (Pearson's Correlation coefficient  $r = 0.7005$ ;  $p$ -value  $<0.0001$ ).

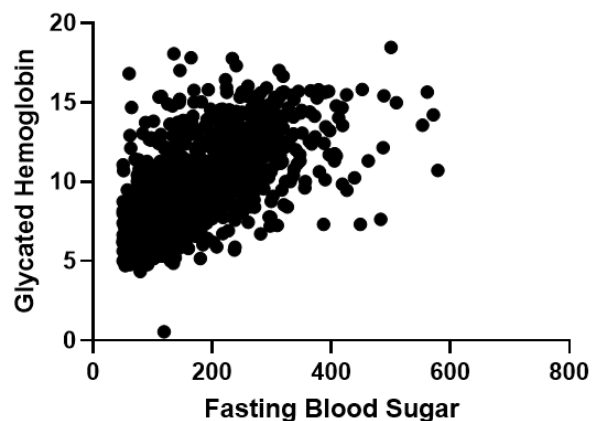
Scatter plot graphs of the same were plotted for the visualization of correlation (Figure 1)

**Figure 1: Scatter plot for correlation between HbA1c and random blood glucose (mg/dl)**

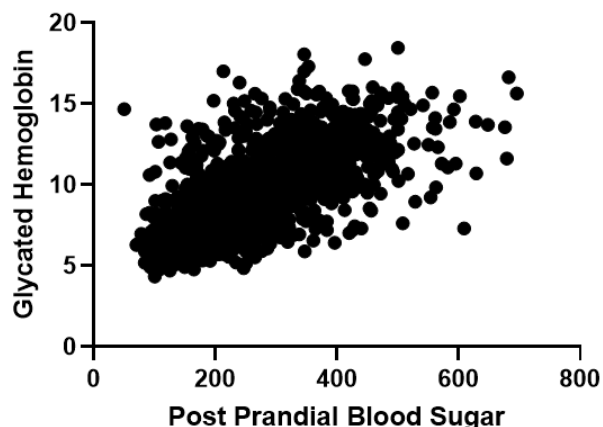
FBS values of 1750 patients correlated significantly with HbA1c values. (Pearson's Correlation coefficient  $r = 0.6903$ ;  $p$  value  $<0.0001$ ).

Scatter plot graphs of the same were plotted for the visualisation of correlation (Figure 2)

PPBS values of 1582 patients also correlated significantly with HbA1c values. (Pearson's Correlation coefficient  $r = 0.6881$ ;  $p$  value  $<0.0001$ ).

**Figure 2: Scatter plot for correlation between HbA1c and fasting blood glucose (mg/dl)**

Scatter plot graphs of the same were plotted for the visualization of correlation (Figure 3)

**Figure 3: Scatter plot for correlation between HbA1c and postprandial blood glucose (mg/dl)**

Patient data was further analysed to check the correlation of HbA1c with FBS values on either side of 126mg/dl. Similarly, patient data was further analysed to check the correlation of HbA1c with PPBS values on either side of 200mg/dl.

Details of analysis are illustrated in Table 2.

Though a statistically significant correlation was observed between HbA1c and blood sugars across decision limits, a significantly higher correlation was observed in FBS  $\geq 126$ mg/dl, PPBS  $\geq 200$ mg/dl and RBS  $\geq 200$ mg/dl.

**Table 2: Correlation of decision limits of blood sugars<sup>1</sup> with HbA1c**

	Total subjects	"r" with HbA1c	"p"
FBS < 126mg/dl	797	0.1543	<0.0001
FBS ≥126mg/dl	953	0.5455	<0.0001
PPBS < 200mg/dl	620	0.2912	<0.0001
PPBS ≥200mg/dl	962	0.5704	<0.0001
RBS <200mg/dl	721	0.2565	<0.0001
RBS ≥200mg/dl	428	0.5384	<0.0001

r = Pearson's Correlation Coefficient; p = statistical significance

## Discussion

Blood glucose estimation had been the mainstay of diabetes diagnosis, monitoring and treatment over years until the emergence of HbA1c. Over the last few decades, HbA1c has assumed its importance as the benchmark in the management of diabetes. However, the cost and technical sophistication of investigative equipment have prevented its widespread use in small and very small clinical or laboratory settings. It has led to speculation of whether traditional fasting, postprandial and random blood sugar estimation can be a substitute during lack of HbA1c.

Data from previous studies with smaller sample sizes yielded ambiguous results about the correlation of HbA1c with blood sugars. So a study with a large sample size was undertaken to obtain statistically unequivocal results about correlation.

Saed MK and coworkers in 2006<sup>[11]</sup>, Gupta S and coworkers in 2014<sup>[12]</sup>, Saiedullah M and coworkers in 2013<sup>[13]</sup> observed that FBS correlated better than PPBS with HbA1c. Their correlation coefficient (r) values for FBS were 0.60 (r=0.20 for PPBS), 0.68 (r=0.62), and 0.81 (r=0.77) respectively. In our study, we observed that FBS correlated significantly with HbA1c. (Pearson's correlation coefficient value r = 0.6903; p-value <0.0001).

Rosediani M and coworkers in 2006<sup>[7]</sup>, Swetha NK in 2014<sup>[8]</sup> Haddadinezhad S and coworkers in 2010<sup>[14]</sup> Datta S and coworkers in 2014<sup>[15]</sup> Avignon A and coworkers in 1997<sup>[16]</sup> and Shrestha L and coworkers in 2012<sup>[17]</sup> observed that PPBS correlated better than FBS with HbA1c. Their correlation coefficient (r) values for PPBS were 0.60 (r=0.58 for FBS), 0.76 (r=0.74 for FBS), 0.43 (r=0.32 for FBS), 0.86 (r=0.84 for FBS), 0.81 (r=0.62 for FBS) and 0.63 (r=0.45 for FBS) respectively. In our study we observed that

PPBS correlated significantly with HbA1c. (Pearson's correlation coefficient value r = 0.6881; p value <0.0001).

Swetha NK in 2014 in a study<sup>[8]</sup> observed that RBS correlated with HbA1c (r=0.601). Similar correlation was also observed in our study (Pearson's correlation coefficient value r = 0.7005; p-value <0.0001).

Shrestha L and coworkers<sup>[17]</sup> and Azim W and coworkers in their study with designs of cut-off points at clinical decision limits as in our study observed that PPBS correlated better than FBS with HbA1c. Their correlation coefficient (r) values for PPBS were significantly higher than their FBS counterparts, i.e 0.63 (r=0.45 for FBS) and 0.44 (r=0.28 for FBS) respectively.

In our pursuit to check whether clinical decision limits of blood glucose values correlate with long-term glycemic control, we divided the study population based on clinical decision limits and analysed the results. We observed that RBS, FBS and PPBS values in the diabetic range showed a significantly higher correlation with HbA1c than RBS, FBS and PPBS values in the non-diabetic range. It indicates the high-reliability index of higher blood sugars in predicting poor long-term glycemic control.

## Limitations of the study

By design, present study was retrospective and could not include patients' full clinical details. Further prospective studies with clinical correlations can add more value.

## Conclusion

Although FBS, PPBS and RBS correlate significantly with HbA1c, none of them seem to have higher clinical utility over the other in predicting long-term glycemic control.

Blood sugar levels higher than clinical decision limits have a high-reliability index of predicting poor long-term glycemic control.

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