Comparison of fasting blood glucose & post prandial blood glucose with HbA\textsubscript{1c} in assessing the glycemic control

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Abstract:

Introduction: Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The aim of the present study was to find the correlation between HbA\textsubscript{1c} with FBS, PPBS & RBS so as to assess their usefulness in monitoring the glycemic control in Diabetic patients.

Material & methods: A cross sectional data survey was undertaken. The data for HbA\textsubscript{1c} with FBS/PPBS/RBS were noted. The study population was divided into three groups based on the HbA\textsubscript{1c} values i.e. Group 1 (HbA\textsubscript{1c}<7%-good control), Group 2 (HbA\textsubscript{1c} 7-9%-fairly controlled), Group 3 (HbA\textsubscript{1c} >9%-Poorly controlled). Glucose was analysed by GOD-POD method using Dirui-CS 400 Clinical chemistry analyzer. HbA\textsubscript{1c} was analysed by the principle of Ion Exchange high-performance liquid chromatography (HPLC) using Biorad D10 Haemoglobin system.

Results: In our study we found that there was significant correlation between HbA\textsubscript{1c} & FBS, PPBS & RBS (’p’value: <0.010) in the study population. However PPBS showed marginally better correlation than FBS & RBS (r=0.764 vs 0.739 & 0.601). There was direct correlation between FBS, PPBS & HbA\textsubscript{1c} levels in both controlled & uncontrolled Diabetic patients. PPBS showed better sensitivity (79% vs. 74%) than Fasting glucose, whereas Fasting glucose showed higher specificity (84% vs. 74%) and positive predictive value (87% vs. 80%) compared to post prandial blood glucose.

Conclusion: HbA\textsubscript{1c} 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 HbA\textsubscript{1c}, FBS & PPBS can be used to monitor the glycemic control.

Key words: HbA\textsubscript{1c}, Glycemic control, FBS, PPBS

Introduction: Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Diabetes causes about 5% of all deaths globally each year. The relatively ineffective insulin in this condition results in hyperglycemia. 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. (1)

The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8%in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. The diabetes mellitus in urban population in developing countries is projected to double between 2000 and 2030. According to the latest World Health Organization (WHO) report, India has 31.7 million diabetic subjects, and the number is expected to increase to a staggering 79.4 million by 2030 (2)

Glycemic control is an important aspect in managing diabetes in order to prevent acute or chronic complications of diabetes mellitus. Many randomized, prospective clinical trials in type 1 and 2 diabetes have clearly shown that achieving glycemic control or reducing hyperglycemia significantly decrease the microvascular complications of diabetes. Each 1% reduction in
haemoglobin $A_1c$ was associated with a 37% decrease in risk for microvascular complications and a 21% decrease in the risk of any end point or death related to diabetes. (3, 4)

The most commonly used assay to measure chronic hyperglycemia is HbA$_1c$ test. However, it is not available in resource poor settings due to its high cost. In some clinical situations that affect red cell life span or hemoglobinopathies, laboratory assessment using the A$_1C$ test may provide unreliable information. There are many reports showing the acceptable correlation between hemoglobin A$_1c$ level and fasting blood glucose (FBS) level (5), whereas few other studies argued that Post prandial blood glucose (PPBS) showed a better correlation (6). The question then arises whether FBS or PPBS is a better predictor of glycemic control.

Hence the aim of the present study was to find the correlation between HbA$_1c$ with FBS, PPBS & RBS so as to assess their usefulness in monitoring the glycemic control in Diabetic patients.

**Materials & methods:**
A cross sectional data survey was undertaken from January 2012 to December 2012 at the Clinical Biochemistry laboratory, Apollo BGS Hospitals, Mysore, India. The laboratory provides tertiary care to patients in and around Mysore. The data for HbA$_1c$ with FBS/PPBS/RBS were noted. Since the data was obtained from the test requests, the clinical history & the purpose of the request (screening, diagnosis, treatment adjustment, follow-up etc) could not be considered, while computing the data. The study population was divided into three groups based on the HbA$_1c$ values i.e. Group 1(HbA$_1c$ <7%-good control), Group 2 (HbA$_1c$ 7-9%-fairly controlled), Group 3 (HbA$_1c$ >9%-Poorly controlled).Glucose was analysed by GOD-POD(7) method using Dirui-CS 400 Clinical chemistry analyzer. HbA$_1c$ was analysed by the principle of ion Exchange high-performance liquid chromatography (HPLC) using Biorad D10 Haemoglobin system.(8)

**Statistical methods used:** SPSS for windows was employed for statistical analysis. The correlation between the parameters was worked out using Pearson’s correlation. ‘p’ value < 0.05 was considered to be statistically significant. The One-Way ANOVA was used for one-way analysis of variance for a quantitative dependent variable by a single factor (independent) variable.

**Results:** Total no of HbA$_1c$ requests (with FBS/PPBS/RBS), received were 1186. Out of these 728 were males & 458 were females. The mean age of the study group was 55.43±19.9 yrs. In our study we found that there was significant correlation between HbA$_1c$ & FBS, PPBS & RBS (’p’ value-: <0.010) in the study population (Table No.1). However PPBS showed marginally better correlation than FBS & RBS. (r=0.764 vs 0.739 & 0.601).

When the study population was divided into three groups based on their glycemic control, we found that there was significant increase in FBS, PPBS & RBS in group 2 &3 compared to group 1(Table No.2). One way ANOVA showed that there was significant correlation (both between groups & within groups) between HbA$_1c$ with FBS, PPBS & RBS (’p’ value - : <0.010) in all the three groups.

From the data, sensitivity, specificity and positive predictive value was also calculated, to predict good control of diabetes (HbA1c<7%, FBS < 130mg/dl, PPBS <180mg/dl) was considered as per American Diabetic association (ADA) guidelines. PPBS showed better sensitivity (79% vs. 74%) than Fasting glucose, whereas Fasting glucose showed higher specificity (84% vs. 74%) and positive predictive value (87% vs. 80%) compared to post prandial blood glucose (Table No.3).The number of requests for RBS were less compared to
FBS & PPBS. So it was not considered for the calculations.

**Discussion:**

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. (5)

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. 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. (8,9,10)

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. (11, 12)

HbA1c is not recommended as a diagnostic or a screening tool because of several factors; lack of standardization, low sensitivity and high cost. The issues of global standardization of HbA1c measurements was improved by introduction of new IFCC standards, with the development of an internationally accepted reference system. Clinical laboratories use methods and analyzers that are traceable to this reference, although many diabetes centers and private practice physicians rely on point-of-care instruments to measure HbA1c with some of them not showing acceptable analytical performance. (12,13,14)

There are many reports showing the acceptable correlation between hemoglobin A1c levels and fasting blood glucose levels. In our study, we found that there was significant correlation between FBS, PPBS, and RBS with HbA1c levels, although PPBS showed marginally better correlation. Our findings agree with the previous studies, who stressed upon the inconvenience caused to diabetic patients, due to overnight fasting & on the contrary, post prandial glucose caused no disruption of daily activities. (6) Studies have also shown that PPBS predicts cardiovascular complications in diabetic subjects. (15)

When the study population was divided into three groups based on their glycemic control, we found that there was significant increase in FBS, PPBS & RBS in group 2, &3 compared to group 1. There was significant correlation (both between groups & within groups) between HbA1c & FBS, PPBS & RBS (*p* value: <0.010) in all the three groups. These findings show that there is direct correlation between HBA1c & blood glucose levels in both controlled & uncontrolled Diabetic patients. From the data, sensitivity, specificity and positive predictive value was also calculated, to predict good glycemic control, (HbA1c<7, FBS < 130mg/dl, PPBS <180mg/dl) was considered as per ADA recommended goals. PPBS showed better sensitivity (79% vs. 74%) than Fasting glucose
whereas Fasting glucose showed higher specificity (84% vs. 74%) and positive predictive value (87% vs. 80%) compared to post prandial blood glucose (Table 1).

The ADA has recognized the fasting plasma glucose (FPG), as the diagnostic test of choice. PPBS values can change due to many variables, such as physical activity, insulin sensitivity, gastric emptying rate, and meal composition etc. (15,16) HbA1c is not recommended as a diagnostic or a screening test because it is considered that HbA1c is inferior to FPG or post-load glucose values at predicting type 2 diabetes because the existence of hemoglobin or red cell abnormalities can increase the variability of HbA1c values. This variability may contribute to its inferior prediction of diabetes compared with fasting or post-load glucose values. FPG and HbA1c may reflect different aspects of glucose metabolism. While HbA1c can reflect a variety of factors in glucose metabolism, FPG levels mainly depend on insulin resistance and hepatic glucose production (17).

**Conclusion:**
HbA1c remains the gold standard in the assessment of glycemic control with availability of standardized methods. The limitation of resource or cost should not be the barrier to provide the good medical care. However in resource poor settings & in conditions with limitations for using HbA1c, FBS & PPBS can be used to monitor the glycemic control. The diabetic patients needs to be educated regarding the importance of achieving good glycemic control (To achieve Hba1c < 7%) so as to reduce the morbidity & mortality due to various complications of diabetes mellitus.

**Table 1:** Correlation between HbA1c with FBS, PPBS & RBS.

<table>
<thead>
<tr>
<th>HbA1c</th>
<th>FBS</th>
<th>PPBS</th>
<th>RBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=1186)</td>
<td>Pearsons Correlation (r)</td>
<td>1</td>
<td>0.739*</td>
</tr>
<tr>
<td>Significance (’p’ value)</td>
<td>-</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>FBS</td>
<td>Pearsons Correlation(r)</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Significance (’p’ value)</td>
<td>-</td>
<td>-</td>
<td>0.000</td>
</tr>
<tr>
<td>PPBS</td>
<td>Pearsons Correlation(r)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Significance (’p’ value)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>RBS</td>
<td>Pearsons Correlation(r)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Significance (’p’ value)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*’p’ value :<0.05 is considered to be statistically significant.*
Table 2: Gender distribution & Mean Fasting, Post prandial, random blood glucose levels in the Study groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1 (n=404)</th>
<th>Group 2 (n=474)</th>
<th>Group 3 (n=308)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>256</td>
<td>283</td>
<td>189</td>
</tr>
<tr>
<td>Females</td>
<td>148</td>
<td>191</td>
<td>119</td>
</tr>
<tr>
<td>Mean FBS</td>
<td>111.320 mg/dl</td>
<td>142.098 mg/dl</td>
<td>217.437 mg/dl</td>
</tr>
<tr>
<td>Mean PPBS</td>
<td>151.518 mg/dl</td>
<td>209.884 mg/dl</td>
<td>318.077 mg/dl</td>
</tr>
<tr>
<td>Mean RBS</td>
<td>155.904 mg/dl</td>
<td>197.800 mg/dl</td>
<td>291.225 mg/dl</td>
</tr>
</tbody>
</table>

Table 3: Sensitivity, specificity and positive predictive value of fasting and postprandial glucose in predicting good glycaemic control

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS</td>
<td>74%</td>
<td>84%</td>
<td>87%</td>
</tr>
<tr>
<td>PPBS</td>
<td>79%</td>
<td>74%</td>
<td>80%</td>
</tr>
</tbody>
</table>

*Good glycemic control: HbA1c < 7%, FBS <130, PPBS<180mg/dl*

References:


