Assessment of Glycaemic control in Diabetic patients Attending Ahmadu Bello University Teaching Hospital, Zaria, Nigeria.

Lawal Nasiru.
Department of Chemical Pathology, Ahmadu Bello University Zaria P.M.B. 0006, Kaduna State Nigeria

ABSTRACT
Important biochemical indices used to assess glycaemic control include fasting blood glucose, 2-hours post prandial glucose and glycated haemoglobin. The objective of this study was to assess glycaemic control in diabetic patients attending medical out-patient Department clinic (MOPD), of Ahmadu Bello university Teaching Hospital (ABUTH), Zaria. The study population was 170 type 2 diabetic patients. Diabetes mellitus (DM) was confirmed according to the new diagnostic criteria based on 2 fasting or 2 random serum glucose levels of more than 7.0 mmol/L and 11.1 mmol/L respectively. A concise history of the patients, physical examination and laboratory findings were recorded on a proforma. Glycated haemoglobin (GHbA1c) and concentrations of serum FBG and RBG were measured. The reference values of glycated haemoglobin was established using a standard protocol. The mean values of GHbA1c and serum FBG as well as RBG were significantly higher in diabetic patients than in control subjects (p<0.01). It was concluded from the findings of the present study that there is poor glycaemic control in the studied patients, which could be as a result of poor compliance of patients to treatment. The established reference value (mean±2SD) for glycated haemoglobin was (6.3-6.7 %).

Key words: Glycated haemoglobin, Glycaemic control, Diabetes mellitus
Correspondence: nasiruacademy@gmail.com

INTRODUCTION
Diabetes mellitus (DM) is a systemic disease caused by absolute or relative deficiency of insulin and is manifested by disorders of carbohydrates, lipid and protein metabolism (1). The hallmark of the disease is fasting hyperglycaemia, characterized by variable occurrence and severity of microvascular (nephropathy, retinopathy, neuropathy) and macrovascular (atherosclerotic cardiovascular complications) (2). The disorder imposes morbidity and mortality (1,3,4). DM is becoming a major health problem in the world including Nigeria with a prevalence of 1.4-2.7% (5,6,7) and over 90% of these are type 2 (7,8).

Several large randomized, control trials have consistently demonstrated that meticulous glycaemic control slows the appearance and/or progression of diabetes mellitus to microvascular as well as macrovascular complications (2,9). Important biochemical analytes that reflect glycaemic control includes fasting blood glucose, 2-hour post prandial glucose and glycated haemoglobin². Excess circulating glucose in diabetic patients is a reactant molecule that is involved in the glycation of other biomolecules and tissues (10). Excessive glycation of a variety of proteins has been widely accepted to be a major (albeit probably not a sole) pathogenic factor in the microvascular complications of DM (11). Glycation of haemoglobin is particularly popular and of great clinical
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Glycated haemoglobin (GHbA1c) expressed as a percentage of total blood haemoglobin concentration gives a retrospective assessment of the mean plasma glucose concentration during the preceding 3-4 months (10). Its measurement is widely accepted as a method of assessing glycaemic control (12,13). Higher percentage of circulating GHbA1c in the blood is indicative of the poor control blood glucose. The present study aimed at revealing the level of compliance of patients in this environment to diabetic care/control measures.

Materials and Methods

The study was conducted in Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Nigeria. This study was approved by the Ethical Committee of the ABUTH, Zaria in accordance with the declaration of Helsinki. A total of 170 diabetic patients attending Medical-outpatients Department (MOPD) and 80 apparently healthy individuals were enrolled for the study. The criteria for diagnosis of type 2 DM was the American Diabetes Association Criteria (2004) which is based on fasting blood glucose of 7.0 mmol/L on two occasions or random blood glucose of 11.1 mmol/L with diabetic symptoms. The diabetic patients were provided with conventional diabetes care/control measures. At the MOPD, arrangement was made with the physicians ensure that inclusion criteria were satisfied. Informed consent for inclusion into the study was obtained from the subjects. The nature of the study was explained to the subjects by the use of appropriate language. A full medical history was obtained from the subjects by the physicians followed by clinical examination, anthropometric measurement and collection of blood specimen. The findings were documented in the Proforma.

Sample collection

Blood specimens (2 cm$^3$) were dispensed into EDTA bottles and (3 cm$^3$) were taken into plain tubes, using sterile technique. The blood (in plain tubes) was centrifuged and the serum was carefully drawn into sample bottles and analysed immediately for glycated haemoglobin (GHbA1c) using the method of Triveli et al. (14) and fasting blood glucose (FBG) as well as random blood glucose (RBG) were assayed using the method of Trinder (15).

Statistical Analysis

Statistical analysis was performed using statistical package for social sciences (SPSS) for Windows, version 15.0. The data were presented as Mean±SEM. Glycated haemoglobin (GHbA1c) levels and serum fasting blood glucose (FBG) as well as random blood glucose (RBG) levels were compared with those of the apparently healthy individuals (controls) using two tailed student t-test. A p-value of equal to or less than 0.05 (p≤0.05) was considered as statistically significant. The reference values of glycated haemoglobin was established using a standard protocol. A value at 95 % confidence interval was adopted.

Results

The results of clinical parameters are presented in table I. The differences in weight and body mass index (BMI) between diabetic patients and controls were statistically significant (p<0.01). GHbA1c and serum FBG as well as RBG in diabetic
patients and controls are presented in table II. The mean values of GHbA1c and serum FBG as well as RBG were significantly higher in diabetic patients than in the control subjects (p<0.01). The result of established reference value is also presented in table III. The GHbA1c value was found to be (6.3-6.7)%(Mean±2SEM).

Table I: Clinical parameters (mean±SEM) in diabetic patients and controls.

<table>
<thead>
<tr>
<th>Subjects</th>
<th>n</th>
<th>Age(years)</th>
<th>Weight (Kg)</th>
<th>BMI(Kg/m²)</th>
<th>D(years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>170</td>
<td>51±0.8</td>
<td>71±0.9</td>
<td>28.2±0.4</td>
<td>6±0.4</td>
</tr>
<tr>
<td>Controls</td>
<td>80</td>
<td>50±1.1</td>
<td>64±1.1</td>
<td>23.0±0.4</td>
<td>NA</td>
</tr>
<tr>
<td>p-value</td>
<td>&gt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

n=Number of subjects, BMI=body mass index, D=duration of diabetes mellitus, SEM=standard error of mean and NA=not applicable.

Table II: Result of biochemical analytes (mean±SEM) in diabetic patients and control subjects

<table>
<thead>
<tr>
<th>Subjects</th>
<th>n</th>
<th>FBG (mmol/L)</th>
<th>RBG (mmol/L)</th>
<th>GHbA1C (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>170</td>
<td>7.0±0.2</td>
<td>9.6±0.3</td>
<td>9.8±0.2</td>
</tr>
<tr>
<td>Controls</td>
<td>80</td>
<td>4.0±0.1</td>
<td>5.4±0.1</td>
<td>6.5±0.1</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

n=Number of subjects, FBG=Fasting blood glucose, RBG=Random blood glucose, GHbA1c=Glycated haemoglobin and SEM=Standard error of mean.

Table III: Mean±SEM and Established reference values in controls subjects

<table>
<thead>
<tr>
<th>Subjects</th>
<th>n</th>
<th>Mean±SEM (%)</th>
<th>Mean-2SEM (%)</th>
<th>Mean+2SEM (%)</th>
<th>Reference value(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>80</td>
<td>6.5±0.1</td>
<td>6.3</td>
<td>6.7</td>
<td>(6.3-6.7)</td>
</tr>
</tbody>
</table>
Discussion
The results obtained in the present study showed that glycated haemoglobin levels and serum fasting blood glucose as well as random blood glucose levels were significantly higher in diabetic patients than in controls. This is in agreement with the reports of Jay\(^9\) and Akinloye et al\(^{10}\). The observation of higher mean level of GHbA1c in type 2 diabetic patients than in control subjects in the present study suggests a poor glycaemic control. Similarly, it was observed in the present study that the mean values of serum fasting glucose were higher in diabetic patients than in control subjects. This also suggests poor glycaemic control. Both GHbA1C and serum fasting glucose can serve as useful indice for glycaemia. While fasting blood glucose may serve as an indices of short-term glcaemia, GHbA1C can serve as an index for long-term glycaemia\(^{16}\). Akinloye et al\(^{10}\) (2007) reported a significant positive correlation between glycated haemoglobin and FBG in both diabetic patients and control subjects. It indicated that the higher the FBG the higher the glycated haemoglobin and thus implies that glycation of haemoglobin increases with increased plasma glucose. This demonstrated a good agreement between the two parameters in the assessment of glycaemia in DM. This is consistent with the observation of the present study. However, GHbA1c appears to be a better reflection of integrated plasma glucose in the preceding days (3-4 months) than the spot plasma glucose determination.

The hallmark of DM is hyperglycaemia and its major consequence is excessive non-enzymatic glycation of proteins. The glycation process begins by the formation of Schiff base followed by the formation an Amadori product. This will then undergo reactions and rearrangement to form advanced glycation end products (AGE)\(^{17}\). Glycated haemoglobin, which measure glycaemic control over a 3-4 weeks period, is best-characterized and best-known Amadori product\(^{17}\). This may be responsible for the increased plasma glycated haemoglobin seen in the present study. Diabetes Control and Complications Trial (DCCT) and United Kindom (U.K). Prospective Diabetes Study (UKPDS), both of them revealed a dramatic risk reduction for microvascular and macrovascular complication of DM\(^9\). The patients under this study were provided with conventional diabetes care/control measures. However, a significantly increased levels of glycated haemoglobin was observed. This demonstrates that there is a possible indication of poor glycaemic control in the studied diabetic patients. This probably implies that these patients only prepared themselves for clinic days. This is in agreement with the observation of Watkins\(^{18}\) and Akinloye et al\(^{10}\).

It is an established fact that fasting blood glucose (FBG) and random blood glucose (RBG) are generally higher in diabetic patients than in apparently healthy individuals. This is in agreement with the observation of the present study. The demonstration of hyperglycaemia through blood glucose tests can be used for short-time monitoring of treatment. In addition, blood glucose tests are also used for the diagnosis and screening of DM or monitoring its treatment\(^1,10,19\).

CONCLUSION
It was concluded from the findings of the present study that there is poor glycaemic control in the diabetic patients which could be as a result of poor compliance of patients to treatment. Measurement of glycated haemoglobin be considered for the management of diabetic patients in ABUTH, Zaria. This could improve the management of these group of patients, and hence reduce the morbidity and mortality for DM.
REFERENCES


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