Glycated albumin and glycated haemoglobin levels as a measure of monitoring glycaemic control in diabetic patients attending out-patient clinic at Kenyatta National Hospital: a comparative study

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ABSTRACT

**Background:** Diabetes mellitus (DM) is a chronic metabolic disease that is characterized by persistent hyperglycemia. Monitoring of glycaemic control in individuals with DM is currently done by a combination of short term, that is daily monitoring of blood glucose and long term biochemical tests especially glycated haemoglobin (HbA1c) which is done every 2-4 months. Glycated albumin (GA) is a new test for intermediate glycaemic control. It measures averaged plasma glucose level over two to four weeks. This enables closer monitoring and evaluation of treatment regimen faster than HbA1c.

**Objectives:** To compare glycated haemoglobin to glycated albumin levels as a measure of monitoring glycaemic control in diabetic patients.

**Design:** A prospective comparative study.

**Methods:** The study was carried out on diabetic patients attending the diabetic clinic at Kenyatta National Hospital.

**Results:** A total of 260 patients were enrolled into the study. The mean age was 52 years with a standard deviation of 12.3. There was a female preponderance of 60.4%. Random blood sugar analysis showed that, the population with good glycaemic control constituted 156 (60%). Majority of the patients had good glycaemic control 170 (65.4%) based on the HbA1c assay, compared to 39.4% in GA. There was a good correlation between HbA1c and glycated albumin with R\(^2\) value of 0.64.

**Conclusion:** More patients showed good glycaemic control based on HbA1c compared to glycated albumin. There was correlation between HbA1c and glycated albumin with R\(^2\) value of 0.64. There is need to introduce glycated albumin as a method of intermediate glycaemic control in the hospital.

**INTRODUCTION**

Diabetes mellitus (DM) is a metabolic disease that is characterized by hyperglycemia. It is caused by a complex interaction of genetic and environmental factors. Hyperglycemia is caused by reduced insulin secretion or resistance, decreased glucose utilization and increased glucose production.

Decades of research have established that prolonged exposure to excess glucose is the cause of diabetic complications and that long term control of blood glucose is required. The process of protein glycation is now understood to be both a marker for the progress of diabetes complications and underlying cause for many of the most serious complications\(^1\).

Monitoring blood sugar levels in individuals with DM is currently done by a combination of short-term that is random blood sugar and long-term methods (glycated haemoglobin).

Glycated albumin is an intermediate method for assessment of glycaemic control which has been used in Japan and other Far East countries but not in Kenya. HbA1c represents time averaged plasma glucose level of over 2-4 months; it requires longer time for HbA1c to improve after improvement of glycaemic control as compared to GA whose time averaged plasma glucose level is 2-4 weeks. GA enables evaluation of treatment regimen faster\(^2\).\(^3\)

American Diabetes Association describes the treatment goals for adults with DM as HbA1c of <7% (53mmol/mol), pre-prandial plasma glucose of 5.0-7.0mmol/l and peak post-prandial plasma glucose of <10mmol/l\(^4\).

Kenyatta National Hospital (KNH) attends to about 8,500 diabetic patients every year. Many of these patients are seen at long intervals (3-6 months). Lately improvements have been made to enable diabetic patients with special...
individual needs to be reviewed more frequently by nurses and clinical officers at the clinic. Random blood sugar of $>11.1\text{mmol/l}$ in symptomatic patients is used as a basis for diagnosis. Those with RBS of between 7.9mmol/l and 11.1mmol/l are subjected to oral glucose tolerance test to determine their diabetic status.

HbA1c is used in monitoring DM patients in most private hospitals. The tests cost between USD15 and 20 USD which is far beyond the reach of many diabetic patients attending the Diabetic clinic at KNH. Glycated albumin is a new useful and rapid method for monitoring DM though, the cost may not be determined at the research level. During the period of data collection, July to September 2011, HbA1c test was not being done at KNH labs but was introduced shortly later at subsidized price of 11 USD.

There is a demonstrable need for an intermediate glycation index. Measurement of GA monitors DM complications by picking poor glycaemic control earlier than when using long term methods. This closes the information gap that exists between daily blood glucose testing and HbA1c testing.

**MATERIALS AND METHODS**

This was a diagnostic accuracy study comparing HbA1c and GA. It was carried out between July and September 2011. The total number of patients, both new and old seen at the clinic yearly are between 8,000 and 9,000 in number and out of these new cases are about 600.

A study population of 260 patients was recruited into the study. Diabetic patients attending the clinic were assessed for eligibility and recruitment done consecutively until the desired number was attained. Screening was done by perusing the files to check for potential study participants who were diabetic patients both type 1 and 2, who gave informed consent to participate in the study. Those who had documented diabetic complications were excluded from the study. After the questionnaires were filled by consenting patients, the patients were seated in a procedure room and the process of blood sampling explained to each one of them by the primary investigator and the research assistant.

The site for venepuncture was cleaned with swabs soaked in 70% alcohol and dried using a dry cotton wool. Approximately 4 ml of blood was drawn from the cubital vein of each participant using a sterile needle and syringe. The sample was then divided into two: 2ml was put in the EDTA bottles and sample mixed well with anticoagulant to avoid clotting of sample. The other 2ml was put in a plain bottle. The EDTA anticoagulated blood was used to run the glycated haemoglobin which was done within 4 hrs of sample collection. The samples in the plain bottle were centrifuged after the daily collection and stored in cryo vials at -20°C. The samples were later run as a batch for analysis of glycated albumin. Both samples were run at the KNH Chemistry laboratories. The KNH lab participates in EQA (HUQAS) for other analytes not glycated albumin because it was being run for the first time.

According to ADA good glycaemic control is defined as, HbA1c of $<7\%$ (53mmol/mol). There is no definition for glycated albumin given hence cut off of 285umol/l was used based on the parameters from the Diazyme Kit assay. The parameters used to describe good diabetic control were: HbA1c of less than 7% (53mmol/mol) and glycated albumin of less than 285umol/l and the parameters for random blood glucose were assessed using the glucose control chart used at the clinic developed by Diabetes Association of Kenya for use in Kenyan public hospitals. Using the HbA1c as the gold standard test, the patients were categorized into two groups: normal HbA1c less than 7% and high HbA1c (more than or equal to 7%), these two categories were used to describe good and poor glycaemic controls. Then the two groups were compared according to their demographic, medical history and physical examination characteristics.

**RESULTS**

During the study period, 272 files were scrutinized. After perusing the files, 5 patients were found to have some complications especially deranged renal function tests and the other 7 declined to consent. Afterwards, 260 patients were recruited into the study. A total of 260 patients met the eligibility and were included in the analysis.

*Figure 1: Age distribution of the patients (n=260)*

The youngest person was 20 years old and the oldest was 90 years old. The mean age was 52.5 years, with a standard deviation of 12.3. Majority of the participants were in the 51-60 years. This group had 81 (31.2%) diabetic patients attending the out-patient clinic.
The range of the random blood sugar was 3.9-29.0. The mean is 9.75 and the SD was 4.39.

Figure 3: Histogram showing distribution of glycated haemoglobin levels in the study population (n=260)

The histogram shows the distribution of glycated haemoglobin level in the study population. The range was 4.1-10.8 and the mean was 6.67 with a standard deviation of 1.18. The patients with good glycaemic control constituted 65.4% of the study population.

Figure 4: Histogram showing distribution of glycated albumin in the population (n=260)

The range was 120-920umol/L. The mean was 352.95umol/L and the SD was 160.4umol/L. Based on a cut off of X, Y (%) patients had good glycaemic control. The linearity is represented in the equation glycated albumin=3.63+97.39 (HbAlc). The R2 value is 0.64. There is a positive correlation between glycated albumin and HbA1c (Figure 5).

DISCUSSION

The main method of monitoring diabetes mellitus at the Kenyatta National Hospital diabetic clinic is the use of self monitoring of blood glucose. This is because the test is cheaper and within the reach of the largely poor population. After analysis of the plasma glucose the results showed that, the population with good glycaemic control constituted 156 (60%), (Figure 2). The Fremantle study of 1,286 type 2 diabetes patients over 5 years as well as a study of nearly 3,000 type 2 patients on oral medication or diet alone in Germany and Austria found no benefit for daily blood glucose testing regardless of treatment.

Self monitoring of blood glucose (SMBG) is especially important for patients treated with insulin to prevent asymptomatic hypoglycemia and hyperglycemia. For most patients with type 1 diabetes and pregnant women taking insulin, SMBG is recommended three or more times daily (ADA). Several recent trials have called into question the clinical utility and cost effectiveness of routine SMBG in non-insulin-treated patients.

In addition to self monitoring of blood glucose some of the patients use HbA1c to monitor their glycaemic control after every 3 months. Results from this study showed that majority of the patients had good glycaemic control 170 (65.4%) based on HbA1c. This is different from a study done by Otieno et al. which was assessing the quality of glycaemic control on ambulatory diabetic patients attending the clinic at Kenyatta National Hospital and found out that more than 60% of the patients attending the clinic had poor glycaemic control. Poor glycaemic control was presumed to be due to sub-optimal medication and deteriorating diabetes.
HbA1c measurements have represented the gold standard for the evaluation of glycaemic control in diabetic patients for the past 30 years. DCCT demonstrated that each 1% increase in HbA1c is associated with an increase in mean blood glucose concentrations of 2mmol/L and this increased the risk of progression and development of microvascular complications in DM. The expert panel of National Committee for Quality Assurance (NCQA) has recently developed new targets of HbA1c target of <8% they considered that target of <6.5% is difficult to achieve. The scoring was thereby revised for the updated standard so that the percentage of patients with acceptable levels HbA1c <8% are 40%. It is recommended that there be need to establish population specific cut-off thresholds according to ethnicity, age, gender and prevalence of DM.

The ADA recommends assessing HbA1c at least 2 times a year in patients who are meeting treatment goals and have stable glycemic control and quarterly in those patients whose hypoglycemic therapy has changed or those who are not meeting glycaemic control goals. The results according to the glycated albumin showed that majority of patients 157 (60.6%) had poor glycemic control while 102 (39.4%) had good glycaemic control (Figure 4). Glycated albumin has been reported as a rapid and useful indicator of glycemic control since the turnover of serum albumin is much shorter (half life of 17 days) than that of HbA1c. Circulating albumin is strongly glycated at 4 sites of lysine residues and the glycation reaction occurs ten times more than in HbA1c. This implies that glycemic fluctuation and excursion would influence glycation in albumin strongly.

The study showed that there is a positive correlation between GA and HbA1c. The linearity is represented in the equation Glycated Albumin=3.63+97.39 (HbA1c). The R^2 value is 0.64. This compares to Nathan et al's study which showed that correlation coefficient between HbA1c and GA was 0.747 and was highly significant (p < 0.001). Another study which had differing results was a Japanese study which was finding out whether GA was a more useful tool to monitor rapidly changing blood glucose than HbA1c. The study was performed on patients hospitalized for diabetes control (51 men and 47 women). Patients were administered oral anti-diabetic drugs and 4-point self monitoring of blood sugar (SMBG) tests daily then 7-point SMBG tests were done the third and tenth hospital day. GA and HbA1c were performed the second and thirteenth hospital day. Results from the second day demonstrated a good correlation of blood glucose with HbA1c and GA (p=0.0001). However, on the thirteenth day only GA correlated well with blood glucose (p=0.0001) as opposed to HbA1c (p=0.019). The study concluded that GA measurement is more accurate for determining rapidly changing blood glucose than HbA1c.

**CONCLUSIONS**

More patients showed good glycaemic control based on HbA1c 170 (65.4%) compared to glycated albumin. There was correlation between HbA1c and glycated albumin with R^2 value of 0.64. There is need to introduce glycated albumin as a method of intermediate glycaemic control in the hospital.

**REFERENCES**


