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VALIDITY OF RANDOM BLOOD GLUCOSE AS A PREDICTOR OF THE QUALITY OF GLYCAEMIC CONTROL BY GLYCATED HAEMOGLOBIN IN OUT-PATIENT DIABETIC PATIENTS AT KENYATTA NATIONAL HOSPITAL
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ABSTRACT

Background: **Patients with diabetes mellitus in Kenya come to the hospital for follow-up visits very infrequently. For most of these patients their blood glucose monitoring is done only on the day of visit to the doctor.**

Objective: **To determine how well the physician-based morning random blood level determines or reflects the quality of glycaemic control.**

Design: **Cross-sectional study (morning, random blood glucose taken between 8.00 a.m. and 12.00 noon).**

Setting: **Out-patient diabetic clinic of Kenyatta National Hospital.**

Subjects: **Patients with diabetes mellitus either type 1 or type 2 attending the out-patient clinic.**

Main outcome measures: **Random blood glucose (morning) and glycated haemoglobin (HbA1c).**

Results: **The morning random glucose level had a linear relationship with glycated haemoglobin levels taken simultaneously. A blood glucose level of 7 mmol/l had 92.7% sensitivity for good control (HbA1c≤7.8%) on a blood sample which was taken simultaneously and 59.8% specific for the same. When blood glucose cut-off level was raised to 10 mmol/l sensitivity fell to 66.3% for HbAlc≤7.8%, and 83.2% specificity for poor glycaemic control (HbAlc>7.8%). There was marked fall in sensitivity of rising random blood glucose level in predicting good glycaemic control in our study, with concomitant rise in specificity of those high cut-off levels of blood glucose in predicting poor glycaemic control.**

Conclusion: **Morning random blood glucose in the ambulatory diabetic patients related well to simultaneously assayed HbAlc. Blood glucose within usual therapeutic targets of 4-8mmol/1 predicted good glycaemic control (HbAlc≤7.8%) with high sensitivity at the range of 86.3-98.4%. In resource-poor settings, the morning random blood glucose assay, which is done in patients who may attend the diabetic clinic in the morning hours, may be used to predict the quality of their diabetic control. However caution should be exercised in its widespread use because its overall applicability may be clinic-specific depending largely on the average metabolic control of the diabetic population using that clinic. Further studies need to be done to relate HbAlc to blood glucose levels obtained at different times of the day in this population to determine the best predictor of good glycaemic control.**

INTRODUCTION

The landmark studies of Diabetes Control and Complication Trial (DCCT)(1) and United Kingdom Prospective Study (UKPDS)(2) have focused attention on the importance of glucose control in preventing and/or retarding the progression of complication in patients with diabetes mellitus. Regular measurements of glycated haemoglobin is now recognised as an essential adjunct to self-measurement of blood glucose in achieving the desired and possible glycaemic control(1,3). Use of glycated haemoglobin as a measure of glucose control in patients with diabetes mellitus in Kenya is limited by its costs per test, currently estimated at US$10-20, while a single physician-based glucose testing costs US$2-3. The machines for home-based self-monitoring of blood glucose retail at approximately US$100-160 excluding testing strips which retail at about US$35-70 for a packet of 50 strips. This estimates to a very costly glucose monitoring, both physician-based

and home-based, which is barely affordable to the average Kenyan diabetic. This means that the majority of patients with diabetes in Kenya have infrequent blood glucose monitoring a scenario occasioned by endemic poverty. Glycated haemoglobin itself is rarely done on these patients because of cost of the assay. However its utility is also low as a test of glycaemia for daily adjustment of medication. Infrequent utilisation of glycated haemoglobin has also been observed in Asia with positive response of utilisation at about 19%(4) compared to Denmark with over 90% utilisation(5).

Blood glucose is therefore the most common laboratory test done on the patient with diabetes attending the clinic in this hospital. The blood glucose done serves two purposes of assessing the point glycaemic status and also offers rough insight on the overall glycaemic control of the patient especially for one who would be unable to afford an assay of glycated haemoglobin. This study was undertaken to assess the latter role.

A morning random blood glucose of physician-based blood glucose testing in an outpatient setting was used because the diabetic clinic here runs in the morning hours. The clinic does not do routine glycated haemoglobin assays.

MATERIALS AND METHODS

Between June and December 1998, patients confirmed to have diabetes mellitus based on the clinical records available of anti-diabetic treatment or newly diagnosed using current WHO guidelines(6) were recruited randomly on each day of the diabetic clinic. Three hundred and five patients were included for evaluation over the seven months. This clinic caters for approximately 2,500 patients yearly, therefore the number of patients included represents more than 10% of the total clinic-attending patients. The patients were seen and examined between 9.00 a.m. and 12.00 noon, on the day of the clinic this interval being the usual clinic time.

A full clinical evaluation was done on each patient in the study. A venous blood sample was obtained from ante cubical vein by venipuncture. From this blood sample 2 ml was collected in fluoride bottle for immediate glucose assay by glucose oxidase method(7). For this study two assays were done on a sample by two different technicians and an average of the two results used for analysis. Another 2ml of blood sample collected in EDTA bottle glycated haemoglobin assay was done using automated IMx system (Abott-Inc); an ion-capture boronate affinity binding assay which is based on complex formation of the glucose cis-diol group and 3-aminophenylboronic acid and reported as percentage glycated haemoglobin (%HbAlc) from the formula(8).

$$\text{Standardised HbAlc} = \frac{\%\text{GHb} + 1.76}{1.49}$$

Its reference for non-diabetic range is 4.4 – 6.4%

Research Design; This was a cross-sectional study which was done on randomly selected patients with diabetes on a single visit to the out patient diabetic clinic of the hospital. There was no prior notification to the patients of their involvement in the study.

Statistical Method: Data was summarised as ranges, mean ± standard deviation and tabulated without transformation. The variable of random blood glucose, its sensitivity and specificity at the optimum cut-off points of glycated haemoglobin were calculated. Receiver operator characteristic (ROC) analysis was done. This method compares the diagnostic properties of a test by expressing sensitivity as a function of 1- specificity(9). In this study, the value of morning random blood glucose to diagnose (identify) the quality of glycaemic control as determined by use of glycated haemoglobin as the gold standard was assessed. The best curve with the highest area under curve (AUC) was obtained with HbA1c ≤ 7.8%.

On the ROC-curve the highest point closest to unity represent the best sensitivity. In this study, the following were the definitions used.

		Glycated Haemoglobin (GHb)	
Blood sugar (mmol/1)		Well controlled ≤7.8%	Not well Controlled >7.8%
≤7.0	Normoglycaemia (Positive)	TP (67)	FP(9)
>7.0	Hyperglycaemia (Negative)	FN(38)	TN(173)

True Negative (TN) = Hyperglycaemia with High GHb (>7.8%)
True Positive (TP) = Normoglycaemia with normal GHb (≤7.8%)

$$\text{Sensitivity} = \frac{TP}{TP + FN} = \frac{\text{Normoglycaemia + Normal HbAlc}}{\text{Normoglycaemia + Hyperglycaemia with high HbA1c}}$$

$$\text{Specificity} = \frac{TN}{TN + FP} = \frac{\text{Hyperglycaemia with high HbA1c}}{\text{Hyperglycaemia with high HbA1c} + \text{Normoglycaemia with high HbA1c}}$$

Table 1

Characteristics of the population included in the study

Characteristics	Number	Proportion %
• Gender		
Male	144	(47.2)
Female	161	(52.8)
• Age(years) Range(17-72)		
<40	57	(18.8)
≥40	246	(81.2)
• Type of Diabetes		
Type 1	41	(13.6)
Type 2	260	(86.4)
• Duration of Diabetes (<1 year to 32 years)		
≤1 year		(22.0)
>1 ≤ 10 years		(53.8)
>10 ≤ 20 years		(20.3)
>20 ≤ 30 years		(3.9)
• Mode of Treatment		
OHA only	181	(62.0)
Insulin only	69	(23.6)
Insulin + OHA	28	(9.6)
Diet only	14	(4.8)
• Glycated Haemoglobin: (range 4.03-17.07)		
≤ 8%	120	(39.5)
> 8% ≤ 10%	92	(30.3)
> 10% ≤ 15%	80	(27.5)
> 15%	13	(4.0)

OHA = Oral hypoglycaemic agents

RESULTS

The population distribution by gender had 47.2% males and 52.8% females This may not however be a true reflection of the national figures of gender distribution for diabetes because of certain biases in utilisation of this health facility.

The age range was 17-72 years and the patients with ≥40 years were the majority (81.2%). Patients with type 2 diabetes were 86.4% of the population studied: this reflected the predominance of type 2 diabetes as seen in the national proportions. The majority (71.6%) of patients were on treatment with OHA only and combined OHA with insulin. These study patients were both type 1 and type 2 diabetes in various stages of their disease. The quality of diabetes control in the study population is shown in Figures 1 and 2.

The quality of diabetes control was noted to be largely poor in the population. Majority (60.5%) had HbAlc >8%. The possible reasons were not the objective of this study. Patients in the study on diet-only had on the whole the best glycaemic control. Figure 3 showes linear relationship of random blood glucose with glycated haemoglobin (HbAlc). Generally, rising hyperglycaemia causes rise in HbAlc (Figures 1 and 2). Alternatively expressed, high glycaemic levels were associated with deteriorating quality of glycaemic control measured by glycated haemoglobin. However the scatter of glycaemia observed imply exceptions to the rule (false poor control) due to various reasons – ranging from post-meal state, missing medication in the morning of the clinic visit, inaccurate machines and other reasons, which were not obvious during the study.

Figure 1

Mean blood glucose of the patients by type of treatment

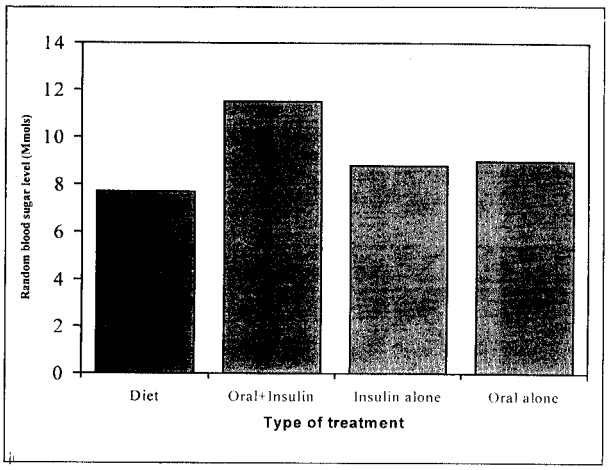

Figure 2

Mean glycated haemoglobin of the patients by type of treatment

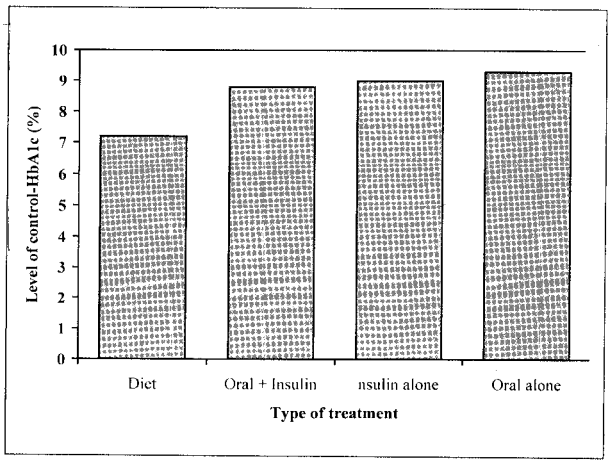

Figure 3

Plot of random blood glucose versus the simultaneously assayed Glycated haemoglobin of the study

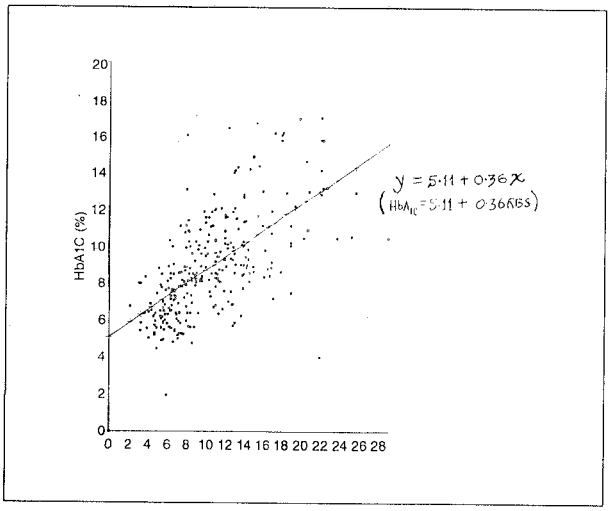

Figure 4

ROC-Curve of random blood glucose against glycated haemoglobin (HbA1c) of the patient included in the study

RBG mmol/l	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Sensitivity	100	100	98.4	98.4	96.8	92.7	86.3	74.7	66.3	58.4	47.3	37.4	31.6	23.2	19.5	15.8	13.2
1-specificity	99.1	99.1	95.3	84.1	64.5	40.2	28	17.2	16.8	14.0	10.3	5.6	2.8	2.8	1.8	2.8	1.9
Specificity	0.9	0.9	4.7	15.9	35.5	59.8	72.0	82.2	83.2	86.0	89.7	94.4	97.2	97.2	97.2	97.2	98.1

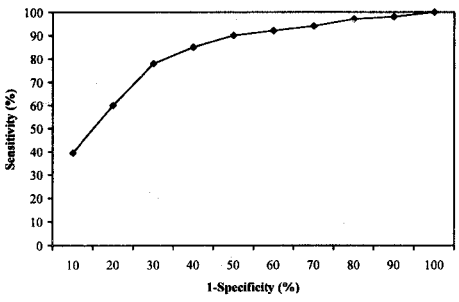

Figure 4 is a ROC-curve expressing sensitivity of morning glycaemia in predicting the quality of glycaemic control. The curve was drawn using the figures in the Table above it. It showed that rising glycaemia predicted good glycaemic control with diminishing sensitivity.

DISCUSSION

Major advances have been made in the diagnosis and treatment of diabetes in the last millennium. In particular the use of self-monitoring of blood glucose and regular monitoring of glycated haemoglobin are now standards of care in the management of diabetes and its complications. These glycaemic parameters provide a more rationalised therapy with either insulin or oral hypoglycaemic agents. Glycaemic monitoring is costly in terms of equipment, supplies and organised health care delivery systems which are barely affordable to patients in developing countries.

Socio-economic status of the patients in the study had earlier been stated as modest. Table 1 refers to patients characteristics. Type 1 diabetes (13.6%) and type 2 diabetes (86.4%) of the population under study was fairly representative of the proportions as known in this country and over the world where patients with type 2 diabetes predominate.

Figure 3 shows a linear relationship that was found between the morning random glucose levels and the corresponding glycated haemoglobin taken simultaneously. The linear equation derived was; HbA1c=0.36 RBG + 5.11. It is prudent to emphasise this observed linear relationship which implies that rising blood glucose levels taken randomly are likely to reflect equally rising glycated heamoglobin levels. However this may not be true always, especially in attempting to use a single blood glucose assay on a clinic day. It has been recognised that reliance on occasional fasting or random laboratory glucose assay provide an incomplete and potentially misleading picture of a patient's glycaemic status(10,11). A patient may also alter behaviour to achieve acceptable glycaemic results to impress the health provider on that day of visit to the out-patient clinic which may serve to complicate the picture. The types, timing and frequency of meals are important determinants of the level of glycaemia taken randomly. The population studied were of people with modest background who may rarely afford three good meals daily and if one did, the meals would be unlikely to vary in content significantly. These observation may support an assumption that 24-hours glycaemic excursions in an individual from this population may not on the whole vary widely over a period of time. A single physician-based blood glucose assay on a clinic visit, which is infrequent in our clinic, showed a linear relationship with glycated haemoglobin similar to the correlation seen between glycated haemoglobin and the means of blood glucose levels obtained over the preceding one to three months in other studies(11-13). This linear relationship also included other measures of glycaemic excursions like fasting plasma glucose and mean post-prandial plasma glucose(11,12,14-17). However instability in glucose control may reduce this correlation(18, 19). Instability of glucose control may arise from glucose dynamics unique to type 1 and 2 diabetes, modes of treatment in use and individual (patient) factors under consideration in a particular time frame. In this study, there were no significant difference in means of glycated haemoglobin in the various groups based on their mode of glycaemic including OHA only, OHA+ insulin and insulin-only treatment except the diet-only group who had the best overall glycaemic control in this study population.

Gebhart *et al.*(20), compared the mean home glucose levels with glycated proteins. They found that the blood glucose levels greater than 11.1mmol/l had abnormal levels of glycated proteins while random blood glucose levels of 8.3 to 11.1 mmol/L were associated with at least one or more normal glycated proteins.

In conclusion, obtaining an accurate estimate of glycaemic control remains a challenge to individuals with diabetes and the physicians that care for them. Records of home-based blood glucose monitoring have become an important tool in diabetic decision-making for both the patient and the clinician. However, the costly nature of this important aspect of diabetes care means that it eludes diabetic patients who are too poor to afford the glucometers, a very familiar and common scenario in the developing countries. These patients are also infrequently monitored in these clinics they attend even in this country.

This study has shown that a physician-based glucose assay in the laboratory may still, in the absence

of the ideal situation be a useful guide for monitoring glycaemic control of patients who may not be able to obtain an assay of glycated haemoglobin.

Further studies are recommended to evaluate usefulness of true fasting, post-lunch and extended post-lunch glycaemic levels then compare them with the morning random glucose assay to ascertain which of these measures of glycaemia predicts the best gycaemic control in this population.

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