ORIGINAL ARTICLE

MONITORING DIABETIC CONTROL BY MEASURING GLYCATED HEMOGLOBIN AND FASTING BLOOD GLUCOSE LEVELS OF DIABETIC PATIENTS ATTENDING JIMMA UNIVERSITY HOSPITAL, JIMMA, ETHIOPIA

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ABSTRACT

BACKGROUND: ***Diabetes is a complex metabolic disorder characterized by increased blood glucose level that leads to hyperglycemia, that results in glycation of a number of proteins, which contributes to diabetic complications. In poorly controlled diabetes, there could be increased glycation of hemoglobin and this form of the protein has lower affinity to oxygen. Fasting blood glucose and glycated hemoglobin levels are the best indicators of the extent of diabetic control.***

METHODS: ***A case control study was made on diabetic patients (both insulin dependent and independent) that have follow up in the diabetic clinic of Jimma University Hospital. To check whether the patients had good or poor glycaemic control, serum glycated hemoglobin, and fasting blood glucose levels of patients were measured by using standard test kits.***

RESULTS: ***In the study, 100 diabetic patients and 158 non-diabetic subjects were employed. Out of the 100 patients 33 were female and 67 were male and 58 were insulin dependent and 42 non-insulin dependent cases. Female diabetic subjects showed an increased serum concentration of glycated hemoglobin (HbA1c) than male subjects. The patients in the age group 30-39 showed the highest blood sugar level and glycated hemoglobin concentration.***

CONCLUSION: ***From the results obtained by measuring glycated hemoglobin (HbA1c), it can be concluded that the patients had a poor glycaemic control in the past three months from the date of collection of blood samples. There is also a general increase in HbA1c with increasing level of fasting blood sugar (FBS) level.***

KEY WORDS: Glycated hemoglobin, Fasting Blood Sugar, glycaemic control, IDDM, NIDDM

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INTRODUCTION

Diabetes mellitus is a debilitating metabolic disorder resulting from the inability of the body cells to use glucose. Long term complications and debilitating sequelae of diabetes mellitus (DM) are the major threats to the quality and length of life in insulin dependent (IDDM) and non-insulin dependent (NIDDM) diabetes mellitus patients (1,2). Hyperglycemia, the primary manifestation of diabetes is associated with the development of some of the diabetic complications. Various cytotoxic roles for glucose have therefore been proposed, including the slow non-enzymatic glycation of proteins (3). This would lead to a change in the conformations and hence change in the function of the proteins. People with diabetes, however well controlled, inevitably accumulate glycated proteins in their tissues. The significance of this process to human diabetes is not clear but recently the extent of tissue browning measured by collagen-associated fluorescence in skin biopsies has been correlated with the incidence and severity of several complications (4,5). It is also well established that these complications are related to the long-term glycaemic status and duration of diabetes (1,6,7). Glycated hemoglobin (HbA1c) concentration is an indicator of average blood glucose concentration over three months and has been suggested as a diagnostic or screening tool for diabetes and its measurement is used as an objective measure of long-term blood glucose control in diabetic patients (7,8,9). Glycated proteins are monitored in the diabetic clinic largely as an indication of glycaemic control (10). Various blood glucose threshold concentrations have been proposed for the diagnosis of diabetes, based on the relation to risk of microvascular complications of diabetes, particularly retinopathy. Moreover, people with diabetes are also at increased risk of macrovascular diseases such as coronary heart diseases and stroke, and it is uncertain whether the relation between blood glucose concentration and such diseases has a threshold or is a continuum (6). Patients with well-controlled diabetes have glycohemoglobin concentrations of 7% HbA1c (0.07 HbA1c/HbA) or less and the diagnostic cutoff for fasting plasma glucose level is 126mg/dl (7.0 nmol/l) (11,12). Research on glycaemic control using glycated hemoglobin as a reliable indicator in the underdeveloped world, especially in Ethiopia, is very scarce and there are bizarre reports. Therefore, this cross sectional study was undergone to assess and report the glycaemic control of diabetic patients at an outpatient diabetic clinic in Jimma, Ethiopia to disseminate information on factors related to the control.

MATERIALS AND METHODS

The study was conducted at the outpatient diabetic clinic of Jimma University Hospital, Jimma, Ethiopia. The clinic serves the people in the town and the surrounding zones with a population of more than 500,000. The hospital is a teaching hospital with 300 beds, which is a specialized hospital staffed with specialists. It is also the main referral hospital in southwest Ethiopia. More than 400 diabetic patients both IDDM and NIDDM attend the diabetic clinic for follow up. The ratio of IDDM to NIDDM is 1.33. From among the patients who have follow up, 100 diabetic patients with an age range of 5-70 were randomly selected for the study between February and December 2002. Blood samples (5ml) were collected after overnight fasting every Wednesday when the patients come on their appointment days with their physician, of which 2.5ml was collected into a vial containing EDTA as anticoagulant and kept at 4^0C for HbA1c determination and the rest 2.5 was used for glucose determination. Blood glucose level was determined at the same day of collection spectrophotometrically using the glucose oxidase test kit (HUMAN, Germany). HbA1c was assayed using Human glycohemoglobin test kit (HUMAN, Germany), an assay that is based on ion resin exchange method. The absorbency of the eluates of the resin after sample application was measured at 415nm using Hitachi-2000 model UV-VIS spectrophotometer. Controls were used for normal and abnormal increased values, which were bought with the kit from the same company.

A questionnaire was also prepared to extract information on the Socio-demographic factors related to the disease like age, sex, duration of disease after diagnosis, locality, occupation, ethnicity, and also information on type of diabetes, type of medication, exercise habit and the type of diet. Weight and height were measured following procedures and BMI was calculated as Weight (Kg)/height^2 (m^2).

Data obtained was analyzed using SPSS software. Differences between means were tested using students t-test and the relations between concentrations of HbA1c and blood glucose with other co-variants were assessed by Pearson's correlation analyses. All possible statistically significant interrelations between different effects and parameters were tested.

RESULTS

A total of 100 diabetic patients, 33 female and 67 male, and 158 non-diabetic controls were included in this study. Of the 100 patients, 58 (58%) were IDDM (Type I) and 42 (42%) were NIDDM (Type II) patients. Out of the total group constituted in the study, 105 were female and 153 were male. Some parameters related to the patient history and characteristics are shown in Table 1. The mean BMI and FBS for Type I and Type II diabetics were 20.01 and 25.18 and 245mg/dl and 204.8mg/dl respectively. The mean FBS level for the diabetic patients and the control group was 228.12 and 91.40 mg/dl respectively. The FBS levels for the controls and the patients were correlated and the analysis showed a significant difference between the two ($p = 0.001$). The average glycated hemoglobin HbA1c level for the patients and control group were 8.5% and 7.0% respectively and when correlated there was a significant difference between them ($p = 0.001$) [Table 2]. The HbA1c and FBS were correlated for different age groups and the relationship between the two was statistically analyzed for the diabetic patients. Generally, the HbA1c level increases with raised FBS level. The distribution of FBS and HbA1c in the different age groups is presented in Table3.

Table 1. Mean values of some parameters measured related to diabetics attending Jimma University Hospital, Jimma, Ethiopia, 2002.

	IDDM	NIDDM	Total
	Mean	Mean	Mean
Age (years)	36.8	50.1	65.1
Height (m)	1.63	1.70	0.13
Weight (Kg)	5.32	69.1	12.5
BMI (Kg/M^2)	20.01	25.18	25.8
FBS (mg/dl)	245	204.8	87.5
HbA1c (%)	8.73	8.23	5.57
Systolic BP	113.9	132.63	15.51
Diastolic BP	70.73	79.26	24.97

Table 2. Mean values and standard deviations (SD) of FBS and HbAlc levels in diabetic (100) and non-diabetic (158) attending Jimma University Hospital, Jimma, Ethiopia, 2002

	Diabetics		Non-Diabetic	
	Mean	SD	Mean	SD
FBS (mg/dl)	228.12	84.1	91.4	15.63
HbAlc (%)	8.52	1.14	7.03	1.50

FBS levels given in mg/dl and HbAlc in %, P (0.000), two tailed T-test

There were 11 patjents in the age group < 20 with mean FBS level of 256mg/dl and mean HbA1c level of 8.7%. There were 20, 9, 21, and 39 patients in the age groups 20-29, 30-39, 40-49 and >50 respectively with FBS and HbA1c levels of 247.4 and 8.775, 290.6 and 9.19, 206.4 and 8.28, 207.6 and 8.33 respectively. The age group 30-39 has the highest FBS level i.e., 290.6mg/dl and the highest HbA1c level, which is 9.19%. As compared to controls the diabetic patients (both IDDM and NIDDM) have increased levels of HbA1c corresponding to increased blood sugar level. The duration of stay with the disease for more than 5 years has an increasing effect on the levels of glycated hemoglobin but the difference is not significant (p =0.2) from the value obtained for patients who have been with the disease for less than 5 years.

Table 3. The FBS (mg/dl) and HbAlc (%) level mean and SD values and distribution of diabetic patients and non-diabetic controls by age

Age group		Fasting blood sugar level		Hemoglobin Alc level	
		Diabetic	Non-diabetic	Diabetic	Non-diabetic
< 20	Mean	256.00	91.62	8.66	7.08
	SD	101.35	13.27	1.03	1.59
	N	11	29	11	29
20-29	Mean	247.40	87.19	8.77	7.11
	SD	79.97	13.57	1.15	1.65
	N	20	58	20	58
30-39	Mean	290.56	92.36	9.19	7.06
	SD	45.29	16.15	0.96	1.33
	N	9	42	9	42
40-49	Mean	206.43	91.64	8.28	6.89
	SD	86.61	15.19	1.58	1.40
	N	21	14	21	14
≥ 50	Mean	207.64	104.33	8.33	7.02
	SD	78.17	20.1	0.85	1.40
	N	39	15	39	15
Total	Mean	228.12	91.4	8.52	7.03
	SD	84.1	15.63	1.14	1.50
	N	100	158	100	158

FBS values and HbAlc levels are given in mg/dl and % respectively. N stands for the number of patients or controls. P values for FBS and HbAlc are 0.005 and 0.05 respectively.

Table 4. The effect of duration of diabetes mellitus (DM) on the levels of FBS and HbAlc

Duration with DM	Fasting blood sugar	Hemoglobin Alc
<5 years Mean	238.14	8.37
SD	87.01	0.90
n	42	42
≥ years Mean	218.28	8.64
SD	84.10	1.33
n	58	58
Total Mean	227.06	8.52
SD	85.52	1.16
n	100	100

FBS and HbAlc levels are given in mg/dl and % respectively

DISCUSSIONS

It is an established fact that diabetes is a debilitating metabolic disorder characterized by high blood glucose level. Although insulin and other oral hypoglycemic drugs can control many aspects of diabetes, numerous complications are common incidents of the disease. Such complications arise due to uncontrolled hyperglycemic state that can lead to glycosylation of blood proteins. The measurement of glycated hemoglobin level in diabetic patients for the detection of glycaemic control is very much uncommon in Ethiopia. Such determination was done twice in the country by researchers i.e., once in Addis Ababa, the Capital, and another time in Gondar (northwestern part of the country) [13,14]. This is the first investigation on metabolic control of diabetics in Jimma area (southwest Ethiopia). In this study, latest kits that constitute standard separation solid supports were used and therefore additional separation techniques were not required. The solid adsorbent efficiently separates glycated hemoglobin from the non-glycated form and the measurement is more reliable than the earlier methods. The mean FBS levels for diabetics and control groups was 228mg/dl and 91mg/dl respectively and this shows that in deed, FBS is the best tool to diagnose .diabetes mellitus. The diagnostic cutoff value is 126mg/dl and therefore the patients have abnormally increased mean FBS level. The highest FBS level obtained in this study was 347mg/dl and the lowest 115mg/dl for the diabetics. The mean FBS level for the female diabetics was 246mg/dl and for the male 219mg/dl and the mean HbA1c level was 9.02% and 8.27% respectively. This shows that the female diabetics had a poorer diabetic control accompanied by an increased HbA1c level than the male. The mean HbA1c level for the diabetics in this study was 8.52% as compared to the control groups whose mean value was 7.8% ($P = 0.001$). There seems to be a direct relationship with increased FBS and hence increased HbA1c. Patients who have a very poor diabetic control will have a high blood sugar level and this in turn could result in an increased glycation of blood proteins including hemoglobin. When looking into the standard normal FBS and HbA1c levels obtained in this study, it can be concluded that the diabetic patients who have follow up in Jimma University Hospital do have a poor glycaemic control. The FBS and HbA1c levels differed on the age group of the patients and the patients in the age group 30-39 had the highest mean values, 290.6mg/dl and 9.2% respectively. Such increase in the level of blood glucose level, hence glycosylation of hemoglobin leads to tissue hypoxia due to decreased transport of oxygen to cells [15]. To see the effect of duration of stay with diabetes, the FBS and HbA1c levels were compared for patients who had known as having the disease less than five years ago and more than five years. The results obtained clearly showed that the values increased with the duration of stay with the disease but the difference was not statistically significant. This could be because the patient distribution in these categories was not proportional and some of the patients might have not been diagnosed as having the disease though they had it earlier. Two tailed correlation analysis was made to check whether or not there is a significant difference in HbA1c and FBS levels between diabetics and non diabetic controls and the results showed a significant difference at $p = 0.01$. The average FBS and HbA1c values for IDDM and NIDDM patients were calculated and the values obtained were 245mg/dl and 8.73% and 204mg/dl and 8.23% respectively. This shows that the IDDM patients have a relatively poor glycaemic control and as a result they also have increased HbA1c level. The reasons for the poor glycaemic control could be many but some of the possible causes could be that the patients did not get enough drugs as required or patients keep their drugs in a very poor manner with the result that the drugs get spoiled and/or may be they did not comply with the recommendations of their doctors. Lack of awareness of drug use, self-care, and proper drug storing most likely contribute to the poor glycaemic control of diabetic outpatients. Therefore, we recommend and suggest that patients must be educated well to make them comply with the advice and recommendations of their doctors and they must also be thought how to store the drugs they are given. For a proper glycaemic control check up, it is mandatory to routinely check FBS and glycated hemoglobin levels as a reliable diagnostic test. Measurement of HbA1c every two months gives a better picture of glycaemic control and the cost is very much affordable. Especially for patients who are very far from their physician, such a checkup is very necessary.

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