Original article

HbA1c as a marker to reduce lower limb amputation in patients with type 2 diabetes mellitus

Abdelmarouf Hassan Mohieldein[1], Abaker Mohamed Abdelkarim[2], Fatin Mohammed Osman[3], Elrasheed Ahmed Abdallah[4], Mahadi Mohammed Ali[5].

Abstract

Background:

Diabetes mellitus is one of the most serious and prevalent chronic diseases worldwide. One of the most common complications of diabetes in the lower extremity is the diabetic foot ulcer which is the precursor to ~85% of lower extremity amputations in persons with diabetes.

Materials and Subjects:

This is a case- control study which was carried out at Jabir Abu-Aliz Specialized Center, Khartoum State, Sudan between October 2006 and April 2007.

Forty type 2 diabetes cases with septic foot (group 1 cases), 40 type 2 diabetes cases without septic foot (group 2 cases), and 40 healthy controls participated in this study. Their demographic data were collected. Serum HbA_{1c} levels were estimated by affinity chromatography method.

Results:

The level of HbA_{1c} was 9.947±1.40%, 7.908±0.45% and 6.462±0.07%. in group 1, group 2, and the healthy control respectively. There was significant increase in percentage level of HbA_{1c} in group 1 cases compared to group 2 cases and healthy control (p = 0.002, 0.001 respectively). We found very low correlation between fasting blood sugar and HbA_{1c} in group 1 cases (r = + 0.331; p=0.042).

Conclusion:

This study indicates that the progression to the complication of foot ulcer in type 2 diabetic patients was correlated to the level of HbA_{1c}. These data may suggest a beneficial effect of considering measurement of HbA_{1c} as a routine test especially for elderly diabetic patients with diabetes for long period. This may help to maintain blood glucose levels in the normal or near normal range and to provide an opportunity for patients to live out their normal life expectancies with minimal complications.

Key words: glycohemoglobin, neuropathy, septic foot, glycemic control.

Diabetes mellitus (DM) is one of the most serious and prevalent chronic diseases worldwide[1].

1. Associate Professor of Biochemistry. Faculty of Applied Medical Science. Al-Qassim University. AlQassim. KSA.
2. A postgraduate student.
3. Medical Officer, Ministry of Health, Sudan.
4. Professor of Surgery. Faculty of Medicine. University of Khartoum.
5. Professor of Medicine. Faculty of Medicine. University of Khartoum.
Correspondence to Dr. Abdelmarouf Hassan Mohieldein, mobile:00966556876251; email: mabdelmarouf@hotmail.com

It has become one of the major health problems with diabetic foot ulcer as one of the most important complications[2].

It is estimated that 15% of patients with diabetes will develop a lower extremity ulcer during the course of their disease[3, 4]. The cumulative effects of neuropathy, deformity, high plantar pressure, poor glucose control, duration of diabetes, and gender are all contributory factors for foot ulceration[5, 6].

While 14–20% of patients with foot ulcers will subsequently require an amputation, foot ulceration is the precursor to approximately

85% of the lower extremity amputations in persons with diabetes[7, 8].

Glycosylated hemoglobin (HbA_{1c}) is the major glycohemoglobin species in human blood[9]. The percentage of HbA_{1c} in human blood depends on the concentration of glucose, the duration of glucose exposure to hemoglobin, and the turnover of erythrocytes[10].

Although not all diabetic foot disorders can be prevented, it is possible to effect dramatic reductions in their incidence and morbidity through appropriate evidence-based prevention and management protocols.

The objective of this study was exploiting HbA_{1c} as a predictive monitoring test of choice to reduce complications of diabetes mainly septic foot in type 2 diabetic patients. This was done by estimating the HbA_{lc} levels in type 2 diabetic patients with and without septic foot compared with healthy controls.

Material and Methods

Study design:

The study is a case- control study.

Study population and sample size:

The study was carried out on 40 type 2 diabetes cases with septic foot (group 1 cases), 40 type 2 diabetes cases without septic foot (group 2 cases), and 40 healthy controls. The ages for diabetic patients and healthy controls range between 50 to 70 years.

Diabetic patients of groups (1 & 2) were randomly selected from the outpatient diabetes clinic at Jabir Abu-Aliz Specialized Center, Khartoum State, Sudan between January 2007 and April 2007. Diabetes was defined according to the World Health Organization (WHO) criteria[11]. Informed consent was obtained for each participant.

Preparation of blood samples:

Blood samples (5ml) were collected from the anticubital veins. The collected blood was allowed to clot for 30 minutes, and then centrifuged at 2000 g for 15 minutes for clear separation of serum.

Estimation for glycated hemoglobin:

Serum HbA_{1c} levels were estimated by affinity chromatography method. After preparing the hemolysate, where the labile fraction is eliminated, hemoglobins are retained by a cationic exchange resin. HA_{1c} is specifically eluted after washing away the hemoglobin A_{1a+b} fraction1 (HbA_{1a+b}) [12].

Statistical analysis:

Statistical Package for Social Studies (SPSS) for Windows Version 10.0 was used to analyse the data. All values were expressed as mean ± S.D. Significant differences between means determined by using the student t-test, and *p* value of <0.05 was considered statistically significant. Pearson correlation was applied to correlate between the fasting blood sugar (mg/dl) and percentage level Hb_{A1c}.

Results

Age, gender, and duration of diabetes (mean±SD) of diabetic patients and healthy control are shown in table 1.

The level of mean HbA_{1c} for group 1, group 2, and healthy control are shown in table 2 and figure 1.

Table 1. Age, gender, and duration of diabetes (mean±S.D) of patients and healthy control

	Group 1	Group 2	Healthy control
Age	58.11±8.2	57.01±6.12	57.68±7.1
Gender			
Male	50% (n=20)	47.5% (n=19)	20% (n=20)
Female	20% (n=20)	52.5% (n=21)	20% (n=20)
Duration of diabetes (years)	8.42±4.7	5.22±2.3	----------

Table 2. The level of mean HbA_{1c} for group 1, group 2, and healthy control

	Group 1 cases	Group 2 cases	healthy control	*P*	
HbA1c levels	9.947±1.40	7.908±0.45	6.462±0.07	0.002[a]	0.001[b]

[a] group 1 cases vs. group 2 cases
[b] group 1 cases vs. healthy control

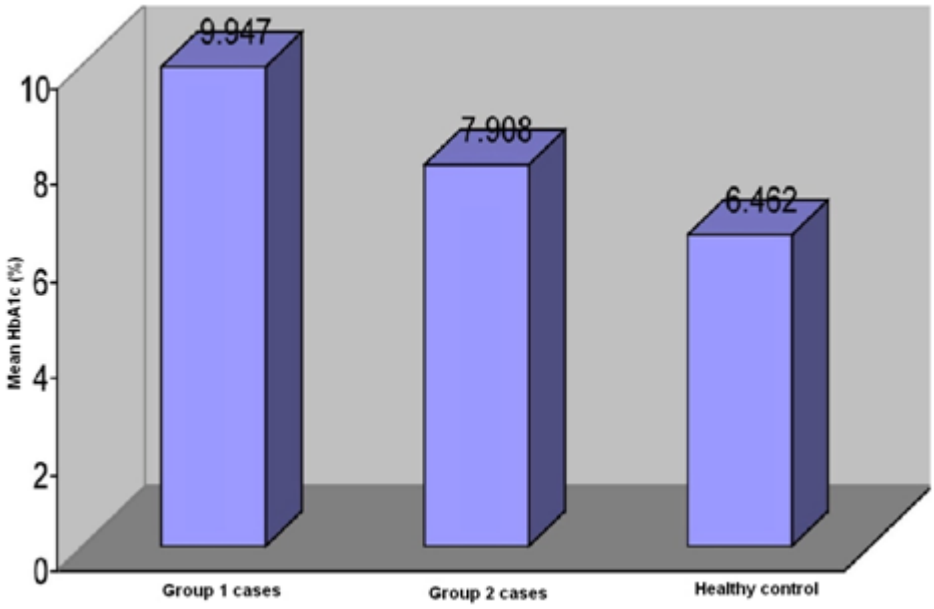

Fig 1. The level of mean HbA_{1c} for group 1, group 2, and healthy control

There was very low correlation between fasting blood sugar and HbA_{1c} ($r = + 0.331$; $p<0.05$) in type 2 diabetes cases associated with septic foot (figure 2).

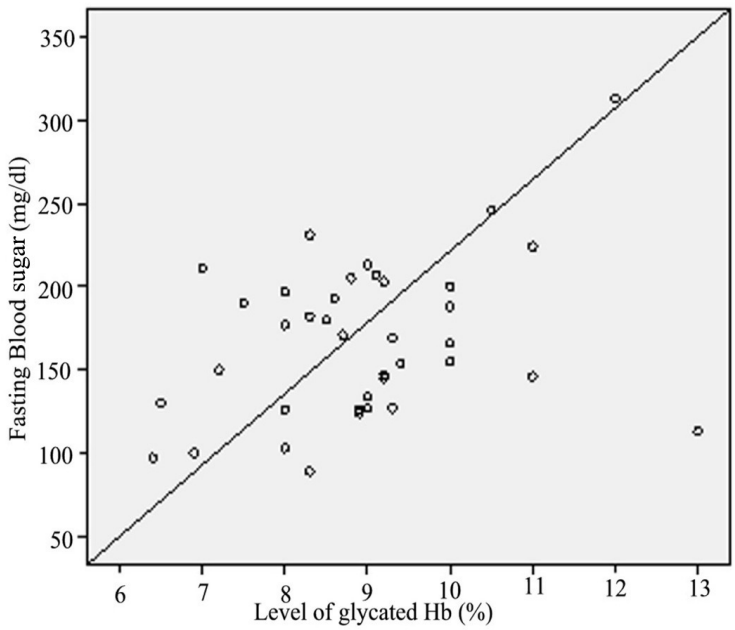

Fig 2. Correlation between level of HbA1c (%) and Fasting blood glucose (mgldl)

Discussion

Type 2 DM is an important health issue in the world. The number of people with type 2 diabetes, especially in developing countries, is expected to double in this and next decade and diabetes will be more prevalent in younger populations than in the past[13,14].

Foot disorders are a major source of morbidity and a leading cause of hospitalization for persons with diabetes mellitus. Costs of treating diabetic foot ulcers increase dramatically if patients require inpatient care and represent a substantial drain on health service resources. Furthermore, diabetic foot ulceration has a profound social impact with patients reporting stigma, social isolation, loss of social role, and unemployment. Quality of life is also reduced, and recent findings suggest that depression is more prevalent than in general diabetes[15].

At present, HbA_{lc} measurements are accepted as the ''golden standard'' for assessing long-term glycemic control. They provide an estimate of the average of blood glucose concentration during the last 2–3 months[16].

However, to our knowledge, there is no data concerning the relationship between HbA_{1c} levels and diabetic complications mainly foot ulcer. From the clinical point of view, it is therefore interesting to analyze the HbA_{1c} levels in relation to diabetes with foot ulcer.

Our study showed that the level of HbA_{1c} (%) in group 1 cases was 9.947±1.40%, while in group 2 cases was 7.908±0.45 compared to healthy control which was 6.462±0.07. There is significant increase in percentage level of HbA_{1c} in diabetic patients with septic foot compared to diabetic patients without septic foot and healthy control ($p = 0.002$, 0.001 respectively).

Fasting blood glucose is routinely tested in most patients who regularly attend the diabetic clinics. However, in the present study we found very low correlation between fasting blood sugar and HbA_{1c} ($r = + 0.331$; $p< 0.05$ "**p= 0.042**") in diabetic patients with septic foot. A single fasting blood glucose measurement only gives an indication of the patient's immediate past (last 1 to 2 hours) condition, and may not represent the true status of blood glucose regulation. In contrast, the level of HbA_{1c} is directly related to the average glucose concentration over the life-span of the hemoglobin in the circulation.

Since uncontrolled hyperglycemia is one of the most frequent risk factors for foot ulceration[17], we may conclude that the progression to the complication of foot ulcer in type 2 diabetic patients under poor glycemic control is correlated to the level of HbA_{lc}. These data suggest a beneficial effect in terms of considering measurement of HbA_{1c} as a routine test instead of fasting blood glucose especially for elderly diabetic patients with diabetes for long time. This may help to maintain blood glucose levels in the normal or near normal range and to provide an opportunity for patients to live out their normal life expectancies with minimal complications.

References:

1. American Diabetes Association. Report of the Expert Committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2000; 23(Suppl. 1):S4–S19.

2. Zimmet PZ. Diabetes epidemiology as a tool to trigger diabetes research and care. Diabetologia 1999; 42: 499 – 518.

3. Andersen CA, Roukis TS. The diabetic foot. Surg Clin North Am. 2007; 87(5):1149-77

4. Albert S. Cost-effective management of recalcitrant diabetic foot ulcers. Clin Podiatr Med Surg. 2002; 19(4):483-91

5. Boulton AJ. The diabetic foot: from art to science. The 18th Camillo Golgi lecture. Diabetologia. 2004; 47(8):1343-53.

6. Abbott, C.A., Vileikyte, L., Williamson, S., et al. Multicenter study of the incidence and predictive risk factors for diabetic neuropathic foot ulceration. Diabetes Care 1998; 21:1071–1075.

7. Gulcan E, Gulcan A, Erbilen E, et al. Statins may be useful in diabetic foot ulceration treatment and prevention. Med Hypotheses. 2007; 69(6):1313-5

8. Wrobel, J. S., Mayfield, J. A., Reiber, G. E. Geographic variation of lower-extremity major amputation in individuals with and without diabetes in the Medicare population. Diabetes Care, 2001; 24: 860−864.

9. Shibata K, Suzuki S, Sato J, et al. Diagnostic accuracy of glycohemoglobin A1c (HbA1c) for postprandial hyperglycemia was equivalent to that of

fasting blood glucose. J Clin Epidemiol. 2005;58(10):1052-7
10. Schwartz Joyce G. The role of glycohemoglobin and otherproteins in diabetic management. Diab Rev 1995; 3:269-287
11. Diabetes mellitus. Report of a WHO Study Group. Geneva, World Health Organization, 1985 (WHO Technical Report Series, No. 727).
12. Klenk DC, Hermanson GT, Krohn RI, et al. Determination of glycosylated hemoglobin by affinity chromatography: Comparison with colorimetric and ion exchange methods and effects of common interferences. Clin Chem 1982; 28: 2088-94
13. Basile, F. The increasing prevalence of diabetes and its economic burden. American Journal of Management Care 2000; 6S: 1077– 1081.
14. Kao, P. C., Wu, T. J., Ho, L. L., et al. Current trends and new approaches in the management of diabetes mellitus. Annals of Clinical and Laboratory Science 2000; 30: 339–345
15. Kirsty Winkley, Daniel Stahl, Trudie Chalder, et al. Risk factors associated with adverse outcomes in a population-based prospective cohort study of people with their first diabetic foot ulcer. Journal of Diabetes and Its Complications 2007; 21: 341–349
16. Matz, R. The target for good glycemic control should be an HbAlc concentration of less than 0.07. Western Journal of Medicine 2000; 173: 179– 180.
17. Reiber GE, Vileikyte L, Boyko EJ, et al. Causal pathways for incident lower-extremity ulcers in patients with diabetes from two settings. Diabetes Care 1999; 22:157-162