HbA1c in Patients with Diabetic Foot: A Prognostic Index.

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ABSTRACT:

BACKGROUND:

Diabetes mellitus (DM) is a common worldwide disease; which if poorly controlled, would be associated with high risk of complications, and diabetic foot is one of them.

Glycated hemoglobin A1c (HbA1c) is an important control index of DM, and nowadays it is used as a diagnostic test.

OBJECTIVE:

To assess the benefit of HbA1c as a prognostic index in patients presented with diabetic foot.

PATIENTS AND METHODS:

This study included 176 patients presented to Al-Hilla Teaching Hospital with diabetic foot during a period of 38 months from 1st March 2007 to 1st May 2010.

HbA1c was measured for all patients at time of enrollment which is mostly day of presentation. Level of 8 was considered a separation control point between good and bad control, and patients were classified into two groups; good control group (GCG) where HbA1c levels < 8, and bad control group (BCG) where levels ≥ 8.

The end points for the study were determined as death, amputation, surgical wound excision without amputation, improvement on medical treatment only. Death and amputation were considered bad prognosis group (BPG), while others were considered good prognosis group (GPG).

Statistical analysis was done using means, independent t-test and F-test.

RESULTS:

One hundred seventy six patients were studied with age range of 35-76 years, 60.15% (107/176) of them were males.

At the end of follow up; 47.7% (84/176) of patients were found in BPG and 52.3% (92/176) in GPG as the following: death (11 patients), amputation (73 patients), wound excision without amputation (52 patients) and medical treatment only (40 patients); while 64.2% (113/176) of patients were found in BCG (HbA1c ≥ 8) and 35.8% (63/176) in GCG (HbA1c < 8).

61.1% (69/113) of BCG patients had bad prognosis; whereas only 23.8% (15/63) of GCG patients had bad prognosis, a statistically significant difference (P-value 0.001);

Higher HbA1c levels were seen in patients with bad prognosis as mean HbA1c was 8.97 in BPG and 7.79 in GPG; a difference that is statistically significant (P-value < 0.001)

CONCLUSION:

HbA1c is a significant prognostic index in patients presented with diabetic foot. Levels greater than 8 were associated with poor prognosis and longer hospitalization. So; diabetic control is a very important factor in preventing and alleviating diabetic complications.

KEYWORDS: diabetes mellitus, hemoglobin a1c, diabetic foot.

INTRODUCTION:

Diabetes mellitus (DM) is a common disorder affecting both sexes at any age. Reportedly 23.6 million (8%) individuals in the United States are affected by diabetes[1]. Many of those with diabetes will develop related co-morbidities such as micro- and macro-vascular complications that involve many organs including lower extremities[2,3].

Controlled clinical trials have established that rigid glycemic control results in improved long-term outcomes and a decreased incidence of diabetic complications[4,5]. Further, many studies have demonstrated a strong correlation among mean levels of glycemia, measured as glycated hemoglobin A1c (HbA1c), and diabetic complications[1]. HbA1c provides an estimation of blood glucose levels over a three- to four-month period[6].

Collectively, this body of knowledge provides the foundation for the recommended treatment goals

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from the American Diabetes Association (ADA) of maintaining HbA1c at less than 7%[2].

HbA1c is the most widely used assay for evaluation of long-term glycemic control and is strongly correlated with adverse outcome risk even in non diabetic patients[7,8]. Elizabeth S. et al found that ideal HbA1c level is less than 4.6%. However, each 1% elevation raises the risk for heart attacks nearly 2.5 times; i.e. people with HbA1c above 4.6% are at increased risk for heart attacks even if they are not diabetic. The reason for this role isn't yet fully understood; however, some elevation in post-prandial sugar may be implicated which may be early sign of diabetes[9].

Moreover, the well established risks of diabetic microvascular and macrovascular complications are strongly associated with the HbA1c level in patients with both type 1 and type 2 diabetes[10,11].

Taking these considerations in mind; HbA1c was examined as a prognostic index in patients presented with diabetic foot.

METHODS:

This study included 176 patients with diabetic foot admitted to Al-Hilla Teaching Hospital or attended it's outpatient clinics (medical, orthopedic or general surgical departments) during a period of 38 months from 1st March 2007 to 1st May 2010.

For all patients; full medical history was taken, thorough clinical examination was done and fasting blood sugar and HbA1c levels were measured.

HbA1c was determined by affinity chromatography test using biosystem kit-USA. The affinity gel columns are used to separate glycated hemoglobin which binds to the column. Aminophenylboronic acid is immobilized from the non-glycated fraction by cross-linking to beaded agars or another matrix e.g. glass fiber, The boronic acid reacts with cis-diol groups of glucose bound to hemoglobin forming a reversible 5-member ring complex thus selectively holds the glycated hemoglobin on the column while the non-glycated hemoglobin doesn't bind. Then sorbitol is added to dissociate the complex and elute the glycated hemoglobin. The absorbance of bound and non-bound fractions measured at 415 nm is then used to calculate the percentage of glycated hemoglobin.

American Diabetes association (ADA) considered HbA1c levels less than 7 as target control levels[1]. In this study; level of 8 was considered a separation control point between good and bad control because the used kit specify level < 8 as good control (in it's enclosed leaflet).

So patients were classified into two groups; good control group (GCG) where HbA1c levels < 8, and bad control group (BCG) where levels ≥ 8.

The end points for the study were determined as:

1. Death: By any cause during follow up period (cerebral or cardiac ischemias, major organ failure, septicemia or others).
2. Amputation: Includes above or below knee, midtarsal or toes.
3. Surgical wound excision without amputation, followed by improvement on medical treatment and discharged better from hospital.
4. Improvement on medical treatment only and discharged in a better condition from hospital.

Death and amputation were considered as bad prognosis group (BPG), while others were considered as good prognosis group (GPG).

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61.1% (69/113) of BCG patients had bad prognosis; whereas only 23.8% (15/63) of GCG patients had bad prognosis, a statistically significant difference (P-value 0.001); i.e. the higher the HbA1c level, the worse the prognosis was seen (Table 1). Higher HbA1c levels were seen in patients with bad prognosis as mean HbA1c was 8.97 in BPG and 7.79 in GPG; a difference that is statistically significant (P-value < 0.001). (Table 2)

Table 1: Diabetic control and prognosis

Control group	No.	%	patients with bad prognosis		P-value
			No.	%	
BCG	113	64.2	69	61.1	0.001
GCG	63	35.8	15	23.8	

P-value: significant if less than 0.05.

Table 2: The association between prognosis and HbA1c

Prognosis group	No.	%	Mean HbA1c	P-value (group statistics)	P-value (Independent t-test)
BPG	84	47.7	8.97	< 0.001	< 0.001
GPG	92	52.3	7.79		

P-value: significant if less than 0.05.

In GPG; age range was 35-72 years and males represented 62.5%(110/176), while in BPG; age range was 38-76 years and males represented 57.4%(101/176). This difference was statistically non significant (Table 3).
In GCG; age range was 38-72 years and males represented 58.7% (37/63), while it was 35-76 years in BCG, and males represented 61.9% (70/113). This difference was statistically non significant (Table 3).
No significant difference was found in fasting blood sugar between variable groups (GPG vs. BPG and GCG vs. BCG) (Table 3).

Table 3: Association of age and sex with different prognosis and control groups.

The group	Average age (years)	Sex (male %)	Mean FBS (mg/dl)
GPG	35-72	62.5	210.6
BPG	38-76	57.4	216.4
P-value	---	NS	NS
GCG	38-72	58.7	208.2
BCG	35-76	61.9	218.8
P-value	---	NS	NS

FBS: fasting blood sugar, P-value: significant if less than 0.05, NS: non significant,

Longer hospital admission was seen in BCG as average duration of hospitalization was 18 days, while it was 9 days in GCG.
HbA1c level wasn't affected by type of DM as 25.6%(45/176) of our patients had insulin dependent diabetes mellitus (IDDM) with mean HbA1c level of 8.19; whereas 74.4%(131/176) of patients had NIDDM with mean HbA1c level of 8.24. This difference was statistically non significant.

Neither the type of DM nor it's duration affected the prognosis as:

1. 48.9%(22/45) of IDDM patients were in BPG, while; 46.6%(61/131) of NIDDM patients were in BPG. This difference was statistically non significant.
2. The average duration of DM since diagnosis was 17.75 years, and it was 26 years for IDDM patients and 15 years for NIDDM patients (Table 4).

Table 4: Relation of DM type with HbA1c and bad prognosis

Type of DM	No.	Mean HbA1c	Average Duration of disease (years)	BPG	
				No.	%
IDDM	45	8.41	26	22	48.9
NIDDM	131	8.35	15	61	46.6
P-value	---	NS	---	---	NS

P-value: significant if less than 0.05, NS: non-significant.

Higher percentage of well controlled patients can be treated without admission to hospitals as 27% (17/63) of GCG were treated as out-patients; while only 5.3% (6/113) of BCG were treated as out-patients and 94.7% (107/113) of them required hospital admission for treatment (Table 4).

Table 5: Mode of treatment according to diabetic control groups.

Control group	No.	Out-patient		In-patients		P-value
		No.	%	No.	%	
GCG	63	17	27	46	73	0.01
BCG	113	6	5.3	107	94.7	

Out-patients: Treated in diabetic clinics as out-patient, In-patient: admitted to hospital for treatment or intervention, P-value: significant if less than 0.05.

The duration from appearance of 1st diabetic foot sign to doctor visit were studied. It's mean was 5.3 days in GPG and 6.9 days in BPG which was statistically non significant as p-value was 0.32 (significant if less than 0.05).

DISCUSSION:

This study found a significant association between HbA1c level and poor prognostic outcome (amputation or death) in patients presented with diabetic foot. Levels of HbA1c more than 8 indicate poor diabetic control during last three to four months prior to presentation and were associated with bad outcome.

To the extent of my knowledge and net search; there is no similar study investigating relation of HbA1c level and outcome in diabetic foot patients. However, many studies emphasized role of HbA1c as diabetic control index and recently as diabetic diagnostic tool[2,4,6,12]. Cederberg et al suggested a predictor role of HbA1c level ≥ 6.5 for developing type 2 diabetes in normal adults after 10 years of follow up[13].

No relation was found between fasting blood sugar (FBS) and HbA1c or prognosis; so no role for presenting FBS as prognostic index.

In this study; the effect of other possible factors were excluded including age, sex and type and duration of diabetes mellitus.

No role for type of diabetes on HbA1c levels and no relation to outcome prognosis was seen.

In spite of a longer disease duration (since 1st diagnosis) in IDDM, there was no significant effect on prognosis.

Most patients in this study were in-patients (admitted to hospital) as outpatients were poor compliant with follow up visits.

The non significant role for duration of seeking medical advice in this study may be explained as most patients were anxious or afraid from diabetic foot even those with bad control history.

CONCLUSION AND RECOMMENDATIONS:

HbA1c is a significant prognostic index in patients presented with diabetic foot. Levels greater than 8 were associated with worse prognosis, complications, longer hospitalizations and more aggressive and costly therapeutic and surgical interventions. This make more burden on health care budget.

Diabetic control is a very important factor in preventing diabetic complications; which if occurred, good control may alleviate their damage.

REFERENCES:

1. American Diabetes Association (www.diabetes/org/diabetes-statistics.jsp).
2. Brownlee M, Hirsh IB. Glycemic variability: a haemoglobin A1c-independent risk factor for diabetic complications. JAMA 2006;295:1707-08.
3. Kalantar-Zade, Kopple JD, Regidor DL, et al. HbA1c and survival in maintenance hemodialysis patients. Diabetes Care 2007;30: 1049-55.
4. Uzu T, Hatta T, Deji N, et al. Target for glycemic control in type 2 diabetes patients on hemodialysis: effects of anemia and erythropoietin injection on HbA1c. Therapeutic Apheresis and Dialysis 2009; 13: 89094.
5. Inaba M, Okuno S, Kumeda Y, et al. Glycated albumin is a better glycemic indicator than glycated haemoglobin values in haemodialysis patients with diabetes: effect of anemia and erythropoietic injection. J Am Soc Nephrol 2007; 18: 896-903.
6. Schwartz KL, Monsur JC, Bartoces MG, et al. Correlation of same-visit HbA1c test with laboratory-based measurements: A MetroNet Study. BMC Family Practice 2005;13: 28.

7. van't Riet E, Rijkelijlhuizen JM, Alssema M, et al. HbA1c is an independent predictor of non fatal cardiovascular disease in a Caucasian population without diabetes. Eur J Cardiovasc Prev Rehabil 2010 ;28. [Epub ahead of print]

8. Thanopoulou A, Karamanos B, Archimandritis A. Glycated haemoglobin, diabetes, and cardiovascular risk in non diabetic adults. N Engl J Med 2010 ;362: 2030-1.

9. Elizabeth S, Josef C, Sherita H, et al. Glycemic control and coronary heart disease risk in persons with or without diabetes. Arch Intern Med. 2005;165:1910-16.

10. Selvin E, Marinopoulos S, Berkenblit G, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med 2004 Sep 21;141: 421-31.

11. Stettler C, Allemann S, Juni P, et al. Glycemic control and macrovascular disease in type 1 and 2 diabetes mellitus. Am Heart J 2006;152: 27-38.

12. Mitka M. HbA1c poised to become preferred test for diagnosing diabetes. JAMA 2009;310: 1528.

13. Cederberg H, Saukhonen T, Laakso M, et al. Post-challenge glucose, HbA1c, and fasting glucose as predictors of type 2diabetes and cardiovascular disease. Diabetes Care 2010 Jul 8. [Epub ahead of print].