

Relationship between HbA1C and Wound Healing in Diabetic Patients

Maitrey Joshi¹, Firdaus Dekhaiya², Samir M. Shah³, Dharmapal Bagate⁴

¹Senior Resident ²Associate Professor ³Professor & Head ⁴Senior Resident, Dept. of General Surgery, Sir T. Hospital & Govt. Medical College, Bhavnagar, Gujarat 364001, India.

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Abstract

Introduction: Diabetes Mellitus is a heterogeneous primary disorder of carbohydrate metabolism with multiple etiologic factors that generally involve absolute or relative insulin deficiency or insulin resistance or both leading to hyperglycemia and various long term complications. The glycated hemoglobin (HbA1C) level, defined as the ratio between HbA1C concentration and total Hb concentration, is considered to be a very useful diagnostic marker for diabetic patient in addition to the measurement of the glucose level and has important relation with the healing process. **Objective:** To find association between HbA1c and diabetic wounds healing rate & decrease Hospital stay in diabetic patients with wounds. **Methods:** Participants were selected from the patients of Sir. T hospital and single baseline measurement of HbA1c using clinically relevant cut-points of <7.0%, 7.0–8.0%, and ≥ 8.0% We determined the location and area of wounds in diabetic patients both at baseline and a second visit a median of 1 month later. **Results:** Among 50 cases studied, percentage of male patients was higher than that of female patients in each age group. In this study Maximum no. of patients (90%) have healing of ulcers, having a range of HbA1c between 7-10%. **Conclusion:** Lower extremity ulcers are frequent occurrence in individuals with diabetes significantly affecting quality of life. HbA1c levels have effects not only on chances of healing but also the rate at which the ulcer heals.

Keywords: HBA1C; Ulcer.

Corresponding Author: Maitrey Joshi, Senior Resident, Dept. of General Surgery, Sir T. Hospital & Govt. Medical College, Bhavnagar, Gujarat 364001, India.

E-mail: dr.maitreyjoshi@gmail.com

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Introduction

Diabetes Mellitus is a heterogeneous primary disorder of carbohydrate metabolism with multiple etiologic factors that generally involve absolute or relative insulin deficiency or insulin resistance or both leading to hyperglycemia and various long term complications [1].

The term diabetic foot mean a group of syndromes & foot lesion in which neuropathy, ischemia and infection lead to tissue break down resulting in morbidity and possible amputation [2]. Both neuropathy and vasculopathy are strong independent risk factors for development of diabetic foot ulcers. About 2.5% diabetic men and women will develop foot ulcer each year [3]. Between 5 to 15% of diabetic foot ulcers will ultimately require amputation [4]. These major amputations will be avoided in 80% such cases.

Also many of the employees will not be able to return to full time employment and they will have to live with impediment that required drastic lifestyle adjustment for the rest of their lives.

Aims and Objective

1. To find association between HbA1c and diabetic wounds healing rate.
2. To differentiate types of lesions in diabetic wounds.
3. To evaluate the result of investigation carried out for patient with diabetic foot.
4. To evaluate the result of surgical treatment of diabetic foot.
5. To accentuate the scope of treatment therapy for non-healing wounds.
6. To reduce overall morbidity of the patient.

Material and Methodology

Fifty cases of Diabetic patients with foot ulcer were admitted, examined and investigated particularly to see the relationship of HbA1C (Glycated Haemoglobin) to Healing rate of that ulcer wound. For that, Over the period of 2 years between 2014-15 and 2015-16, those cases admitted at Sir T. Hospital, Bhavnagar, were followed and detail history according to proforma like age, sex, status of smoking, significant complaint, other co-morbidities like Hypertension, Chest disease, IHD, liver disease were obtained. And those all patients undergone basal investigation like complete hemogram, LFT, RFT, Chest and Local part X-ray to rule out confounding factors and to reduce bias.

Then HbA1C value of all patients obtained at initiation and followed to monitor the patient. For that complete horizontal and vertical dimensions of wound measured at admission and healing status of wound was noticed. Subsequently on Next visit of one and two month interval all ulcers are reexamined following the same medical treatment (Antibiotics, Glycemic Control) and Conventional Dressing and minor surgical procedures. After that results were obtained and analyzed.

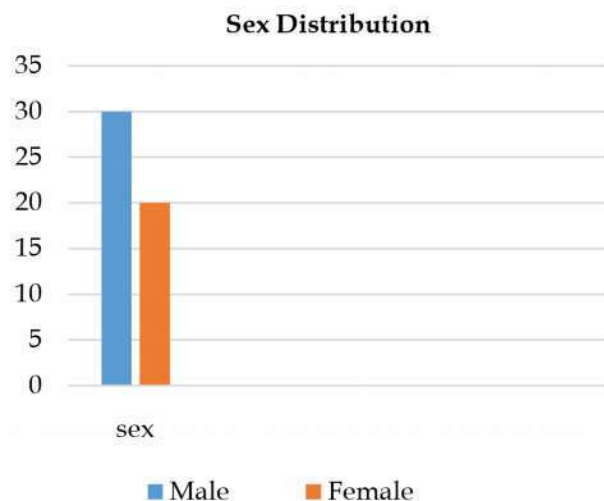
Observations & Results

Sex Distribution

It shows male predominance in diabetic wounds. Male to female ratio 3:2 (Table 1 and Graph 1).

Table 1:

Sex	Cases	%
Male	30	60
Female	20	40



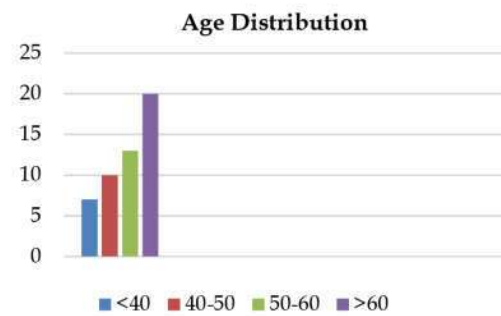
Graph 1:

Age Distribution

Table shows cases are more prevalent in the age group of >60 years followed by age group of 50-60 years (Table 2 and Graph 2).

Table 2:

Age group	cases	%
<40	07	14
40-50	10	20
50-60	13	26
>60	20	40



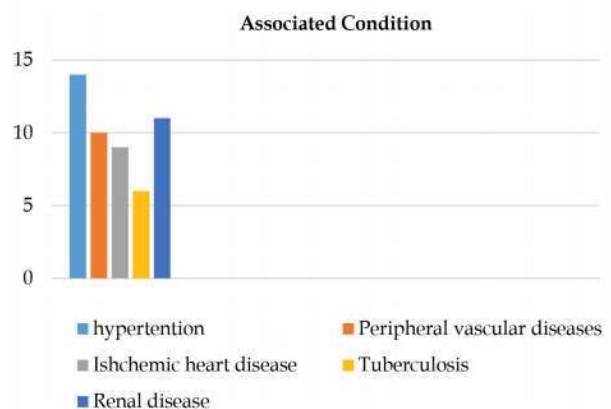
Graph 2:

Associated Condition

As evident from table hypertension also most common associated disease either present alone or in association with other cardiovascular pathology. Hypertension play a major role in the development of peripheral vascular disease. Tuberculosis has no specific response on diabetic wound but it reduces the resistance to infection (Table 3 and Graph 3).

Table 3: Associated Condition

Associated condition	cases	%
Hypertension	14	28
Peripheral vascular diseases	10	20
Ishchemic heart disease	09	18
Tuberculosis	06	12
Renal disease	11	22



Graph 3:

Smoking

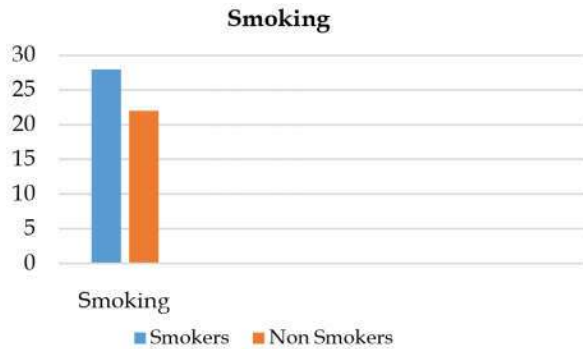
In Study 28 patients (56%) were found smokers while 22 patients(44%) were found non smokers (Table 4 and Graph 4).

Precipitating Factors

20% patients had history of trauma while two patients presented with a history of thorn injury. However, maximum number of patients (66%) presented with history of unknown injury (Table 5 and Graph 5).

Table 4:

Smoking	No. of cases	%
Smoker	28	56
Nonsmoker	22	44



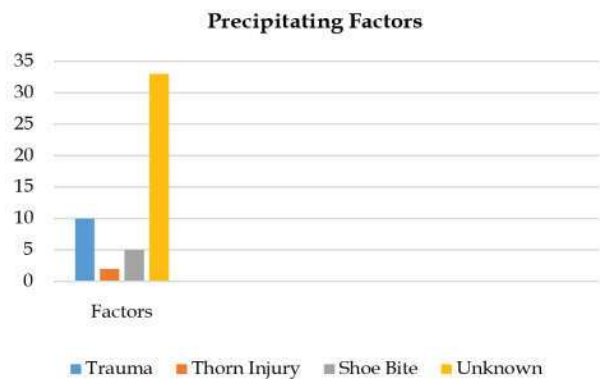
Graph 4:

Healing Time in Relation to HbA1C Value

The healing time of Maximum number of case (10) in HbA1C value between 4-7 gm % is below 30 days. And patients having HbA1C value of 4-7gm % have also healing period of 30 days. Whereas HbA1C value >10gm% have longer healing period (>30 days) (Table 6 and Graph 6).

Table 5:

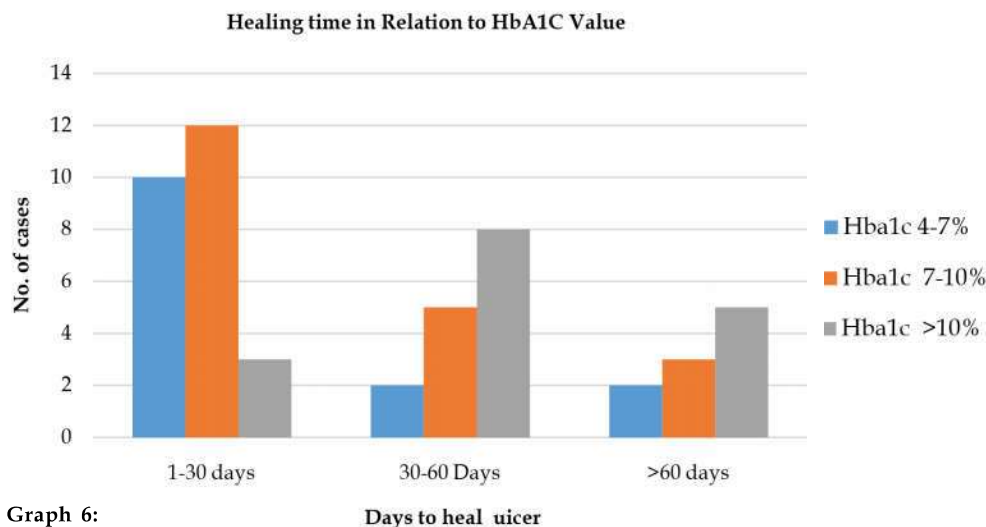
Precipitating Factors	No. of Cases	Percentage
Trauma	10	20%
Thorn Injury	2	4%
Shoe Bite	5	10%
Unknown (Spontaneous)	33	66%



Graph 5:

Table 6:

No. of Days of healing	Value of HbA1C (gm%)	No. of Cases	Percentage
1-30 days	4-7	10	20
	7-10	12	24
	>10	3	6
30-60 days	4-7	2	4
	7-10	5	10
	>10	8	16
>60 days	4-7	2	4
	7-10	3	6
	>10	5	10



Graph 6:

Discussion

Age Incidence

Maximum no. cases (48%) presented in fifth and sixth decade of life. This was contrary to study by John Malil⁵ where majority of the cases presented in seventh decades of life. The result however correlate with the findings of Samal et al. [6] in whose study, majority of patient belong to 41 to 70 year age group.

The average age of presentation in this series was 41-60 years of age similar to that observed by Ramchandran et al. [7] and Jbour A.S. et al. [8]. In whose series the average age was 45-65 and 46-66 years respectively. One probable cause of such discrepancy in the result could be earliar occurrence of peak incidence of diabetes and probably lesser no. of admissions for geriatric patients in small parts of country.

Sex Incidence

Comparison of sex incidence of diabetic foot between present study and other studies reveals that like most of studies, females were conspicuously less than male with a male: female ratio of 3:2. Increased exposure of male to precipitating factors, irrespective of the socio-economic class and profession and thus making them more prone to trauma and callosities.

Co Existing Condition & Other Factors

Almost most of the patient have hypertension while ADA states that 75% of patient have hypertension or taking medication for that. Almost 70% of patients have peripheral vascular diseases and more than 40% have renal diseases. Peripheral vascular diseases is more common in diabetic than non-diabetic. In addition ADA suggests that 20% to 40% of patients have nephropathy. The presence of renal diseases, peripheral vascular diseases and hypertension all are suggestive of micro-vascular complication.

In this sample of diabetic individuals seen at the study, only elevated HbA1c was significantly independently associated with wound-area healing rate. This relationship was stronger for the wounds located on the foot, which were insensate neuropathic wounds (approximately 60% of all wounds). Our results suggest that HbA1c is an important clinical predictor of wound healing rate, particularly in those with diabetic wound.

To our knowledge, a strong association between HbA1c and wound healing over time in a large clinic population of diabetic individuals is previously unreported. Previous studies have found either no association [8,10] or have reported a trend, but have had small sample size and did not statistically analyze data [11].

Previous studies have used need for amputation [9] or total time to complete healing [11,12] as the outcome of interest. The innovative use of a quantitative endpoint (healed area per day) might contribute to our success in demonstrating the correlation between HbA1c and wound healing. Although our endpoint differs from endpoints used in previous studies, all are assessing the same underlying wound healing process. The formation of advanced glycation end products have also been associated with impaired wound healing in diabetic mice [16,17].

We did not find an association between any other demographic, clinical, and laboratory variables and wound-area-healing rate per day. Reports in the literature about an association between sex and wound healing have been mixed. Marston et al. report female patients as being more likely to heal [14], but Margolis et al. [12], Golinko et al. [13], Ince et al. [17] and Oyibo et al. [16-28] did not find an association. Margolis et al. [12] report that foot ulcers are more likely to heal in nonwhite individuals (odds ration: 0.64, 95% CI: 0.43, 0.96) [12]. The literature on age is also mixed, Apelqvist and Agardh [11] reported a higher risk of amputation with increasing age, but Ince et al. [17], Golinko et al. [13] and Margolis et al. [12] reported no association with age.

Our results are similar to Golinko et al. [13] who reported no association with cholesterol or white blood cell count between foot amputee patients and non-amputee patients. Although the associations between demographic, clinical, laboratory variables and healing in the literature are not consistent, our study is largely in agreement with existing reports where the majority of clinical data are not associated with wound healing.

Previous reports associated faster wound healing with smaller wound size [12,19,20]. While our study showed a similar trend, HbA1c better predicted healing rates than baseline wound size.

Several previous studies have not fully adjusted for HbA1c [19] or did not include HbA1c in their model [20,21] when exploring the association between healing rates and wound size.

Consistent with a recent consensus statement which states that wound healing outcomes should be the rate of total wound closure, we used daily wound healing rate as our outcome [22].

In summary, of the clinical, laboratory and demographic variables commonly measured in diabetic patients in wound clinics, only elevated HbA1c was significantly associated with poor wound-area healing rate per day.

Our study suggests that hyperglycemia, as assessed by HbA1c is associated with slower wound healing in patients with diabetes. Future prospective studies should assess the effect of tight glycemic control to decrease-HbA1c levels in wound healing.

Conclusion

Lower extremity ulcers are frequent occurrence in individuals with diabetes significantly affecting quality of life. HbA1c levels have effects not only on chances of healing but also the rate at which the ulcer heals.

Despite being the smallest size at baseline, wounds at the highest level of HbA1c healed at the slowest. Conversely, the ulcers with larger baseline size in the lowest and intermediate HbA1c categories both had greater healing rates than the ulcers with smaller baseline size in the highest HbA1c category. Although, there trends to be an inverse association between baseline wound size and healing rate, statistical significance was not reached after adjusting for HbA1c and other variables in our model ($p > 0.2$).

HbA1c was inversely related to healing rate. For each 1.0% point increase in HbA1c, the wound-area healing rate per day decreased by 0.028 cm² (95% CI: 0.003, 0.054, $p = 0.027$).

Age, sex, race/ethnicity, smoking, body mass index, wound number, cholesterol, triglycerides, systolic blood pressure, pulse, temperature, white blood cell count and peripheral artery disease, neuropathy showed no association. Therefore, the only characteristic significantly associated with wound-area-healing rate per day was HbA1c.

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