

Original Research Article

Prospective study to correlate the level of glycosylated haemoglobin with wound healing, vasculopathy and neuropathy in diabetic foot patients

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Received: 11 July 2016

Accepted: 10 August 2016

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ABSTRACT

Background: Diabetes mellitus is a prevalent global health problem and diabetic foot represents one of its dreadful complications. Early aggressive approach and multidisciplinary intervention prevent limb loss and disease fatality. Glycosylated haemoglobin (HbA1c) reflects long term glycaemic control and helps in prediction of complications as well as response to treatment.

Methods: A total of 50 patients with diabetic foot ulcer (Wegner grade 1, 2) made nucleus of this study. Every patient underwent proper clinical, hematological and sonological assessment. Optimum treatment was provided and the effect of improvement in HbA1c value was correlated with duration of wound healing, vasculopathy and neuropathy over a 12 week follow up.

Results: Mean age of presentation was 53.4 years and patients developed diabetic ulcers (Wegner grade 1, 2) at a mean HbA1c value of 6.6. Foot trauma was inciting event in 70% cases. 70% patients had neuropathy and 30% had vasculopathy at presentation. Mean duration of healing was 42.6 days. Healing was faster in the group with lower HbA1c; however there was no improvement in neuropathy or, vasculopathy in 12 weeks duration.

Conclusions: Based on the observations of present study it may be submitted that lower HbA1c value contributes to faster wound healing, however it doesn't improve neuropathy and/or vasculopathy over duration of 12 weeks.

Keywords: Diabetic foot, Foot ulcers, Glycosylated haemoglobin, Neuropathy, Vasculopathy, Wound healing, Wegner grade

INTRODUCTION

Diabetes mellitus is one of the commonest global non-communicable health-care problem, carrying a predicted pandemic score of 366 million population by 2030.¹ According to the ICMR-INDIAB study, there are 62.4 million people living with diabetes in India alone, making it "diabetic capital" of the world.² About 15% of all such patients develop a foot ulcer in their lifetime.³ Neuropathy and ischemia, two common complications of

diabetes, have been implicated as the primary underlying risk-factors in the development of foot-ulcers while hyperglycemia contributes to delayed and impaired wound healing.⁴

Treatment of diabetic foot syndrome involves multidisciplinary approach in achieving euglycemia and needs serial debridement/ disarticulation/ amputation as per the grade of ulcer/ foot gangrene, else it could be life-threatening to the patient.

Glycosylated haemoglobin (HbA1c) is a measure of 'beta-N-1-deoxy fructosyl component' of haemoglobin, which is formed by non-enzymatic glycation pathway, due to hemoglobin's exposure to plasma glucose, depicting the average blood glucose level over previous 2-3 months span.⁵ American Diabetic Association has included HbA1c in the diagnosis of diabetes mellitus, with a cut-off value of 6.5.⁶ Although it is clear from literature review that strict glycaemic control prevents complications, the relationship amongst HbA1c value, wound healing, vasculopathy and neuropathy in diabetic foot patients is less well defined.

The objective of this study was to co-relate the influence of level of glycosylated haemoglobin on wound healing, vasculopathy and neuropathy in diabetic foot patients.

METHODS

The proposed study was conducted in the department of surgery, Vardhman Mahavir medical college and Safdarjung hospital, New Delhi, in collaboration with the department of biochemistry, department of radio diagnosis and department of microbiology over a period of 18 months.

Patients presenting to surgical emergency, surgical outpatient department and diabetic foot clinic with lower limb ulcers were selected on the basis of clinical history, physical examination, blood investigation and duplex ultrasound. Proper treatment was provided and they were re-assessed at 12 weeks.

Inclusion criterion

- Diabetic foot ulcers grade 1 & 2 (Wagner Classification).

Exclusion criteria

- Pregnant ladies
- Age >80 years
- Patients with S. creatinine > 2 mg/dl
- Diabetic foot ulcers grade 3, 4 and 5 (Wagner classification).

Study protocol submitted for approval to local ethical committee. All patients were informed about the intervention and written informed consent taken.

Data was collected at presentation and at 12 weeks of holistic treatment using proper history, thorough examination of patient, limb and ulcer, HbA1c assessment as well as duplex arterial sonography of lower limb.

Patient work-up (At presentation and at 12 weeks following treatment)

History

Duration and family history of diabetes, compliance to treatment, history of numbness, decreased sweating, corns/callosities and ulcer/abscess of lower limb.

Clinical examination

Clinical nutritional assessment, palpation of all peripheral pulses, signs of chronic limb ischemia, ulcer evaluation and neurological examination using pinprick sensation, touch sensation by Semmes Weinstein filament, vibration sensation by 128 Hz tuning fork and ankle reflex.

Haematological investigations

Haemogram, fasting and post-prandial blood sugar level, renal function test and HbA1c assessment.

Radiological investigations

Vasculopathy assessment by ankle brachial pressure index (ABPI) using hand held Doppler and duplex arterial sonography of both lower limbs.

Treatment approach

Under strict glycemic control, patients were followed up at regular intervals and ulcers were debrided surgically. Appropriate antibiotic(s) was advised as per the tissue culture-sensitivity report, and moist dressings applied. At 12th week of treatment, patients were re-assessed by history (for improvement in symptoms), clinical examination (for ulcer healing, peripheral pulsations, features of limb ischemia and neurological deficits), biochemically (HbA1c value) and sonologically (ABPI as well as Duplex arterial flow pattern).

Statistical analysis

Data was fed into Microsoft excel format in computer and was analyzed using SPSS statistical software, version 16. Categorical variables were presented as numbers and continuous data was presented as Mean (+/- standard deviation) or, median (min-max) as appropriate. The comparison between qualitative data was determined by applying chi-square or Fischer exact test. Continuous data was compared by student T-test/ Man Whitney U-test wherever required. P-value less than 0.05 were considered significant.

RESULTS

Total 54 patients, complying with inclusion criteria, were enrolled in the study and received optimal treatment from department of surgery at Safdarjung hospital, New Delhi, India. All had unilateral limb involvement. 4 patients lost to follow-up. They were assessed at the time of first presentation and at 12th week of treatment. The mean age of presentation was 53.4 years with a male (70%) preponderance. 60% had short history of diabetes (less than 5 years) and there was preceding history of foot

trauma in most (70%) cases. 84% had Wagner’s grade 1 diabetic ulcer and 16% had grade 2 ulcers. Neuropathy (predominantly sensory) was noted in 70% patients, while 30% had vasculopathy (Figure 1, 2). Mean glycosylated haemoglobin level of study population was 6.6 and 25 patients had value higher than 6.5 (mean 7.23).

Following 12 weeks of holistic treatment, though the glycemic status of population improved (mean HbA1c 6.4), yet 25 patients retained their value higher than 6.5 (Table 1).

Table 1: Age, sex, grade of foot ulcer, pre and post treatment HbA1c values.

Total number of patients		Mean Age (years)±std. dev.	Number of patients and grade of foot ulcer at presentation		Mean glycosylated haemoglobin +/- std. dev.		Number of patients at presentation with HbA _{1c} value		Number of patients at 12 weeks with HbA _{1c} value		Mean HbA _{1c} (±std. dev.) of patient group with value more than 6.5	
			Wegner Grade 1	Wegner Grade 2	At 0 week	At 12 week	Less than or equal to 6.5	More than 6.5	Less than or equal to 6.5	More than 6.5	At 0 week	At 12 weeks
Male	Female	53.4±11.9 years										
35	15		42	08	06.6±0.7	06.4±0.7	25	25	25	25	07.2±0.5	07.1±0.5
N = 50			N = 50		P-value = 0.16		N = 50		N = 50		P-value = 0.48	

Table 2: Mean duration of wound healing and its correlation with HbA1c value.

Mean duration (days) of wound healing +/- std. dev.	Mean duration (days) of wound healing in two groups ±std. dev.	
	Mean duration (days) of wound healing in patient group with HbA _{1c} up to 6.5	Mean duration (days) of wound healing in patient group with HbA _{1c} more than 6.5
42.6±17	39±13.1	46.5±20
P-value	0.13	

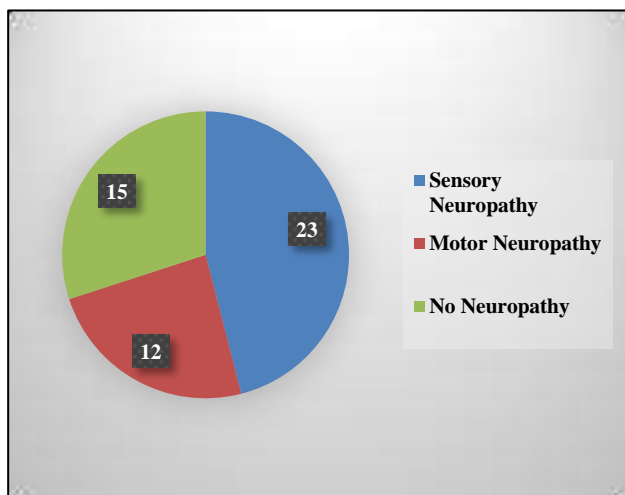


Figure 1: Number of patients with neuropathy.

Mean duration of wound healing was 42.6 days (Wagner grade 0). Healing was earlier in patients whose HbA1c was less than or equal to 6.5 (39 days versus 46.5 days). In two patients foot ulcer worsened to higher grade and needed amputation. Both these patients had pre-treatment

mean glycosylated haemoglobin value 8.65, which remained 8.5 at 12 weeks of treatment. However no subjective or, objective change was noted in vasculopathy and neuropathy in follow-up (Table 2).

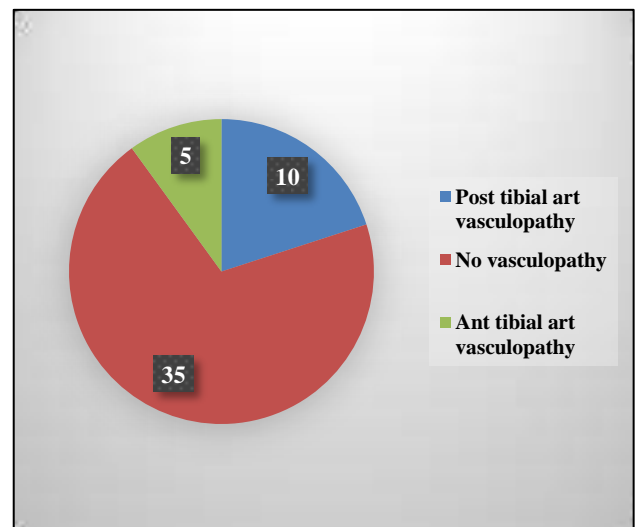


Figure 2: Number of patients with vasculopathy.

DISCUSSION

Diabetes has become one of the largest global healthcare problems of the century and the burden of disease is predicted to double between 2000 and 2030.¹ Diabetic foot syndrome is a complex and heterogeneous disorder which affects 1 out of 7 patients with diabetes at least once in their lifetime with relevant consequences both on lower limb and general morbidity.³ Presently there is no absolute way to prevent the development of this disastrous disease, however a good glycemic control has been proven to retard the progression of complications like neuropathy, angiopathy, foot infections etc.

HbA1c reflects glycemic control over past 2-3 months and its role in management of diabetes is well established.⁶ In ADVANCE trial, a target 6.5 HbA1c value was found to drastically reduce the macro and microvascular complications.⁷

Prevalence of diabetic foot complications increases with age and duration of disease. In contrast to the West, where mean age of presentation is 61 years, here the presenting population is younger, which is in accordance with the demographic data obtained during a study conducted in North India over 678 diabetic patients in which mean age with foot ulcer was 55.3 years with male preponderance (71.1%).^{8,9} Usually patients with 8 or more HbA1c have foot ulcers, however they were present at a mean value of 6.6 in our study.^{8,10} In present study, the average duration of diabetes mellitus was 4.5 years, which was of relatively shorter duration. Shailesh et al in their study over prevalence of diabetic foot ulcer and associated risk factors in North India, found mean duration of diabetes to develop foot ulcers 11.5 years.⁹ 70% of our patients had preceding history of foot trauma. *Staphylococcus aureus* was the commonest microbe (in 50% patients) isolated from tissue culture specimen. Neuropathy was noticed in 70% cases. Estimate of diabetic peripheral neuropathy varies from 9.6-78% in different populations.¹³ Our 30% patients had features of vasculopathy. Similar prevalence of vasculopathy has been reported in other studies over diabetic foot ulcers.^{9,14} There was early healing (mean duration 39 days) in the sub-group, where glycosylated haemoglobin was up to 6.5 during treatment. Christman et al in their study at John Hopkins Wound Center, USA found similar inverse association between it and rate of healing. For each 1.0 unit increase in HbA1c, the wound area healing rate per day decreased by 0.028 cm².⁸ Though association between high HbA1c and peripheral vasculopathy as well as neuropathy is well established since long, but there was no improvement in vasculopathy or, neuropathy with improvement in HbA1c over 12 week span.^{11,12}

CONCLUSION

In this study, we noticed that presentation of diabetic foot patients in India is different from western counter-part. Here patients are developing complications like

neuropathy, vasculopathy and foot-ulcers at an early age, despite shorter duration of this disease well as at relatively lower HbA1c value. So, shorter duration of diabetes, even mild, is harmful. It is advisable to screen the population for diabetes at an early age. With early detection and prompt intervention, limb loss and other morbidities could be minimized. Patients, as well as family members, should be educated about importance of strict glycemic control, foot care and early reporting of changes to health care professionals.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Bhawna for her assistance in analyzing the statistics of this study.

Funding: Funded by Hospital

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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Cite this article as: Kumar B, Mishra MK, Sinha A, Soni RK, Patel DK. Prospective study to correlate the level of glycosylated haemoglobin with wound healing, vasculopathy and neuropathy in diabetic foot patients. *Int Surg J* 2016;3:2087-91.