A PROSPECTIVE STUDY ON THE IMPACT OF HbA1c (GLYCOSYLATED HAEMOGLOBIN) ON DIABETIC FOOT MORBIDITY AND IT'S CORRELATION WITH CLINICAL VARIABLES

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***Abstract*- This prospective study investigates the potential impact of glycated hemoglobin (HbA1c) levels on diabetic foot morbidity and explores its potential correlation with a range of clinical factors. Diabetic foot complications present a significant healthcare challenge, and HbA1c serves as a well-established marker for long-term glycemic control. Gaining insights into the potential relationship between HbA1c levels and foot morbidity holds the promise of enhancing patient care and management. The study employs [describe the study design, sample size, and Inclusion criteria], with a focus on categorizing participants' HbA1c levels. Concurrently, clinical variables including neuropathy, vascular status, and foot deformities are evaluated.**

***Index Terms*- HBA1C (Glycosylated Hemoglobin).**

I. INTRODUCTION

GLYCOSYLATED HEMOGLOBIN & DIABETIC FOOT: The healing process of diabetic foot ulcers can be significantly impacted by the levels of HbA1c, also known as glycosylated hemoglobin. Prolonged exposure to high blood sugar levels can lead to damage to blood vessels and nerves, resulting in reduced blood flow to the feet and compromised immune function. These factors collectively contribute to delayed healing of foot ulcers. To promote effective healing, it is essential for individuals with diabetic foot ulcers to achieve and maintain optimal blood sugar control, as indicated by HbA1c levels that closely align with the target range set by their healthcare provider. Additionally, proper wound care techniques, diligent infection control measures, and appropriate offloading of weight from the affected foot are crucial in supporting the healing process. In summary, the levels of HbA1c play a significant role in influencing the healing potential of diabetic foot ulcers. It is imperative for individuals with diabetes to prioritize good blood sugar control and adhere to appropriate wound care practices in order to facilitate effective healing of foot ulcers and prevent further complications. For an HbA1c test to classify as normal, or in the non-diabetic range, the value must be below 5.7 %. Anyone with an HbA1c value of 5.7 % to 6.4 % is considered to be prediabetic, while diabetes can be diagnosed with a HbA1c of 6.5% or higher. [1]

ETIO-PATHOGENESIS OF DIABETIC FOOT ULCERS:

Recent studies have identified several risk factors associated with the development of diabetic foot ulcers.

These risk factors include: male gender, a diabetes duration of more than 10 years, advanced age, high Body Mass Index (BMI), and coexisting conditions such as retinopathy, diabetic peripheral neuropathy, peripheral vascular disease, and elevated levels of glycosylated hemoglobin (HbA1c). Other contributing factors include foot deformities, high plantar pressure, infections, and inadequate foot self-care practices. Most diabetic foot ulcers can be attributed to Ischemic, neuropathic, or a combination of both neuro-ischemic abnormalities. [2]

ASSOCIATION WITH CLINICAL VARIABLES:

Diabetic individuals face significant threats to their well-being due to the potential development of various complications in the feet, such as neuropathy, peripheral arterial disease (PAD), foot ulcers, and infections. Among the multitude of factors that contribute to the progression of these complications, heightened levels of glycated hemoglobin (HbA1c) have emerged as a vital clinical indicator of sustained glycemic control over time. HbA1c provides valuable insights into the long-term management of diabetes and its potential repercussions on the health of diabetic feet . To comprehensively address the intricate interplay underlying diabetic foot complications, it is imperative to grasp the relationship between HbA1c levels and other clinical parameters.

- **Neuropathy:** Diabetic neuropathy, or nerve damage, can lead to loss of sensation in the feet and increase the risk of injury and infection.
- **Peripheral Vascular Disease:** Poor blood flow to the feet can slow the healing of cuts and sores, increasing the risk of infections and foot ulcers.
- **Foot deformities:** People with diabetes are at higher risk of developing foot deformities, such as hammertoes and Charcot foot, which can put pressure on certain areas of the foot and increase the risk of ulcers and infection.
- **Poor glycemic control:** High blood sugar levels can damage blood vessels and nerves, increase inflammation, and impair the immune system, all of which can contribute to the development of diabetic foot complications.
- **Smoking:** Smoking has been shown to increase the risk of diabetic foot complications by decreasing blood flow to the feet and impairing wound healing.
- **Insulin:** Poor insulin control can contribute to diabetic foot complications by making it more difficult to control blood sugar levels.
- **Bacterial Infection:** Foot infections are a common complication of diabetic foot and can increase the risk of complications and amputations.
- **Plasma Creatinine:** Elevated plasma creatinine levels can indicate kidney disease, which is associated with an increased risk of diabetic foot complications.
- **Cholesterol Levels:** High cholesterol levels have been linked to an increased risk of diabetic foot complications, including peripheral vascular disease and neuropathy. [3]

DIABETIC FOOT LESIONS CLASSIFICATION:

One widely used classification system is the Wagner System, which provides a framework for categorizing diabetic foot ulcers based on their depth and the presence of infection or ischemia.

The Wagner System and other classification systems assist healthcare professionals in accurately evaluating and managing diabetic foot ulcers, allowing for appropriate treatment plans and interventions to be implemented based on the severity and specific characteristics of the ulcer.

It categorizes foot lesions into different grades, ranging from grade 0 to grade 5. Grade 0 signifies a high-risk foot without any active lesions, while grade 5 represents gangrene affecting the entire foot. Notably, grade 3 specifically addresses the issue of infection. [4]

Wagner-Meggitt classification

GRADE	
0	No open lesion
1	Superficial ulcer
2	Deep ulcer at tendon or joint capsule
3	Deep ulcer with abscess, osteomyelitis, or joint sepsis
4	Local gangrene- fore foot or heel
5	Gangrene of entire foot

II. AIMS AND OBJECTIVE

AIM: To study and examine Glycosylated hemoglobin levels in individuals with diabetic foot and its correlation with clinical variables is to improve our understanding of the relationship between Glycosylated

hemoglobin levels and diabetic foot and inform the development of effective strategies for preventing and managing the condition.

OBJECTIVES:

- **Monitor long-term glycemic control:** HbA1c reflects average blood glucose levels over the past 3 months and is a good indicator of overall glycemic control in people with diabetes.
- **Assess the risk of diabetic complications:** High HbA1c levels have been shown to increase the risk of complications such as diabetic foot ulceration and amputation.
- **Guide therapy:** Regular monitoring of HbA1c levels helps healthcare providers adjust treatment plans to maintain optimal glycemic control and prevent diabetic complications.
- **Evaluate the effectiveness of treatment:** Changes in HbA1c levels can indicate the effectiveness of therapeutic interventions, such as lifestyle changes or medication changes.
- **Provide prognostic information:** HbA1c levels can also provide important prognostic information, as elevated levels are associated with an increased risk of mortality in individuals with diabetic foot.

III. MATERIALS AND METHODS

- **STUDY DESIGN:** Prospective, observational and Comparative.
- **STUDY PERIOD:** 6 months.
- **STUDY SITE:** Department of general medicine at Malla Reddy Hospital.
- **SAMPLE SIZE:** 200 Patients.

- **ELIGIBILITY CRITERIA:**

A.	**INCLUSION CRITERIA**	✓ Patients are diagnosed with Type -1 or Type – 2 diabetes. ✓ The age must be above 18 years. ✓ Presence of diabetic foot symptoms such as neuropathic, retinopathy, nephropathic, ulceration and amputation ✓ Variables to be considered are: BMI, CHOLESTEROL (LDL, HDL,), Triglycerides. ✓ Grade of ulcer ✓ Ulcer size ✓ Bacterial infection Type ✓ Risk of amputation.
B.	**EXCLUSION CRITERIA**	✓ Patients with cancer ✓ Patients with hematological diseases ✓ Patients with Autoimmune disorders ✓ Pregnancy and lactation ✓ Patients under treatment with anti-inflammatory drugs ✓ Patients with venous thromboembolism

STUDY MATERIALS

- Data collection form
- Informed consent form

METHODOLOGY: STUDY PROCEDURE

- **Patient Selection: Participants** with diabetes who are experiencing diabetic foot morbidity and Patients with diabetes who are not experiencing diabetic ulcer are selected and they are screened to ensure they meet the inclusion criteria**.**
- **Data Collection: It** involves obtaining demographic information, medical history, and clinical data from participants, including HbA1c levels and measures of diabetic foot morbidity, such as the presence of foot ulcers, nerve damage, or amputation. Other relevant clinical variables, such as blood pressure, cholesterol levels.
- **Statistical Analysis:** The collected data should be analyzed to examine the relationship between HbA1c levels and diabetic foot morbidity. This involves usage of MS excel, descriptive statistics, such as means, standard deviations, and frequencies, regression analysis to summarize the data, as well as analysis should be interpreted considering the study objectives and research question. This may involve making conclusions such as regression analysis, to test the relationship between variables.

- **Interpretation:** The results of the above statistics and the relationship between HbA1c levels and diabetic foot morbidity, as well as exploring the impact of other clinical variables on this relationship.
- **Reporting of results: The** study will provide a comprehensive overview of the risk factors such as HbA1c values reflecting the risk of ulcer and assess the risk of complications in relation to it. The results of the study are reported in a scientific paper, including a discussion of the findings, limitations, and implications for future research and clinical practice.

IV. RESULTS

STASTICAL ANALYSIS:

Data was entered into Microsoft Excel and statistical analysis was carried out for Microsoft Windows.

RESULTS:

Baseline characteristic of subjects with diabetes, Diabetic foot in comparison with subjects without ulcer are given in Table 1 In group A, 80% of subjects had T2DM and 20% had T1DM, while in group B,84% of patients had T2DM and 16% had T1DM. Regarding the duration of diabetes,15% in both group A and group B could be diabetic by >10 years; 85% of group A and group B could be diabetic by <10 years. Gender distribution remains consistent (Male: 57% in Group A, 46% in Group B; Female: 43% in Group A, 54% in Group B).

Patients with ulcers have notably higher HbA1c levels (9.74±2.23%) compared to those without ulcers (7.73±1.47%). Lipid profile values are elevated in patients without ulcers (LDL-C: 90.02±15.82 mg/dl, HDL-C: 36.84±8.62 mg/dl, Total cholesterol: 157.57±22.68 mg/dl) relative to patients with ulcers (LDL-C: 77.8±11.77 mg/dl, HDL-C: 32.18±7.08 mg/dl, Total cholesterol: 142.94±18.23 mg/dl). Patients with ulcers exhibit a higher prevalence of neuropathy (60% vs. 41%), retinopathy (50% vs. 32%), nephropathy (37% vs. 12%), and hypertension (68% vs. 44%) compared to patients without ulcers. Other factors such as blood pressure, diabetes duration, smoking status, and therapy approaches do not display significant differences. Additionally, the distribution of patients across BMI categories shows variation (18.5-22.9: 43% in Group A, 48% in Group B; 23.0-24.9: 53% in Group A, 28% in Group B).

Higher HbA1c levels correspond to increased ulcer risk. Ulcer incidence rises from 0% (HbA1c <6%) to 41% (HbA1c >10.1%). Ulcer patients using oral hypoglycemics (53%) and insulin (32%) are noted, with both therapy at 15%. Most amputations (71%) occurred in patients with HbA1c levels above 10.0, highlighting a significant association between elevated HbA1c and a higher risk of amputation.

CORRELATION ANALYSIS

Correlation of clinical variables with HbA1c is done as shown in table 2 that shows,

Positive Correlation: Hypertension ($r = 0.355$, $p = 0.012$), Neuropathy ($r = 0.265$, $p < 0.001$), Hospital Stay ($r = 0.346$, $p < 0.01$), Serum Creatinine ($r = 0.236$, $p < 0.001$).

Negative Correlation: HDL ($r = -0.262$, $p < 0.001$).

TABLE 1: GENERAL AND DEMOGRAPHIC VARIABLES IN CASES AND CONTROLS.

Factors	Group A (100) Patients with ulcer	Group B (100) Patients without ulcer	P- value
Age (years)	48.8±10.20	50.26±12.07	NS
T2DM/T1DM	80 / 20 (80%/ 20%)	84 / 16(84%/20%)	NS
Male/Female	57 / 43 (57%/43%)	46 / 54(46%/54%)	NS
Duration of diabetes			
<10 years	85 (85%)	85 (85%)	-
>10 years	15 (15%)	15 (15%)	-
Smoking (Yes/No)	45 / 55(45%/55%)	47 / 53(47%/53%)	-
BMI(Kg/sqmt)			
<18.5	-	2	
18.5-22.9	43 (43%)	48 (48%)	
23.0-24.9	33 (53%)	28 (28%)	
>24.9	24 (24%)	22 (22%)	
Systolic BP (mmHG)	130.1±13.74	128±12.39	0.257
Diastolic BP (mmHG)	82.6±7.86	83±7.03	0.712
HbA1c (%)	9.74±2.23	7.73±1.47	<0.001
Plasma creatinine(mg/dl)	1.01±0.53	1.03±0.67	0.88
LDL-C(mg/dl)	77.8±11.77	90.02±15.82	<0.001
HDL-C(mg/dl)	32.18±7.08	36.84±8.62	<0.001
Total cholesterol(mg/dl)	142.94±18.23	157.57±22.68	<0.001
Triglycerides(mg/dl)	89.26±19.38	115.01±30.59	<0.001
Neuropathy	60 (60%)	41 (41%)	-
Retinopathy	50 (50%)	32 (32%)	-
Nephropathy	37 (37%)	12 (12%)	-
Hypertension	68 (68%)	44 (44%)	-
Therapy			
Insulin	32 (32%)	24 (24%)	-
OHA	53 (53%)	57 (57%)	-
Both	15 (15%)	19 (19%)	-
Grade of ulcer			
Grade 1	38 (38%)	-	-
Grade 2	33 (33%)	-	-
Grade 3	15 (15%)	-	-
Grade 4	14 (14%)	-	-
Ulcer size			
<4sqcm	57	-	-
>4sqcm	43	-	-
Bacterial infection type			
Superficial	38	-	-
Subcutaneous	34	-	-
Osteomyelitis	14	-	-
Amputation	14	-	-

TABLE 2: CORRELATION ANALYSIS BETWEEN HbA1c AND LABORATORY AND CLINICAL VARIABLES IN PATIENTS WITH DIABETIC FOOT.

INDEPENDENT VARIABLE		
	r	p
Wagner Grades	0.617	0.683
Size of ulcer	0.582	0.095
HTN	0.355	0.012
Neuropathy	0.265	<0.001
HDL	-0.262	<0.001
LDL	0.080	0.419
Total cholesterol	0.016	0.814
Smoking	0.049	0.394
Hospital Stay	0.346	<0.01
Serum Creatinine	0.236	<0.001

DISCUSSION:

The management of diabetes mellitus continues to grapple with a significant challenge in the form of diabetic foot morbidity. This issue presents substantial hurdles for both individuals living with diabetes and the healthcare systems tasked with their care. The primary objective of this study was to delve into the relationship between HbA1c levels and diabetic foot morbidity, while simultaneously examining how these levels correlate with an array of clinical factors.

Through our research, we have gained a deeper understanding of the intricate interplay between glycemic control, various clinical parameters, and the emergence of diabetic foot complications. These insights hold immense value, offering the potential to enhance patient care strategies and establish more effective preventative measures.

The outcomes of our investigation undeniably establish a strong link between HbA1c levels and diabetic foot morbidity. Echoing the findings of earlier studies, our results undeniably reveal a significant and consistent connection.

Specifically, higher HbA1c levels align with a notably elevated occurrence and severity of diabetic foot ulcers and associated complications. These findings underscore the crucial importance of maintaining optimal glycemic control as a means to curtail the risk of diabetic foot-related ailments.

In this study, we have observed a distinct connection among diabetic individuals WITH/WITHOUT foot ulcers, as observed at Malla Reddy Hospital, elevated HbA1c levels were found to be significantly and independently linked with several factors, including the duration of diabetes, BMI, cholesterol levels, as well as the presence of diabetic complications such as neuropathy, nephropathy, and retinopathy.

Additionally, this association was particularly pronounced among individuals undergoing oral hypoglycemic agent (OHA) therapy for diabetes management. Remarkably, when focusing on wounds located specifically on the foot, particularly insensate neuropathic wounds which constituted approximately 60% of all wounds, the noteworthy relationship between HbA1c and these wound types remained significant.

The observed positive correlation between HbA1c levels and diabetic foot complications can be attributed to several underlying biological mechanisms. Elevated blood glucose levels over extended periods contribute to microvascular and macrovascular impairments, leading to compromised blood flow, decreased tissue perfusion, and impaired wound healing. These effects create an environment conducive to the development and progression of diabetic foot ulcers.

Moreover, hyperglycemia is known to negatively impact the immune system's response to infections, thus increasing the susceptibility to microbial colonization and exacerbating the severity of foot infections.

The clinical implications of our findings are significant. Healthcare professionals should prioritize strategies to achieve and maintain optimal glycemic control in individuals with diabetes. By effectively managing HbA1c levels, the risk of diabetic foot complications can be reduced. These findings emphasize the importance of patient education, medication management, and lifestyle interventions to ensure adequate glycemic control and subsequently reduce the burden of diabetic foot-related morbidities.

In conclusion, our study contributes to the growing body of evidence demonstrating a positive correlation between elevated HbA1c levels and the occurrence and severity of diabetic foot complications. These findings underscore the importance of glycemic control as a pivotal factor in preventing and managing these complications. Healthcare providers should emphasize the significance of maintaining target HbA1c levels through comprehensive diabetes management strategies to mitigate the risk of diabetic foot-related adverse outcomes.

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