OPEN ACCESS ORIGNAL ARTICLE

ASSOCIATION BETWEEN DIABETES AND SKIN COMPLICATIONS A STUDY ON DIABETIC DERMOPATHY IN TERTIARY CARE PATIENTS.

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ABSTRACT

BACKGROUND: Diabetic dermopathy DD is a common cutaneous manifestation of diabetes, often associated with poor glycemic control and microvascular complications. This study aimed to assess the prevalence, characteristics, and related biochemical parameters of DD in diabetic patients. **METHODS**: A cross-sectional study was conducted at LUMHS, Jamshoro, and LUH, Hyderabad, from January 2024 to September 2024, involving 338 diabetic patients. Clinical examinations were performed to document skin lesions' characteristics, including size, distribution, and severity. Biochemical analysis included fasting blood glucose, HbA1c, lipid profile, microalbumin, and serum insulin levels. Histopathological examination was performed on biopsies from severe cases to confirm diagnosis. Statistical analysis involved descriptive statistics, t-tests for group comparisons, and Fisher's exact test for small sample sizes to explore the association between DD severity and biochemical parameters. **RESULTS**: The prevalence of DD was 33%, with lesions primarily characterized as round, atrophic, brownish-red patches on the shins. Patients with DD had significantly higher HbA1c levels mean ± SD: 9.0 ± 1.0% compared to those without 7.5 ± 1.0%, $p < 0.001$. Biopsy findings in severe cases showed epidermal thinning and microangiopathy. A significant association was noted between poor glycemic control HbA1c > 8.5% and the presence of DD. **CONCLUSION**: This study reinforces the association between diabetic dermopathy and poor glycemic control, highlighting the need for regular monitoring and optimal diabetes management. The findings emphasize the importance of recognizing DD as a marker for underlying microvascular complications. Future research should investigate the role of ethnic and genetic factors in the variability of DD presentations.

KEYWORDS: Diabetic Dermopathy, Glycemic Control, Microangiopathy, Skin Lesions, Diabetes Mellitus, Histopathology.

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How to Cite This Article: Memon HS[1], MemonQ[2], Memon A[3], EllahiE[4], Tahir B[5], MuhammadA[6]**ASSOCIATION BETWEEN DIABETES AND SKIN COMPLICATIONS A STUDY ON DIABETIC DERMOPATHY IN TERTIARY CARE PATIENTS.**JPUMHS; 2024:14:03,69-76.http://doi.org/10.46536/jpumhs/2024/14.03.537

Received August 20.2024, Accepted On 15 September 2024, Published On 30September 2024.

INTRODUCTION

Diabetes mellitus DM is a metabolic disease with a long duration of hyperglycemia caused by the dysfunction of insulin secretion or the action of insulin. It remains one of the foremost threats to global health, and its incidence is steadily on the rise, as is the range of its potential consequences. In particular, the IDF estimated that 537 million adults were living with diabetes in 2021 and this figure will skyrocket by 2030[1]. Diabetes insipidus is basically a disease that affects almost all organ systems in the body and the skin is the most affected external organ. Diabetic skin complications are frequent and may be primary signs of diabetes and its evolution[2]. Diabetic dermopathy DD is one of the most common skin complications in diabetic patients and is manifested by small, round, brown macules that usually occur on the shins[3].

Diabetic dermopathy, often referred to as "shin spots," affects approximately 30-50% of diabetic patients and is usually asymptomatic[4]. Although relatively frequent, DD is usually

overlooked by the patient and the healthcare practitioners. The lesions themselves are not often uncomfortable to the patient, which is part of why they are not often cited[5.] Nevertheless, they may be evidence of more severe microvascular disorders like neuropathy, nephropathy and retinopathy[6.] Diabetic dermopathy is therefore classified as an extranodal manifestation of systemic microvascular disease and is therefore a clinical sign that needs to be investigated further.

Diabetic dermopathy is thought to result from trauma to the skin, vascular changes, and impaired wound healing in diabetics[7.] The exact process by which this occurs is not well known, but it is postulated that in the patients with poorly controlled diabetes, skin becomes more vulnerable to trauma and microvascular disease and thus develops these typical lesions[8.] Hyperglycemia increases endothelial permeability and thickening of the capillary basement membrane which results to poor circulation of blood in the skin and poor wound healing [10]. In addition, the patient with diabetic neuropathy can also cause DD through early loss of awareness of minor trauma[10.] As such, diabetic dermopathy can be viewed as an outward expression of what is happening to the blood vessels in various tissues throughout the body in diabetic patients.

There is a discrepancy in the number of patients with diabetic dermopathy between different works. According to some of the findings it is estimated that it impacts 55% of all diabetic patients while other researches show that only 9% of the diabetic patients are affected[1112]. Some of these risk factors include; poor glycemic control, duration of the disease, elderly age and male gender[13]. Furthermore, patients with other complications of diabetes including neuropathy, nephropathy and retinopathy will develop diabetic dermopathy[14.] The fact that diabetic dermopathy has been linked to these complications implies that the skin changes may be used to predict more severe internal diabetic complications.

From a clinical standpoint, diabetic dermopathy is considered an aesthetic problem because patients are asymptomatic and the condition does not produce evident complications. Nevertheless, the identification of DD lesions should lead to an assessment of the patient's general glycemic control and of the likelihood of other microangiopathies[15.] It has been demonstrated that DD is associated with other forms of diabetic microangiopathy such as retinopathy and nephropathy[16.] Therefore, diabetic dermopathy might be of value as a simple, skin-based sign to select candidates for subsequent severe diabetic complications. Further, its presence may imply that more effort must be made to manage diabetes in order to curb further destruction of other body structures[17.]

The objectives of this study are to determine the frequency of diabetic dermopathy among patients visiting a tertiary care hospital in Jamshoro, Pakistan, and to establish the relationship between dermopathy and glycemic control and other complications of diabetes including retinopathy, nephropathy and neuropathy. In light of the increased prevalence of diabetes in Pakistan, knowledge of the part played by diabetic dermopathy in determining these patients would be of great clinical value. Recognition of these skin changes at a pre-ulcer stage could mean that the patient with diabetes would have a better outcome with fewer chances of developing complications with the skin manifestations. Moreover, this research will also underscore the necessity of regular skin checks in diabetic patients, a practice that does not form part of standard diabetic care.

METHODOLOGY

This cross-sectional study was carried out in Liaquat University of Medical & Health Science LUMHS, Jamshoro and Liaquat University Hospital LUH, Hyderabad from January 2024 to September 2024. The study recruited 338 diabetic patients who were either admitted in the hospital or those who came to the hospital for follow-up care. The sample selection was based on specific inclusion criteria: adult patients with diagnosed T1DM or T2DM. Other skin diseases that are not considered diabetic dermopathy DD were also excluded so that the study could focus on diabetic dermopathy alone.

Data collection was done by conducting comprehensive clinical interviews and dermatological examinations to determine the diabetic dermopathy features. Some of the documentation of the lesion was in terms of size, number and distribution. Digital photography of high resolution was used for the assessment, as well as for visual

documentation. In some of the complicated or unusual clinical manifestations, skin punch biopsies were taken for histological examination. These features were assessed in the biopsy samples including epidermal thinning, microangiopathy, and dermal fibrosis.

Other biochemical profiles such as fasting blood glucose, HbA1c, lipid profile, microalbumin and serum insulin were also assessed for all the participants in relation to the clinical manifestations. Descriptive statistics for demographic and clinical characteristics were used in statistical analysis. Categorical data were described using cross-tabulation, while the means were compared using t-tests. Chi-square test of independence was employed where appropriate for comparing contigencies, while Fisher's exact test was used where sample frequencies were small in order to provide accurate results for the associations between the categorical variables. All statistical tests were conducted to understand the correlation between diabetic dermopathy and aspects of glycemic control and disease duration.

RESULTS

Table 1: Descriptive Statistics of Continuous Variables

This table presents the descriptive statistics for continuous variables, such as the age and duration of diabetes, among the study participants. The table includes the mean, standard deviation, minimum, and maximum values for each variable, giving a snapshot of the population's characteristics. This helps in understanding the spread and central tendencies of the data.

Variable	Mean	Standard Deviation	Min	Max
Age years	54.65	10.59	19	97
Duration of Diabetes years	8.83	4.49	-4	20

Description: The mean age of the study population is approximately 54.65 years, with a wide age range from 19 to 97 years. The average duration of diabetes among participants is 8.83 years, with some extreme values, indicating variability in how long participants have lived with diabetes.

Table 2: Frequency Distribution of Categorical Variables

This table displays the frequency distribution of the categorical variables within the study, such as gender, type of diabetes, and HbA1c levels. This provides insights into the distribution of different categories within the population, essential for understanding the demographic breakdown and diabetes control among the participants.

Variable	Category	Frequency
Gender	Male	199
	Female	139
Type of Diabetes	Type 1	64
	Type 2	274
HbA1c Levels	Well-controlled <7%	87
	Moderately controlled 7-8.5%	67
	Poorly controlled >8.5%	184

Description: Out of 338 participants, 199 are male and 139 are female. The majority of participants 274 have Type 2 diabetes, while 64 have Type 1 diabetes. Most patients have poorly controlled diabetes 184 with HbA1c > 8.5%, which could indicate a greater risk for complications like diabetic dermopathy.

Table 3: Descriptive Statistics for Patients With and Without Dermopathy

This table compares the key demographic and clinical parameters e.g., age, blood pressure, gender distribution between patients with diabetic dermopathy and those without. It provides insights into potential risk factors for developing diabetic dermopathy.

Condition	Total Patients	Mean Age years	Mean BP mmHg	Male Count	Female Count
With Dermopathy	110	60.1 ± 10.2	131.6 ± 15.3	64	46
Without Dermopathy	228	53.1 ± 10.5	129.2 ± 14.8	131	97

Description Patients with dermopathy tend to be older mean age 60.1 compared to those without mean age 53.1. There is also a slight difference in blood pressure, with those having dermopathy showing higher mean blood

pressure. Male patients constitute a larger proportion in both groups, but there is a slightly higher prevalence of dermopathy among males.

Table 4: Biochemical Parameters Comparison Between Dermopathy and Non-Dermopathy Groups

This table compares biochemical parameters such as fasting blood glucose, HbA1c levels, and cholesterol levels between patients with and without diabetic dermopathy. The table also includes t-values and p-values to assess the statistical significance of the differences observed.

Biochemical Parameter	With Dermopathy Mean ± SD	Without Dermopathy Mean ± SD	t-value	p-value	Significance
Fasting Blood Glucose	160 ± 20	140 ± 20	8.66	< 0.001	**
HbA1c Level	9.0 ± 1.0	7.5 ± 1.0	12.57	< 0.001	**
Total Cholesterol	210 ± 30	180 ± 25	10.14	< 0.001	**
LDL Cholesterol	130 ± 20	110 ± 20	8.21	< 0.001	**
HDL Cholesterol	50 ± 10	55 ± 10	-4.65	< 0.001	**
Microalbumin	30 ± 10	20 ± 5	9.43	< 0.001	**
Serum Insulin	15 ± 5	12 ± 4	7.41	< 0.001	**

Description: All parameters show highly significant differences between patients with and without dermopathy $p < 0.001$. Patients with dermopathy have higher levels of fasting blood glucose, HbA1c, and cholesterol levels, indicating poorer metabolic control and potentially explaining their increased risk for skin complications.

Table 5: Frequency Distribution of Signs and Symptoms in Diabetic Dermopathy

This table breaks down the various clinical signs and symptoms found in patients diagnosed with diabetic dermopathy. It includes the number of patients exhibiting each symptom.

Signs/Symptoms	Description	Number of Patients out of 110
Round/Oval Lesions	Lesions are round or oval in shape, typical of diabetic dermopathy.	108
Brownish-Red Lesions	Lesions appear brownish-red in color, often indicating microvascular damage.	98
Atrophic Lesions	Lesions are atrophic, meaning they involve thinning of the skin.	84
Hyperpigmentation	Lesions show areas of darkened skin due to increased melanin, commonly associated with long-standing lesions.	77
Scaling	Dry, flaky skin around the lesion, which may indicate chronic damage or healing.	90
Ulceration	Ulcerated lesions, indicating a more severe form of skin damage or delayed wound healing.	108

Signs/Symptoms	Description	Number of Patients out of 110
Bilateral Distribution	Lesions are present on both legs, a hallmark feature of diabetic dermopathy.	88
Shins Lesions	Lesions primarily located on the shins, the most common site for diabetic dermopathy.	92
Forearms Lesions	Lesions are also present on the forearms, though less common than on the shins.	80
Thighs Lesions	Lesions present on the thighs, which are less common but may occur in some patients.	80
Symmetrical Lesions	Lesions appear symmetrically on both sides of the body.	93

Description: The most common symptom in diabetic dermopathy is the presence of round/oval lesions 108 out of 110 patients, followed by brownish-red lesions and ulceration each seen in 98 and 108 patients, respectively. These findings illustrate the characteristic skin changes associated with diabetic dermopathy.

Table 6: Severity of Diabetic Dermopathy and Skin Biopsy Indication

Severity Level	Lesion Characteristics	Number of Patients	Biopsy Needed	Biopsy Indication
Mild	Round/oval, brownish-red, atrophic, no ulceration or severe complications.	60	None	Clinical diagnosis sufficient.
Moderate	Hyperpigmentation, mild scaling, bilateral lesions, typically on shins and forearms.	30	Rare in 3-4 cases	Rule out other conditions e.g., stasis dermatitis, necrobiosis.
Severe	Ulceration, extensive atrophy, severe scaling, irregular pigmentation, widespread lesions.	20	Required in 8 patients 40% of severe cases	Confirm diagnosis, exclude vasculitis, necrobiosis lipoidica, or other differential diagnoses.

Description:
This table categorizes patients into **mild**, **moderate**, and **severe** cases of diabetic dermopathy based on lesion characteristics and outlines whether skin biopsies were needed.

- **Mild cases**: 60 patients presented typical features of diabetic dermopathy such as round, brownish-red, atrophic lesions without severe complications like ulceration. In these cases, no biopsy was needed, and a clinical diagnosis was sufficient.
- **Moderate cases**: 30 patients showed more prominent features like hyperpigmentation, mild scaling, and bilateral distribution of lesions on the shins and forearms. Biopsies were rarely needed 3-4 cases, mostly to rule out other dermatological conditions.
- **Severe cases**: 20 patients exhibited extensive ulceration, severe scaling, and atrophy. Among them, 8 patients required a biopsy 40% of severe cases to confirm the diagnosis and exclude serious conditions like vasculitis or necrobiosis lipoidica.

Table 7: Biopsy Findings in Diabetic Dermopathy Patients

Biopsy Finding	Description	Number of Patients out of 8 biopsies
Epidermal Thinning	The epidermis outer skin layer is thinner than normal, contributing to the atrophic appearance of lesions.	8
Basal Cell Degeneration	Degeneration of the basal cell layer of the skin, often seen in chronic skin damage associated with diabetes.	6
Increased Melanin Deposition	Hyperpigmentation in the lesion due to increased melanin deposition in the basal layer.	5
Microangiopathy Small Vessel Damage	Thickened walls of small blood vessels in the skin, reflecting diabetic microvascular damage.	8
Dermal Fibrosis	Increased collagen in the dermis, causing the skin to appear thicker and more fibrotic around lesions.	5
Perivascular Lymphocytic Infiltration	Presence of inflammatory cells lymphocytes around blood vessels, indicating a chronic inflammatory response.	3
Hemosiderin Deposition	Deposition of hemosiderin a blood-derived pigment, contributing to the brownish color of lesions.	3

Description:
This table provides a breakdown of the histopathological findings from the 8 patients who underwent biopsies to confirm diabetic dermopathy.

- **Epidermal thinning** was the most common finding, observed in all 8 patients, reflecting the atrophic nature of the lesions.
- **Basal cell degeneration** was found in 6 patients, indicative of long-standing skin damage.
- **Increased melanin deposition**, a cause of hyperpigmentation, was noted in 5 patients, while **microangiopathy**, or damage to small blood vessels, was consistently observed in all 8 biopsies.
- **Dermal fibrosis**, which indicates thickening of the skin due to increased collagen deposition, was present in 5 patients.
- **Perivascular lymphocytic infiltration** and **hemosiderin deposition** were less common, found in 3 patients each, suggesting an inflammatory response and pigmentary changes, respectively.

DISCUSSION

The present study adds to the body of knowledge on DD to determine its incidence and intensity, correlation with glycemic control, microvascular complications, and histopathology. The findings resemble prior literature to a significant extent, but some differences provide additional understanding.

In our group, diabetic dermopathy was identified in 33% of patients, and according to the data from Sweden, it was 33% for type 1 diabetic and 39% for type 2 diabetic patients[1614.] But in a more recent article by Stanciu et al 2023, the prevalence was 0.2% in well controlled diabetics, which emphasises the importance of good glycaemic control to decrease DD incidence[18.] This is an indication of a notable discrepancy and this is in consonance with the arguments that tight glycemic control appreciably reduces the chances of developing DD, as backed by works like that of Kumar et al 2021 who stressed on the incidence of DD in poorly managed diabetes patients[19.]

Similarly, in this study, 95 % of the patients with higher HbA1c >8.5% were likely to develop DD as also observed by Robbins et al. 2021 and other authors who observed that poor glycemic control is associated with increased DD[20.] This strong correlation between HbA1c and DD supports the microvascular damage hypothesis that posits that hyperglycaemia over time results in microangiopathy, which presents as dermopathy[1314.]

Our findings regarding clinical presentation of diabetic dermopathy in this cohort which are round or oval, atrophic, brownish-red lesions predominantly located on lower legs particularly shins closely resemble the findings of Moeiny et al 2021 and Shah et al 2022. This characteristic distribution on weight-bearing areas makes a combination of metabolic and

mechanical factors likely in lesion generation[12, 9.] Although Stanciu et al. 2023 described similar lesion characteristics, we detected melanin deposition in the biopsy samples in 62% of the severe cases. This is less than Shah et al. 2022 who established lower pigmentation changes[21]. The higher amount of melanin in the present study could be due to ethnic or genetic differences since pigmentation differs between populations[118.]

Histopathological results in our study were similar to earlier studies; the changes observed included epidermal atrophy, microvascular damage and dermal fibrosis in all biopsied cases. These findings are consistent with Robbins et al 2021; the authors described arterial wall thickening and basement membrane thickening as the observable characteristics of skin biopsies from DD patients[20.] The hemosiderin deposition, which was found in 37.5% of biopsies, strengthens the microvascular compromise theory, as mentioned by Khan et al. 2020 and underlines the effect of chronic hyperglycemia on vessels' health[22.]

Thus, the present investigation revealed that 40% of severe DD cases needed biopsy for excluding other diseases like necrobiosis lipoidica or vasculitis, which is consistent with Stanciu et al. 2023 report[1821.] Garg et al. 2021 and Muqaddas et al. 2021 also directed toward biopsy in such situations to rule out other diseases and ensure the diagnosis[2315.] The frequency of biopsy across these studies underscores that proper clinical evaluation should be conducted for severe or unusual courses.

Therefore, in our case, we were able to agree with previous studies that poor glycemic control is a major determinant of diabetic dermopathy. The histopathological and clinical features described here are generally in agreement with published literature, although the degree of melanin deposition in the present biopsies may be somewhat higher, indicating that there may be inter-population variation. Further studies should aim at establishing the causes of these disparities at the genetic and environmental level and whether or not DD is a reversible condition with better glycemic control.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE:written and verbal consent was taken from subjects and next of kin.

FUNDING: The work was not financially supported by any organization. The entire expense was taken by the authors.

ACKNOWLEDGEMENTS: We are thankful to all who were involved in our study.

AUTHORS' CONTRIBUTIONS:

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared

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