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***Original Article***

# Non-Infectious Dermatological Manifestations among Patients with Diabetes Mellitus in Basrah, Iraq

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**Abstract**

Diabetes mellitus (DM) is a clinical illness usually linked to a wide range of skin manifestations; however, skin, as the greatest organ in the body, has received little attention. As a result, this study aimed to detect the prevalence and pattern of non-infectious skin disorders among patients with diabetes. This study was carried out at the Faiha Specialized Diabetes, Endocrine, and Metabolism Center, Basrah Province, Iraq, from September 2020 to September 2021. The data were collected from 347 patients with Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM). The exclusion criteria were patients with skin changes due to some medications, pregnancy, iatrogenic factors, skin infections, established hypo- or hyper-thyroidism, Cushing or adrenal insufficiency, pituitary disorders, end-stage renal impairment, malignancy, and established rheumatological disease and those who were on chemotherapy. Full dermatological examinations and screenings were performed under the supervision of a dermatologist expert and all clinically definable cutaneous lesions were recorded. The prevalence of skin lesions was estimated at 71.5% in patients. Pruritus, xerosis, acrochordon, diabetic dermopathy, acanthosis nigricans, and insulin-related lipohypertrophy were the commonest skin lesions reported among the patients. The occurrence of skin lesions in diabetic patients was proportional to the female gender, duration of disease, obesity, insulin therapy, and worse glycemic control. There was a broad spectrum of skin lesions in both T1DM and T2DM with corresponding prevalence.

**Keywords:** Iraq, Skin lesion, T1DM, Pruritus, T2DM, Xerosis

## 1. Introduction

Diabetes mellitus (DM) is a long-term illness, which affects people's well-being all over the world. Diabetes mellitus is among the top 10 reasons for adult mortality (1). Type 1 diabetes mellitus (T1DM) is caused by autoimmune-cell destruction that results in absolute insulin deficiency; however, type 2 diabetes mellitus (T2DM) is induced by a progressive loss of insulin secretion in the context of insulin resistance (2). In most countries, the proportion of individuals having T2DM is increasing, as in low- and middle-income nations, one out of every five individuals over the age of 65 has diabetes (3).

According to the results of several studies, 30-82% of diabetic patients suffer from various skin problems over the chronic course of their condition, and certain anti-diabetic medications might cause skin problems (4, 5). The overall skin disease prevalence in both types of DM varies from 51% to 97% in different regions worldwide (6). Therefore, controlling the body's metabolism may prevent some of these manifestations and support the treatment (7). Dermatologic manifestations generally appear after the development of diabetes; however, since it may even precede the diagnosis by several years, the dermatologist can be the first to notice hidden diabetes on a patient (8).

Skin can be affected by DM in several ways as reaching high levels of glycemia, various protein, lipid, and nucleic acid molecules can be glycated resulting in advanced glycation end products that contribute to a variety of DM problems, including skin problems, and fibrotic process, skin aging, and immunological suppression by reducing collagen elasticity and solubility (6, 9).

Chronic pruritus is a frequent skin symptom of a person who has diabetes, which is frequently linked to xerosis cutis and affects 3-49% of persons with diabetes reducing their life quality significantly (10). Diabetic polyneuropathy may impact developing diabetic pruritus by causing sweating failure due to sympathetic nervous system damage (11). Xerosis, frequently observed in patients with DM, is caused by abnormal, persistent cohesion between corneocytes, which results in secondary thickening of the stratum corneum (SC), impaired moisturization of the uppermost SC layers, increased corneocyte transit time in the SC, and altered skin barrier function; diabetic xerosis appears to be linked to microangiopathy (12, 13). Acanthosis nigricans (AN) is a hyperpigmented velvety thickening of skin folds, which presents predominantly in the neck, axilla, and groin areas (14). Insulin-related allergies, urticaria, painful nodules, and granulomas are examples of localized allergic responses to insulin and analogs (15). Therefore, this study aimed to assess the prevalence and pattern of non-infectious skin disorders in patients with diabetes.

## 2. Materials and Methods

### 2.1. Ethical Considerations and Data

This cross-sectional research was conducted on diabetes individuals attending the Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) in Basrah Province, Iraq, from September 2020 to September 2021.

### 2.2. Inclusions Criteria

The T1DM or T2DM patients who attended FDEMC were subjected to diagnosis according to the American Diabetes Association criteria a year prior to data collection. Their symptoms were collected during the first hour of the clinic's working time. On the other hand, the exclusion criteria were patients with skin change secondary to drugs, pregnancy, iatrogenic factors, skin infections, hypo- or hyper-thyroidism, Cushing's syndrome or adrenal insufficiency, pituitary disorders (e.g., hypopituitarism, acromegaly, or hyperprolactinemia), end-stage renal disease, cancer, and rheumatological disease and on chemotherapy.

### 2.3. Clinical Evaluation

The subjects were asked about any dermatological problems they could have, and a full history was obtained, including the age of diagnosis of diabetes, duration of diabetes, any complications developed during this period, type of diabetes, history of medication administration, and mode of treatment for diabetes, such as oral antidiabetic drugs (OADs) only or insulin±OADs. The body mass index (BMI) was determined by dividing weight by height then squaring them using kilogram for weight and meters for height. The body mass index was divided into two groups, namely non-obese with a BMI of less than 30 $kg/m^2$ and obese with a BMI of equal to or greater than 30 $kg/m^2$. All study participants were subjected to dermatological examination and screening under the supervision of a dermatologist expert. Complete clinically definable skin lesions were recorded according to their presentation rather than on the basis of their underlying cause or relationship to diabetes. The demographic information of all of the subjects was also documented.

### 2.4. Laboratory Tests

After overnight fasting of each patient for 8-10 h, 10 ml of venous blood was taken at early morning, 7 ml into free-anticoagulant glass gel-tube that centrifuged for 10-15 min to separate the serum to be tested by the electrochemiluminescence immunoassay using the COBAS INTEGRA 400 plus analyzer (Roche, Germany) to estimate the fasting blood sugar, serum creatinine, lipid profile, and liver function tests. Furthermore, the sera were examined by the COBAS e 411 analyzer (Roche, Germany) to obtain the thyroid-

stimulating hormone (TSH) and free thyroxine (FT4). Normal values for TSH and FT4 were set at 0.27-4.2 μIU and 0.93-1.7 ng/dl, respectively. A total of 3 ml of each blood sample was collected into plastic ethylenediaminetetraacetic acid tubes to estimate glycated hemoglobin (A1c) by high-performance liquid chromatography using the BIO-RAD VARIANT II TURBO system (BIO-RAD, USA).

### 2.5. Statistical Analysis

The continuous variables were studied using the analysis of variance and independent student t-tests, whereas non-parametric variables were analyzed using the Chi-square test. Qualitative variables were summarized as numbers (n) and frequencies (%) and quantitative variables were described as mean and standard deviation (Mean±SD). The collected data were analyzed in SPSS-26, and the occurrence frequencies of various cutaneous manifestations were obtained. The *P*-values of $< 0.05$ were considered statistically significant.

## 3. Results

The study included 347 diabetic patients at the age range of 14-75 years old, with a mean age of 49.2±14.4 years. Table 1 provides a summary of the basic characteristics of the participants. Accordingly, 194 (55.9%) patients were female, and non-infectious skin lesions were detected in 248 (71.5%) individuals. The mean age at which diabetes first appeared was estimated at 39.8±14.4 years. Diabetes mellitus duration was 9.4±6.8 years, and 275 (79.3%) subjects were affected with T2DM. The BMI was obtained at 29.9±5.7 kg/m$^2$, with 168 (48.4%) patients being obese. It was found that 220 (63.4%) patients administered insulin with or without OADs, while the rest of the cases used OADs only. The mean insulin duration was calculated at 9.38±6.8 years, and A1c was 9.9±5.2 percent. Poor glycemic control accounted for a large proportion of the patients, accounting for 304 (87.6%) subjects (Table 1).

**Table 1.** Baseline characteristics of the patients

| Factor | Category | Value |
|---|---|---|
| Age (years) | | 49.2±14.4 |
| Gender | Women | 194 (55.9%) |
| | Men | 153 (44.1%) |
| Patients with skin lesions | | 248 (71.5%) |
| Age at onset (years) | | 39.8±14.4 |
| Duration of DM (years) | | 9.4±6.8 |
| Type of DM | Type 2 | 275 (79.3%) |
| | Type 1 | 72 (20.7%) |
| BMI | Mean (Kg/m$^2$) | 29.9±5.7 |
| | Obese | 168 (48.4%) |
| | Non-obese | 179 (51.6%) |
| Treatment type | Insulin±OADs | 220 (63.4%) |
| | OADs only | 127 (36.6%) |
| Insulin duration (years) | | 9.38±6.8 |
| A1c | Mean (%) | 9.9±5.2 |
| | <7 | 43 (12.4%) |
| | ≥7 | 304 (87.6%) |

DM: Diabetes mellitus; BMI: Body mass index; OADs: Oral antidiabetic drugs; A1c: Glycated hemoglobin
Values are presented as either number (%) or Mean±SD.

The observed non-infectious skin lesions in this study included 6 lesions, namely pruritus (37.9%), xerosis (27.0%), acrochordon (25.8%), diabetic dermopathy (25.4%), AN (25.4%), and lipohypertrophy (15.3%) (Figure 1 and Table 2).

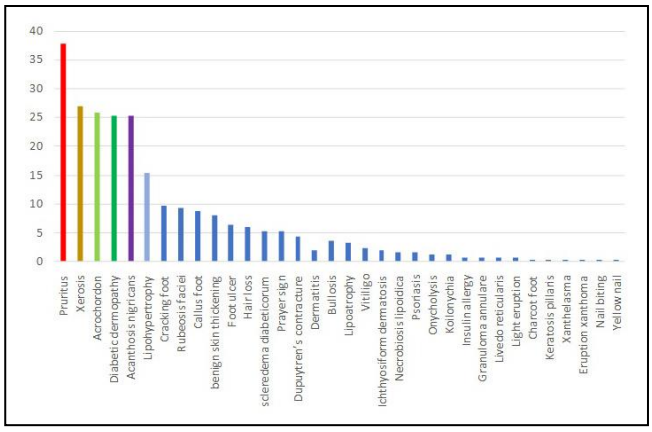


**Figure 1.** Frequency of multiple non-infectious skin lesions for patients with skin lesions

**Table 2.** Frequency of non-infectious skin lesions

| Type of skin lesion | No. | Percentage (%)/Total patients (n=347) | Percentage (%)/Patients with skin lesions (n=248) |
|---|---|---|---|
| Pruritus | 94 | 26.8 | 37.9 |
| Xerosis | 67 | 19.1 | 27.0 |
| Acrochordon | 64 | 18.2 | 25.8 |
| Diabetic dermopathy | 63 | 18.15 | 25.4 |
| Acanthosis nigricans | 63 | 17.9 | 25.4 |
| Lipohypertrophy | 38 | 10.8 | 15.3 |
| Cracking foot | 24 | 6.8 | 9.67 |
| Rubeosis faciei | 23 | 6.6 | 9.27 |
| Callus foot | 22 | 6.3 | 8.87 |
| Benign skin thickening | 20 | 5.7 | 8.0 |
| Foot ulcer | 16 | 4.6 | 6.45 |
| Hair loss | 15 | 4.3 | 6.0 |
| Scleredema diabeticorum | 13 | 3.7 | 5.24 |
| Prayer sign | 13 | 3.7 | 5.24 |
| Dupuytren's contracture | 11 | 3.1 | 4.43 |
| Dermatitis | 10 | 2.88 | 2.03 |
| Bullosis | 9 | 2.6 | 3.62 |
| Lipoatrophy | 8 | 2.3 | 3.22 |
| Vitiligo | 6 | 1.7 | 2.41 |
| Ichthyosiform dermatosis | 5 | 1.4 | 2.0 |
| Necrobiosis lipoidica | 4 | 1.1 | 1.61 |
| Psoriasis | 4 | 1.1 | 1.61 |
| Onycholysis | 3 | 0.9 | 1.20 |
| Koilonychia | 3 | 0.9 | 1.20 |
| Insulin allergy | 2 | 0.6 | 0.80 |
| Granuloma annulare | 2 | 0.6 | 0.80 |
| Livedo reticularis | 2 | 0.6 | 0.80 |
| Light eruption | 2 | 0.6 | 0.80 |
| Charcot foot | 1 | 0.3 | 0.40 |
| Keratosis pillaris | 1 | 0.3 | 0.40 |
| Xanthelasma | 1 | 0.3 | 0.40 |
| Eruption xanthoma | 1 | 0.3 | 0.40 |
| Nail biting | 1 | 0.3 | 0.40 |
| Yellow nail | 1 | 0.3 | 0.40 |

The effect of some variables on the occurrence of skin lesions was presented in this study (Table 3). The mean age of patients with and without skin lesions were 49.49±14.03 and 48.37±15.25 years, respectively, which was not significantly different (*P*=0.512). According to gender, it was revealed that women got skin lesions at a higher rate than males (77.3% vs. 64.1%, respectively, odds ratio [OR] 1.913, 95% confidence interval [CI]: 0.326-0.837, *P*=0.007). Age of onset of DM diagnosis did not affect the appearance of diabetic skin complications. The mean ages of diagnosis were obtained at 39.35±14.18 and 40.87±14.86 years in patients with and without skin lesions, respectively (*P*=0.375). The mean DM duration had a more significant effect on skin lesions development; accordingly, it was 10.13±6.84 years for people suffering from skin lesions, in comparison to 7.49±6.32 years for those without skin lesions (*P*=0.001). Individuals with a mean DM duration of 10 years or more had more skin lesions than those with a DM duration of less than 10 years (88.0% vs. 64.6%, respectively, OR 2.194, 95% CI: 1.341-3.589, *P*=0.002). It was found that DM type did not affect skin lesions development between the two groups (70.8% of T1DM compared to 71.6% of T2DM, *P*=0.893). Mean BMI had a significant effect on the appearance of skin lesions between the two groups (30.42±9.52 vs. 28.86±4.78 for patients with and without skin lesions,

respectively, *P*=0.02). More skin lesions were observed in obese patients (BMI≥30, 79.2%) than in non-obese ones (BMI<30, 64.2%) with doubled risk OR 2.11 (*P*=0.002). The type of DM treatment had a significant effect on the presence of skin lesions; in this respect, those with insulin treatment (77.3%) have had more skin lesions than those on OADs (61.4%; OR 2.13, 95% CI: 1.32-3.44, *P*=0.002). The mean scores of A1c for individuals with and without skin lesions were estimated at 10.37±5.86 and 8.91±2.62, which showed that the difference was significant (*P*=0.018). Patients with uncontrolled A1c had more skin lesions than controlled ones (73.7% vs. 55.8%, respectively; OR 2.217, 95% CI: 1.153-4.262, *P*=0.015).

**Table 3.** Effect of some variables on any skin lesion

| Factor | Category | With any skin lesion | Without lesion | Statistics | |
|---|---|---|---|---|---|
| | | Value | Value | OR (95% CI) | *P*-value |
| Age (Year) | | 49.49±14.03 | 48.37±15.25 | - | 0.512 |
| Gender | Women | 150 (77.3%) | 44 (22.7%) | 1.913 (1.194-3.065) | 0.007 |
| | Men | 98 (64.1%) | 55 (35.9%) | | |
| Age at onset (Year) | | 39.35±14.18 | 40.87±14.86 | - | 0.375 |
| Duration of DM (Year) | | 10.13±6.84 | 7.49±6.32 | | 0.001 |
| Duration of DM category (Year) | ≥10 | 124 (80%) | 31 (20%) | 2.194 (1.341-3.589) | 0.002 |
| | <10 | 124 (64.6%) | 68 (35.4%) | | |
| Type of DM | Type 2 | 197 (71.6%) | 78 (28.4%) | 1.040 (0.587-1.842) | 0.893 |
| | Type 1 | 51 (70.8%) | 21 (29.2%) | | |
| BMI | Mean (Kg/m$^2$) | 30.42±9.52 | 28.86±4.78 | - | 0.02 |
| | Obese | 133 (79.2%) | 35 (20.8%) | 2.115 (1.306-3.424) | 0.002 |
| | Non-obese | 115 (64.2%) | 64 (35.8%) | | |
| Type of treatment | Insulin±OADs | 170 (77.3%) | 50 (22.7%) | 2.136 (1.326-3.44) | 0.002 |
| | OADs | 78 (61.4%) | 49 (38.6%) | | |
| A1c | Mean | 10.37±5.86 | 8.91±2.62 | - | 0.018 |
| | <7 | 24 (55.8%) | 19 (44.2%) | 2.217 (1.153-4.262) | 0.015 |
| | ≥7 | 224 (73.7%) | 80 (26.3%) | | |

DM: Diabetes mellitus; OR: Odds ratio; CI: Confidence interval; OADs: Oral anti-diabetic drugs; BMI: Body mass index; A1c: Glycated hemoglobin

Values are presented either as a number (%) or Mean±SD. The *P*-values of < 0.05 are considered significant.

## 4. Discussion

Our findings confirmed the hypothesis that identifiable skin conditions had a higher prevalence amongst patients with diabetes. Non-infectious skin lesions were found in nearly three-quarters of the enrolled patients, which was higher than what was observed in two previous studies conducted in Iraq. In the first one, Strak (16) (Basrah, 2006) found a prevalence of 55.3%, and in the second, Yasso, Yaso (17) (Baghdad, 2013) reported the prevalence of 55%, both of which included patients with infectious and non-infectious skin lesions. The prevalence of skin lesions in the current research was similar to those reported in a study conducted by Chatterjee, Chattopadhyay (18), in which the prevalence of skin lesions was estimated at 73.9% among Indian patients with T1DM and T2DM. A meta-analysis and systematic review was performed in 2020, evaluating 22 final articles of a total sample size of 8,406 patients with diabetes; accordingly, skin lesions were prevalent in 70.3% of the population (19).

The findings of the present study showed that the most predominant skin lesions were pruritus, xerosis, acrochordon, diabetic dermopathy, AN, and lipohypertrophy with a descending pattern. The results of a local study investigating 532 diabetic patients (16) demonstrated that the most frequent skin patterns were xerosis, diabetic dermopathy, bacterial infections, pruritus, bullosis, drug-induced lipohypertrophy or lipoatrophy, diabetic ulcer, and necrobiosis lipoidica (NL) in descending order; nevertheless, AN was not reported a skin lesion, which was more prevalent in a quarter of patients in our study. Additionally, NL was rare in both the current (2.4%) and previously performed studies (1.6%). However, in the present research, it was impossible to calculate the exact percentage of each skin lesion pattern after excluding bacterial infections due to the overlapping of skin manifestations.

The higher frequency of non-infectious lesions in this study, compared to the results of the research conducted by Strak (16), might be attributed to the fact that our patients were older, and regarding this, aging leads to an increase in skin problems (20) and affected more female than male (21). Moreover, considering the DM duration, there was a wide range of DM durations in the current study, compared to that in a previous study (22). It was also revealed that there were more patients with inadequate glycemic control in the present research than in another study (23). Furthermore, obesity may be associated with higher prevalence; nonetheless, it was not addressed in the results of the study performed by Strak (16). Another research in Iraq was conducted by Yasso, Yaso (17) at several medical institutions in Baghdad on 200 patients with diabetes. The results of the mentioned research showed that the most common documented skin lesions were pruritus (27.2%), waxy skin (21.8%), thick skin (16.3%), diabetic dermopathy (14.5%), ulcers (7.27%), and NL (1.8%) in descending order, which was consistent with those of our study; however, the lesions of GA, AN, and vitiligo were not observed. Based on the findings of a study conducted in Jedda, Saudia Arabia, on 558 patients with T1DM and T2DM over a year, the prevalence of skin lesions was 96.1%. In the mentioned research, the most frequent skin disorders were reported to be xerosis (77.79%), pruritus (39.92%), diabetic dermopathy (31.34%), finger pebbles (26.67%), scleroderma (23.13%), skin tags (19.40%), and AN (12.5%). The proportion was recalculated based on the number of patients having skin lesions (n=536) rather than the total of patients (24).

The most prevalent type of lesion observed in the present study was pruritus, which was ranked the highest after infectious causes in another study (17). The results of a study carried out in Kuwait revealed that pruritus was significantly prevalent (25). Pruritus cause and effect in DM remain unproven autonomic dysfunction, metabolic abnormalities, anhydrosis, and diabetic neuropathy all may share (26).

Xerosis was the second most common skin lesion recorded in the current study. Zimmo (24) reported that xerosis was the most common lesion seen in Saudi Arabia with a prevalence rate of 74%. In another Indian study, Mishra (27) found that xerosis was the most common skin lesion accounting for the prevalence of 26.5% among 102 patients with diabetes. Other less common skin manifestations identified in this study in association with diabetes included Scleroderma diabeticorum, Necrobiosis lipoidica, and Granuloma annulare. Other lesions either were associated with diabetes or discovered by chance and warrant further research. Our study archived all skin lesions according to what was observed on each patient rather than on the basis of etiological background or whether they were associated with diabetes or not.

Skin lesions were found to be higher in females than in males at a ratio of 1.2:1 as recorded in previous studies (21, 28). This might be explained by the greater number of women consulting doctors indicating that females were more ill or more concerned about their health status (29). The chance

of getting skin manifestations rose as the duration of diabetes grew longer, and this fact was visible in this study, which was in line with the findings of other pieces of research (22, 30). Although in the present study, no significant difference was found between both types of DM in the formation of skin lesions, in other studies, T2DM had more diabetes-related skin disorders than T1DM (31). In the current study, a two-fold increase was observed in skin manifestations among obese subjects, compared to non-obese cases. Obesity was prevalent among people with diabetes since it could predispose them to metabolic syndrome, which is one of the risk factors of T2DM. Ozlu, Uzuncakmak (32) has shown the effect of obesity on DM and diabetic cutaneous manifestations; however, this effect was not significant with the BMI of less than 30 $kg/m^2$, which was in agreement with the results of our study. In this study, patients who received insulin therapy had more skin complications than those without insulin therapy, possibly because insulin users had poor glycemic control (33) and longer DM duration (34). According to our findings, poor glycemic control was associated with increased diabetic skin lesions, which was consistent with those of other studies (29, 35).

Skin lesions were reasonably common in both T1DM and T2DM with a similar percentage. The most common skin lesions to be aware of in adults with diabetes were pruritus, xerosis, diabetic dermopathy, acanthosis nigricans, acrochordon, and insulin-related lipohypertrophy. It was revealed that female gender, prolonged diabetes duration, and worse glycemic control resulted in more diabetes skin complications. Limitations of this study included that some skin lesions required biopsy confirmation; however, it was seldomly performed due to difficulties or patient's refusal. Since this study was single tertiary center research, its results cannot be applied to the entire population.

## Authors' Contribution

Study concept and design: K. I. A. H.
Acquisition of data: A. S. A. B.
Analysis and interpretation of data: A. S. A. B.
Drafting of the manuscript: A. A. M.
Critical revision of the manuscript for important intellectual content: A. S. A. B.
Statistical analysis: A. S. A. B.
Administrative, technical, and material support: A. S. A. B.

## Ethics

Ethical approval was taken from the Research Ethics Committee at College of Medicine, University of Basrah, Iraq, and written consent was recorded for each patient.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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