



# International Journal of Dermatology, Venereology and Leprosy Sciences

E-ISSN: 2664-942X

P-ISSN: 2664-9411

[www.dermatologypaper.com](http://www.dermatologypaper.com)

Derma 2020; 3(2): 88-92

Received: 07-05-2020

Accepted: 10-06-2020

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## A clinical study of cutaneous manifestations in diabetes mellitus

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**DOI:** <https://doi.org/10.33545/26649411.2020.v3.i2b.49>

### Abstract

**Background:** Diabetes mellitus (DM) is the most common endocrine disorder<sup>1</sup>. At least 30% of diabetics have some cutaneous involvement during the course of their disease<sup>1</sup>. Type II patients do develop more frequent cutaneous infections, whereas type I patients develop more autoimmune- type cutaneous lesions<sup>2,3</sup>.

**Objective:** To evaluate the prevalence and pattern of skin manifestations among diabetic patients.

**Methods:** 100 patients of diabetes mellitus with skin manifestations who consecutively attended DVL outpatient department and willing to participate in the study were enrolled in this study. Skin examination was done and findings entered to computer database for analysis.

**Results:** Among 100 patients, there were 56 males and 44 females the youngest patient being 19 years old and eldest was 77 years old. Cutaneous infections were the most commonly observed dermatoses (51%), followed by dermatoses more commonly associated with diabetes mellitus (36%), non specific dermatoses (23%), neuropathic and ischemic diabetic skin disease (5%), due to microangiopathy (4%), metabolic disorders (3%) and cutaneous reactions to therapy (3%). Among cutaneous infections, fungal infections (38%) are the most common dermatoses followed by bacterial infections (11%) and viral infections (2%). Tinea corporis was the most common fungal infection and furunculosis (3%) was most common bacterial infection. Among the common dermatoses associated with diabetes mellitus (36%) majority presented with pruritus secondary to xerosis (12 patients, 12%) followed by 11 cases (11%) of psoriasis, 4 cases of vitiligo, 2 patients each (2%) of acrochordons, lichen planus and macular amyloidosis, 1 patient each (1%) of acanthosis nigricans, alopecia universalis and kyrles disease. Among patients with non specific dermatoses, eczema was most common followed by pemphigus, acne vulgaris and hidradenitis suppurativa.

### Conclusion

Infections were the most common cutaneous manifestations in diabetes, followed by dermatoses most commonly associated with diabetes. Cutaneous manifestations are more common in patients who have overall poor glycemic control. Cutaneous manifestations can heighten the suspicion of a physician regarding the diagnosis of diabetes and help to prevent systemic derangements by early institution of appropriate treatment.

**Keywords:** Clinical study cutaneous manifestations diabetes mellitus

### Introduction

Diabetes mellitus is a heterogeneous group of disorders characterized by chronic hyperglycemia due to disturbance in carbohydrate, protein and fat metabolism, which result from either a defect in insulin action or secretion or combination of the two. It can affect all age groups and all socio-economic segments of the population. Though mechanism of most of the skin diseases in diabetes remains unknown, the pathogenesis of others is linked to abnormal carbohydrate metabolism, altered metabolic pathways, atherosclerosis, microangiopathy, neuron degeneration, and impaired host mechanism<sup>[4]</sup>.

Skin findings may be the first sign of a metabolic disturbance caused by undiagnosed diabetes, suboptimal management of known disease, or even a prediabetic state. Skin complications of diabetes can provide clues to current and past metabolic status. Recognition of cutaneous markers enables earlier diagnosis and treatment, which may slow disease progression and ultimately improve the overall prognosis<sup>[5]</sup>.

Most documented studies have shown the incidence of cutaneous disorders associated with diabetes to be in between 30% and 71%<sup>[6]</sup>.

Although, the overall prevalence is the same in IDDM and NIDDM, the former more frequently develop autoimmune type lesions, while the latter have frequent cutaneous infections [7]. No diseases of the skin are absolutely peculiar to the diabetes, yet there are diseases with higher incidence in diabetes than in non-diabetes individuals [6]. According to the study conducted in DVL department of Wenlock district hospital, Mangalore the incidence of skin diseases were more during the first five years of the diabetes compared to that of chronic diabetics. Infections both bacterial and fungal were seen in majority of patients. Infections were common in early diabetics whereas metabolic changes and specific cutaneous markers were noted in patients with diabetes for a prolonged period [8]. According to the study conducted by DK Timshina, D. Mohan Tappa *et al.*, most of the dermatoses occurring in diabetic patients were seen in the fifth decade. The distribution of dermatoses was found to be similar between males and females [9]. We did this study to evaluate the prevalence and pattern of skin manifestations among diabetic patients.

**Materials and Methods**

This is a descriptive study. 100 patients of diabetes mellitus with skin manifestations attending the Department of Dermatology, Venereology, Leprosy OPD at NRI Medical College and General Hospital, Chinakakani, Guntur were enrolled in 18 months study period from January 2019 after approval from institute ethics committee. Informed consent was taken from all patients. Inclusion Criteria included both female and male of any age group, All confirmed (old and new) cases of Diabetes Mellitus (irrespective of duration of illness). Exclusion Criteria included Patients with HIV/AIDS, Patients on immunosuppressive drugs, Patients with internal malignancy and other terminal illness, Pregnant and lactating women. In the selected patients, a detailed history with particular reference to demographic details, family history of similar complaints and of DM, duration of DM, treatment details, duration of various symptoms and evolution of lesions was taken. The diagnosis of DM was based on the International Expert Committee by the American Diabetes Association, the European Association for the Study of Diabetes, and the International Diabetes Federation has issued diagnostic criteria for DM [10].

- A Fasting Plasma Glucose level  $\geq 7.0$  mmol/L (126 mg/dL),
- A Plasma Glucose level  $\geq 11.1$  mmol/L (200 mg/dL) 2 hrs after an oral glucose challenge, or
- A Random Plasma Glucose level  $\geq 11.1$  mmol/L (200 mg/dL) accompanied by classic symptoms of DM (polyuria, polydipsia, weight loss) also is sufficient for the diagnosis of DM.
- HbA1C  $\geq 6.5\%$  warrant the diagnosis of DM.

**Following investigations were done in all the patients**

- 1) Fasting blood sugar, post prandial blood sugar, random blood sugar
- 2) Glycosylated haemoglobin (HbA1c)
- 3) Lipid profile – serum total cholesterol, serum triglycerides, VLDL, HDL, LDL.

**Results**

In the present study, peak prevalence (32%) was seen in the age group of 50-59. The youngest patient was 19 years old

and eldest was 77 years old. Number of Male patients (56%) outnumbered the females (44%). 48% Of the patients had diabetes for a duration of 1-5 years, 27% for 6-10 years and 18% for more than 10 years. Majority of the patients had type 2 diabetes (96%), while type 1 diabetes was seen in 4% of patients. 44 patients (44%) had positive family history of diabetes mellitus. Majority of the patients (36%) had random blood sugar levels in the range of 210-279mg/dl followed by 30% patients with levels 140-209mg/dl and 17% patients with levels 280-349 mg/dl.

Four patients (4%) had random blood sugar levels above 420 mg/dl. 59 patients (59%) had HbA1c levels  $>8\%$  followed by 19% patients with 7.1-8% levels and 15% patients with 6.5-7.0%. Out of the 100 patients, 55% had associated systemic illness. Among these Hypertension (48%) was the most commonly associated systemic illness followed by coronary artery disease (6%) and hypothyroidism (5%).

Some of the patients had more than one associated systemic illness. Cutaneous infections were the most commonly observed dermatoses (51%), followed by dermatoses more commonly associated with diabetes mellitus (36%), non-specific dermatoses (23%), neuropathic and ischemic diabetic skin disease (5%), due to microangiopathy (4%), metabolic disorders (3%) and cutaneous reactions to therapy (3%). Some patients had more than one type of cutaneous manifestation.

**Table 1:** Pattern of Cutaneous Manifestations

Dermatoses	No. of patients	%
Cutaneous infections	51	51
Dermatoses asso with microangiopathy	4	4
Neuropathic and ischemic diabetic skin disease	5	5
Metabolic diseases	3	3
Disorders of collagen	0	0
Dermatoses more commonly asso with dm	36	36
Cutaneous reactions to therapy for dm	3	3
Non-specific dermatoses	23	23

Amongst the 51 patients with cutaneous infections, majority had fungal infections (38%), followed by bacterial infections (11%) and viral infections (2%).

Among the 38 patients who had fungal infections, most commonly observed infection was tinea corporis in 14 patients (14%), followed by tinea cruris in 11 patients (11%), 4 cases (4%) Of candidal balanoposthitis, 3 cases each (3%) of candidal intertrigo, p.versicolor, 2 cases (2%) of candidal vulvovaginitis and 1 case (1%) of chronic paronychia. Some patients presented with more than one fungal infection.

Among the 11 patients who had bacterial infections the most commonly observed infection was furunculosis in 3 patients (3%) followed by 2 patients each (2%) of folliculitis and cellulitis. 1 patient each (1%) of ecthyma, erysipelas, abscess and carbuncle.

**Table 2:** Bacterial infections

Bacterial infections	No. Of cases
Furunculosis	3
Folliculitis	2
Cellulitis	2
Ecthyma	1
Erysipelas	1
Abscess	1
Carbuncle	1

**Table 3:** Fungal infections

Fungal infections	No. of cases
T. Cruris	11
T. Corporis	14
Candidial intertrigo	3
P. Versicolor	3
Candidial Balanoposthitis	4
Candidial Vulvo vaginitis	2
Chronic paronychia	1

Out of the hundred patients studied, 4 patients (4%) presented with dermatoses due to microangiopathy of which 3 patients had diabetic dermopathy and 1 patient had diabetic bullae. Out of 100 patients, Six patients presented with neuropathic and ischemic diabetic skin disease. 3 patients (3%) had diabetic foot ulcers and (3%) patients had fissure feet. Three patients (3%) presented with metabolic conditions associated with diabetes mellitus. One case each of xanthomas, scleredema adultorum of buschke and xanthelasma palpebrarum was reported. Among the common dermatoses associated with diabetes mellitus (36%), majority presented with pruritus secondary to xerosis (12 patients, 12%) followed by 11 cases (11%) of psoriasis, 4 cases of vitiligo, 2 patients each (2%) of acrochordons, lichen planus, macular amyloidosis, 1 patient each (1%) of acanthosis nigricans, alopecia universalis and kyrles disease. Some of the patients had more than one type of dermatoses which are commonly associated with DM. Among patients with cutaneous reactions to diabetic therapy (3%), 3 patients (3%) presented with acute urticaria secondary to insulin therapy. Out of 100 patients, 23 patients (23%) presented with non specific dermatoses. Among them eczema was the most common dermatoses observed in 9 patients (9%), followed by 2 patients each (2%) of pemphigus, acne vulgaris and hidradenitis suppurativa.

**Table 4:** Dermatoses commonly associated with Diabetes Mellitus

Dermatoses	No. of cases
Pruritus sec to xerosis	12
Psoriasis	11
Vitiligo	4
Acrochordons	2
Lichen planus	2
Macular amyloidosis	2
Acanthosis nigricans	1
Alopecia universalis	1
Kyrles disease	1

### Discussion

In the present study of 100 patients of DM with cutaneous manifestations, majority belonged to the 5<sup>th</sup> and 4<sup>th</sup> decade with 32% and 24% respectively. The frequencies of patients with cutaneous manifestations in the first, second, third, sixth and seventh decade is 1%, 3%, 8%, 19% and 13% respectively. Similar frequencies were reported by various studies carried out by Mahajan *et al.*<sup>11</sup>, Sawhney *et al.*<sup>12</sup> and Nigam *et al.*<sup>13</sup>, which are well in accordance with the above frequencies. The relative increase in the incidence of cutaneous involvement with age in diabetic patients may be attributed merely to the decreased resistance of body as well as long duration of diabetes in these patients.

### Sex distribution

In the present study male diabetics were more prone for

cutaneous manifestations than females (56% vs 44%), which was also observed by sawhney *et al.*<sup>12</sup>, Rao *et al.*<sup>14</sup>, Al-Mutairi *et al.*<sup>15</sup>.

Mahajan *et al.*<sup>11</sup>, Bhat *et al.*<sup>16</sup> and Nigam *et al.*<sup>13</sup> reported that female diabetic patients had significantly higher incidence of cutaneous manifestations.

### Duration of diabetes

In the present study 48% of the patients had diabetes for a duration of 1–5 years and 27% patients for 6–10 years. According to Bhat *et al.*<sup>16</sup>, majority of diabetic patients with cutaneous manifestations had 1–5 years of duration of DM (37.37%) followed by 6–10 years (24.24%). Rao *et al.*<sup>14</sup> reported that majority of skin manifestations occurred within five years of diagnosis of diabetes. As duration of diabetes increases there is non- enzymatic glycosylation of dermal collagen and mucopolysaccharides, leading to various cutaneous manifestations<sup>16</sup>. Infections were more common during early diabetes, probably due to decrease in the host defense mechanism and decreased phagocytic activity, which is noticed immediately in uncontrolled diabetes.

### Type of diabetes mellitus

Non-insulin dependent diabetes mellitus (type 2 DM) was most commonly observed (96%) as compared to insulin dependent diabetes mellitus (type 1DM) (4%). This reflects the general distribution pattern of type 1 and type 2 DM cases in world population. No difference in the prevalence of cutaneous disorders between type 1 and type 2 DM has been noted<sup>15,16</sup>.

Similar observations of type 2 diabetes being more common was observed in studies conducted by Mahajan *et al.*<sup>11</sup> (98%), Sawhney *et al.*<sup>12</sup> (80%), Bhat *et al.*<sup>16</sup> (97.7%), Nigam *et al.*<sup>13</sup> (82.1%) and Al-Mutairi *et al.* (93%)<sup>15</sup>.

### Random blood sugar levels:

Majority of the patients had random blood sugar levels in the range of 210-279 mg/d (36%), followed by 30% patients with levels 140-209 mg/dl.

### Hba1c levels

Among the 100 diabetic patients with cutaneous manifestations, 19 patients (19%) had moderate control of DM with Hba1c levels in the range of 7.1%-8%, while 59 patients (59%) had a poor control of DM with Hba1c levels >8%. In a study conducted by Nigam *et al.*<sup>13</sup>, uncontrolled diabetes was observed in 52% of cases. The incidence of cutaneous diseases in patients with uncontrolled diabetes mellitus was 70.2% while it was only 51% in patients with controlled diabetes. Studies conducted by Bhat *et al.*<sup>16</sup>, Sawhney *et al.*<sup>12</sup>, Yosipovitch *et al.*<sup>17</sup> also found majority of diabetic patients with skin lesions having uncontrolled diabetes. Uncontrolled diabetes increases the risk of development of microangiopathy related complications or sequelae<sup>16</sup> and predisposes skin for various infections<sup>13</sup>. A study conducted by Raghunatha *et al.*<sup>18</sup> showed well controlled diabetes in majority of the patients.

### Associated systemic illnesses

Of the 100 patients, 55 patients (55%) had associated systemic co-morbidity, such as hypertension in 48 patients (48%), coronary artery disease in 6 patients (6%) and hypothyroidism in 5 patients (5%). According to Mahajan *et*

*al.* <sup>[11]</sup>, 53.1% patients were hypertensive. Similar frequencies were reported by Bhat *et al.* <sup>[16]</sup> (46.46%), Al-Mutairi *et al.* <sup>[15]</sup> (44%) and Nigam *et al.* <sup>[13]</sup>, where in hypertension was the most common associated systemic disease. Hypertension has been hypothesized to accelerate the process of microangiopathy in diabetics <sup>[15]</sup>.

### Pattern of cutaneous manifestations

In the present study, among the various dermatological manifestations, infections were the most common dermatoses (51%), followed by dermatoses more commonly associated with diabetes mellitus (36%), non-specific dermatoses (23%), neuropathic and ischemic diabetic skin disease (5%), due to microangiopathy (4%), metabolic disorders (3%), cutaneous reactions to therapy for diabetes (3%). Some patients had more than one type of cutaneous manifestations. Similar findings were reported by other studies (Mahajan *et al.* <sup>[11]</sup>, Rao *et al.* <sup>[14]</sup>, Bhat *et al.* <sup>[16]</sup>, Nigam *et al.* <sup>[13]</sup>, Al-Mutairi *et al.* <sup>[15]</sup>).

High incidence of infections was due to following factors:

1. Hyperosmolality of the hyperglycemic serum which causes diminished chemotaxis.
2. There is impaired release of cytokines as a consequence of lack of insulin.
3. Impaired phagocytosis may be due to diminished leucocyte response caused by thickening of capillary valves.
4. Microangiopathy, atherosclerosis, micro aneurysms, increased mast cells in the upper dermis and elevated glucose levels <sup>[19]</sup>.

### Cutaneous infections

Amongst the 51 patients (51%) with cutaneous infections, majority had fungal infections (38%), followed by bacterial infections (11%) and viral infections (2%). This is accordance with other studies where fungal infections were more common, as observed by Mahajan *et al.* <sup>[11]</sup> (54.68%), Bhat *et al.* <sup>[16]</sup> (34.34%) and Al-Mutairi *et al.* <sup>[15]</sup> (68%). Amongst the 51 patients (51%) with cutaneous infections, majority had fungal infections (38%), followed by bacterial infections (11%) and viral infections (2%). This is in accordance with other studies where fungal infections were more common, as observed by Mahajan *et al.* <sup>[11]</sup> (54.68%), Bhat *et al.* <sup>[16]</sup> (34.34%) and Al-Mutairi *et al.* <sup>[15]</sup> (68%). 4 patients presented with dermatoses due to microangiopathy of which 3 patients (3%) had diabetic dermopathy and 1 patient (1%) had diabetic bullae.

Most of the western studies report a high frequency of diabetic dermopathy (50%), as compared to 17.8% in Indian patients. Nigam *et al.* <sup>[13]</sup> reported 6 cases (3.5%) of diabetic dermopathy and 2 cases (1%) of diabetic bullae. Similarly, Mahajan *et al.* <sup>[11]</sup>, in their study of 100 diabetics, found diabetic dermopathy in 6 patients and 2 cases of diabetic bullae. While a comprehensive review on the subject considers diabetic dermopathy to be the most common manifestation, we did not observe it to be so common. Skin manifestations due to diabetic microangiopathies are usually seen in chronic diabetes because the deposition of PAS-positive material within the lumina of the blood vessels occurs slowly in the disease process.

### Neuropathic and ischemic diabetic skin disease:

Six patients presented with neuropathic and ischemic diabetic skin disease. 3 patients (3%) had diabetic foot

ulcers and (3%) 3 patients had fissure feet. Bhat *et al.* <sup>[16]</sup>, in their study, observed 4 cases of diabetic foot ulcers. According to Mahajan *et al.* <sup>[11]</sup>, Rao *et al.* <sup>[14]</sup>, Nigam *et al.* <sup>[13]</sup>, Al-Mutairi *et al.* <sup>[15]</sup>, diabetic foot ulcers were reported in frequencies of 8,1, 6 and 2% respectively. In the present study, 3 cases of diabetic foot ulcers were observed, which is well in accordance with the study by Bhat *et al.* <sup>[16]</sup> and Al-Mutairi *et al.* <sup>[15]</sup>.

### Metabolic conditions affecting diabetic skin

Out of the 100 diabetic patients 3 patients (3%) each had xanthomas, scleredema adultorum of buschke and xanthelasma palpebrarum. Rao *et al.* <sup>[14]</sup> reported 2 cases of xanthelasma palpebrarum, whereas Bhat *et al.* <sup>[16]</sup> observed xanthelasma palpebrarum in 4 cases. Eruptive xanthomas-though rare are found mainly in untreated DM and hypertriglyceridemia, whereas xanthelasma palpebrarum is very frequently associated with DM and hyperlipidaemia. Eruptive xanthoma mainly occurs in type 1 DM, but no definite relations between DM and hyperlipidaemia can be ascertained as they are also found in normal subjects <sup>[20]</sup>.

### Dermatoses more commonly associated with diabetes:

Majority presented with pruritus secondary to xerosis (12 patients, 12%) followed by 11 cases (11%) of psoriasis, 4 cases of vitiligo, 2 patients each (2%) of acrochordons, lichen planus, macular amyloidosis, 1 patient each (1%) of acanthosis nigricans, alopecia universalis and kyrles disease. Some of the patients had more than one type of dermatoses which are commonly associated with DM. The above mentioned dermatoses have been reported previously in studies conducted by Paron *et al.* <sup>[21]</sup> and Al-Mutairi *et al.* <sup>[15]</sup>. Autonomic neuropathy or age of stratum corneum proteins has been attributed to the pathogenesis of xerosis and pruritus <sup>[18]</sup>.

Acanthosis nigricans and acrochordons are manifestations of insulin resistance, which may be present before the expression of DM. Increased levels of insulin act on insulin like growth factor (IGF) receptors, resulting in the development of acanthosis nigricans. Association between multiple acrochordons and DM has been reported.

Skin tags often associated with obesity were observed in 26% of type 2 DM as stated by Kahana *et al.* <sup>[22]</sup>. This study showed that incidence of skin tags in diabetes was 2% (2 cases) and mostly associated with obesity, acanthosis nigricans and type 2 DM. Acanthosis nigricans may be considered as a prognostic indicator for the development of type 2 DM as stated by Stuart CA *et al.* <sup>[23]</sup>. Again acanthosis nigricans occurred in 66% of children who weighed 200% more of their ideal body weight.

In the diabetic population, the incidence of lichen planus has been recorded as 1.6% by Lozada-Nur *et al.* <sup>[24]</sup> and Jain *et al.* <sup>[25]</sup>. This study showed that incidence of lichen planus was 2%. An association between psoriasis and increased cardiovascular risk and metabolic syndrome has been reported <sup>[18]</sup>. In a study by Nigam *et al.* <sup>[13]</sup>, dermatoses associated with an increased incidence of DM, like vitiligo (4), lichen planus (2) and acquired perforating dermatoses (3) were detected. Certain dermatoses with underlying pathogenesis like vitiligo are known to occur in DM as a part of polyglandular autoimmune syndrome. Oral lichen planus has been suggested to occur with increased frequency in DM <sup>[18]</sup>. However, such an association was not noticed in several other studies including the present one.

### Cutaneous reactions to therapy for diabetes

Of the 98 patients on diabetic treatment, only 3 patients (3%) presented with acute urticaria secondary to insulin therapy. The use of highly purified and recombinant insulin reduces the prevalence of insulin reactions. Lower prevalence of insulin reactions in the present study may be due to the use of human insulin. Lipodystrophy either in the form of lipoatrophy or lipohypertrophy is associated with insulin of older type and is rare with the newer, purified human insulin these days. The prevalence of skin rashes in patients on oral hypoglycemic agents (OHAs) are 1% to 5% mainly with sulfonylureas, and maculopapular rash was the commonest form as stated by Paron *et al.* [21].

### Conclusion

Infections were the most common cutaneous manifestations in diabetes, followed by dermatoses most commonly associated with diabetes. Cutaneous manifestations are more common in patients who have overall poor glycemic control which in turn is reflected by high HbA1c value.

Cutaneous manifestations can heighten the suspicion of a physician regarding the diagnosis of diabetes. This further helps to prevent systemic derangements by early institution of appropriate treatment. Proper skin care and long-term control of blood glucose levels may reduce the risk of some of the skin lesions in diabetic subjects. Dermatologists play an important role in reducing dermatologic morbidity, improvement of quality of life and management strategy of diabetic patients.

### Declarations

**Funding:** No funding sources

**Conflict of interest:** None declared

**Ethical Approval:** The study was approved by the institutional ethics committee

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