

Study on Cutaneous Manifestations of Diabetes Mellitus and to Correlate these with Complications of Diabetes

Venkatavishnu Veeravalli¹

¹Faculty, Department of Dermatology, Calicut University, Thenhpalam, Kerala 673635, India

Sri Sathya Naga Mallika Bokka²

²Oral Pathologist, Department of Oral Pathology, NTR University, Hyderabad, Telangana 500075, India

Umarajan³

³Professor, Department of Dermatology, Calicut university, Thenhpalam, Kerala 673635, India

ABSTRACT

Diabetes is the most common endocrine disorder, affecting 8.3% of the population. Skin disorders will be present in around 60 % to 90% of people with diabetes. A study of 300 patients with diabetes found that the most common skin manifestations were cutaneous infections, xerosis, and inflammatory skin diseases. Individuals with type 2 diabetes are more likely than those with type 1 diabetes to develop cutaneous manifestations. Cutaneous disease can appear as the first sign of diabetes or may develop at any time in the course of the disease. This review provides a brief overview of skin conditions that primary care providers (PCPs) may encounter when treating patients with diabetes.

INTRODUCTION

Long standing diabetes mellitus can lead to permanent and irreversible functional changes in the cells of the body leading to various complications involving multiple organ systems.

Abnormal carbohydrate metabolism, atherosclerosis, microangiopathy, neuronal degeneration and impaired host mechanisms, all contribute to the pathogenesis of cutaneous complications.¹⁸ Though cutaneous manifestations of DM generally appear subsequent to the development of the disease, it may be the presenting sign, or may even precede the primary disease manifestation.²⁰⁰

CUTANEOUS MANIFESTATIONS OF DIABETES

Classification¹⁵

Cutaneous lesions and other visible disorders associated with diabetes mellitus.

1. Infections:

- **Bacterial infections**– Primary bacterial infections mainly by staphylococcus aureus, Malignant external otitis (Pseudomonas aeruginosa), Necrotizing fasciitis (gram-positive, gram

negative and anaerobic mixed infections), and Erythrasma.

- **Mycotic** - Superficial (Dermatophytosis and candidiasis)
- Deep (mucormycosis).

2. Skin changes thought to be related to microangiopathy:

- Punched out skin ulcers on lower legs
- Necrobiosis lipoidica diabetorum
- Diabetic dermopathy
- Bullous eruptions of diabetes
- Rubeosis

3. Skin changes thought to be related to neuropathy

- Neuropathic ulcers (mal perforans)
- Charcot joints

4. Skin changes thought to be related to macrovascular insufficiency

- Ischemic skin ulcers and digital gangrene
- Erysipelas – like erythema

5. Skin changes related to lipodystrophy

- Insulin injection sites lipodystrophy

- Syndromes of lipodystrophy and diabetes [seip– Bernardinelli syndrome) and acquired lipodystrophy (Lawrence-Seip syndrome)]

6. Other skin diseases that may be associated with diabetes

- Granuloma annulare
- Scleredema diabeticorum (adultorum)
- Eruptive xanthomas
- Perforating cutaneous diseases of diabetes
- Pruritus
- Vitiligo
- Acanthosis nigricans

7. Drug reactions

AIM OF THE STUDY

- To analyze the pattern of various cutaneous manifestations in diabetes mellitus
- To correlate these findings with complications of diabetes mellitus.

MATERIALS AND METHODS

Three hundred known diabetic patients irrespective of age, sex, type of diabetes and treatment attending the diabetes clinic, Medicine O.P.D and wards at Calicut Medical college were included in the study.

The study was conducted from march 2011 to march 2012. Pregnant women and those on systemic corticosteroid therapy were not included in the study.

Detailed general examination, systemic and dermatological examinations were done in every case. The details were recorded on a proforma for each patient.

Relevant investigations for the diagnosis of cutaneous manifestations & for assessing the complications of diabetes were done in all patients wherever necessary.

RESULTS

1. 126 (42%) patients were males and 174 (58%) patients were females. The majority of patients (90%) were above 39 years age. Maximum (33%) patients were 5-10 years duration of diabetes.
2. 288 (94.12%) patients were suffering from type-2 diabetes and only a small number 12 (5.88%) patients were with type-1 diabetes.

3. Of the total, 186(62%) patients were having uncontrolled, and 114(38%) patients had controlled diabetic status.
4. Cutaneous manifestations were observed in 270(90%) patients and 30(10%) patients did not have any associated skin lesions.
5. Cutaneous manifestations were the initial presentation of diabetes in 36(12%) patients.
6. Major systemic complications were present in 100(33.33%) cases.
7. Most common systemic complication observed was hypertension seen in 91(49.1%) cases and the least common complication was peripheral vascular disease seen in 4(1.48%) cases.
8. Majority 160 (59.25%) patients with cutaneous manifestations and Most of the 69 (69%) patients with complications had uncontrolled diabetes mellitus.
9. In our study a higher percentage (68.11%) of patients with cutaneous manifestations had systemic complications.
10. None of the patients with no cutaneous manifestations had complications except the one with hypertension (3.33%).
11. Most common cutaneous manifestations observed were candidal infections 111 (37%), followed by bacterial infections 78(26%) patients. And the least common was diabetic bullae seen in one (0.37%) patient.
12. Higher percentage of bacterial and fungal infections was seen especially in patients with complications like nephropathy & neuropathy.
13. Among cutaneous manifestations related to microangiopathy, dermatopathy in 36(12%) & necrobiosis lipoidica diabeticorum in 6 (2%) cases were observed.
14. All dermatopathy (100%) patients showed some form of renal involvement and 50% patients had retinopathy and 33% had neuropathy.
15. 50% patients with necrobiosis lipoidica had combined diabetic nephropathy, neuropathy, retinopathy and also hypertension.
16. Only one patient had diabetic bullae and was associated with peripheral neuropathy.
17. Disseminated granuloma annulare -both annular & papular types were observed in the study.
18. Nine (3%) patients had scleredema in that three (33.33%) patients had combined

- nephropathy, neuropathy, retinopathy and hypertension.
19. 2 (0.7%) patients had waxy skin and stiff joints both are young and not associated with any systemic complications
 20. Finger pebbles were observed in 2 (0.7%) patients; both were males and manual labourers.
 21. Changes like Waxy skin with stiff joints, and Finger pebbles are less commonly associated with systemic complications.
 22. Dupuytren's contracture was observed in six (2%) patients
 23. Xanthelasma palpebrarum was seen in six (2%) patients. All were with elevated serum cholesterol & three (50%) patients had coronary artery disease and hypertension.
 24. 12(4%) patients had Kyrle's disease out of which 8(66.66%) had coexisting nephropathy and hypertension.
 25. Three (1%) patients had earlobe crease, all were associated with coronary artery disease & two (66.66%) patients had retinopathy.
 26. 33(11%) had generalized pruritus and all patients had dryness with associated nephropathy or neuropathy.
 27. Acanthosis nigricans with multiple skin tags was a common finding in diabetics.
 28. 18(6.66%) patients had trophic ulcers & all had associated peripheral neuropathy.
 29. Three (1%) patients had lichen planus & all had coexisting hypertension making the triad of Grinspan's syndrome with diabetes.
 30. Both insulin lipoatrophy & lipohypertrophy were observed in this study and all patients complicated with neuropathy, retinopathy and nephropathy.
 31. Yellow nails were seen in 18(6%) patients. Three (1%) patients showed nephropathy and had white nails with Beau's lines.
 32. Pedal oedema was observed in 49(13%) patients. Among them 24 (61.54%) patients had associated nephropathy and or neuropathy. In the remaining 15(38.46%) patients, no obvious cause could be found out.

DISCUSSION

The study population comprised of 42% males & 58% females. Majority (94.1%) of patients were

suffering from type-2 diabetes and only a small number (5.88%) patients were with type-1 diabetes. Of the total 62% patients were having uncontrolled, and 38% patients had controlled diabetic status. These results are similar to reports by Shawney et al.⁵² Majority (59.2%) patients with cutaneous manifestations and most of the (69%) patients with complications had uncontrolled diabetes mellitus.

90% patients in this study had some kind of cutaneous manifestations. The most common cutaneous manifestations observed were candidal infections (37%), followed by bacterial infections (26%) and the least common was diabetic bullae seen in one (0.3%) patient.

Major systemic complications were present in 33.33% cases and most common systemic complication observed was hypertension (49.1%) followed by Neuropathy & coronary artery disease (12.9%) each respectively. Nephropathy in (11.8%), Retinopathy in (10.8%), cases were observed and the least common complication was peripheral vascular disease seen in 1.4% cases.

Our study showed a higher percentage (68.1%) of patients with cutaneous manifestations had systemic complications like hypertension, coronary artery disease, peripheral vascular disease, nephropathy, retinopathy and peripheral neuropathy as compared to diabetic patients without cutaneous manifestations (3.33%), none of the patients with no cutaneous manifestations had complications except the one patient was having hypertension (3.33%).

Bacterial Infections

Bacterial infections were found in 26% patients. 92.3% of patients with bacterial infections had uncontrolled diabetes.

Hypertension was seen in (38%) patients and (13.5%), (16.2%), (6.4%), (1.8%) patients had nephropathy, neuropathy, retinopathy, and peripheral vascular disease respectively.

Majority of nephropathy (68%), neuropathy (66%) and (50%) PVD patients had some or the other bacterial infections.

Candidal Infections

37% patients had candidal infections. Among them 83.8% of patients had uncontrolled diabetes. 26% patients had chronic paronychia.

Intertrigo was observed in 12% patients. It is reported to be more common in diabetics²⁸. Vaginitis was found in only 1% patient. Balanoposthitis was present in 2% patients. In one of them it was the presenting manifestation of diabetes. It is reported that balanoposthitis may be the presenting manifestation of diabetes.

Tinea versicolor

Tinea versicolor was found in 10% patients. Mendel et al³⁹

Dermatophytosis

Dermatophytosis was found in 5% patients. Onychomycosis was observed in 5% patients. 15% patients in the present study had dystrophic toe nails. In the present study, all patients with onychomycosis had uncontrolled diabetes. The commonest presentation was distal subungual onychomycosis. All together superficial fungal infections were noted in 57% patients. Of the total, (28.8%), (13.5%), (16.2%), (4.5%), (1.8%) patients had hypertension, nephropathy, neuropathy, retinopathy, and PVD respectively in all superficial fungal infections. Like bacterial infections, majority of nephropathy (68.1%), neuropathy (75%), and half of the peripheral vascular disease patients had superficial fungal infections.

Diabetic Dermopathy

In the present study 12% patients were found to have diabetic dermopathy. All patients were above the age of 30 and the maximum number of cases (75%) were seen in age group over 60 years. The constant site of dermopathy noted in this study was the legs. Three patients had lesions over thighs and forearms. All the (100%) patients with the dermopathy had some form of renal involvement as evidenced by overt nephropathy in 25% and microalbuminuria in the remaining 75% cases. 50% had retinopathy and 33% had neuropathy.

Necrobiosis lipoidica diabetorum (NLD)

2% patients had NLD. The reported prevalence of NLD is 0.3%⁶². 66% patients were females and 34% were males. The patients were over 60 years of age. All patients had multiple lesions,

bilaterally and asymmetrically distributed over both legs. In this study 33.33% patients had ulceration.

50% patients had combined diabetic nephropathy, neuropathy, retinopathy and also hypertension.

Diabetic bullae

Only one (0.37%) patient had diabetic bullae. 51-year-old male was having history of 7 years duration of diabetes. Lesions were present bilaterally symmetrically over the dorsum of the feet.

Patient also had peripheral neuropathy. It is reported to be associated with neuropathy.^{4,79}

Granuloma annulare

Disseminated granuloma annulare was found in 2% patients. The male to female ratio in the present study was 1:1. In the present study 83.3% patients had annular lesions and 16.6% had papular lesions. Dabski and Winkelmann¹⁰⁵ has reported that 67% of their patients had annular lesions and 33% had non-annular lesion. Related to complications 66% patients had hypertension.

Scleredema diabetorum

9(3%) of patients had scleredema diabetorum. The male to female ratio was 2:1 in the present study. All patients were above 50 years of age. In this study also all patients had duration of diabetes more than 6 years and two (66.66%) patients had duration of 15 years. This study shows that scleredema is more common in male patients with prolonged duration of diabetes and increasing age.

In this study 33.33% patients had combined nephropathy, retinopathy, neuropathy and hypertension. This is comparable to the usual observation that scleredema is more in middle aged patients with a high frequency of other diabetic end organ damage⁵ and 66.66% patients had uncontrolled diabetes in the present study.

Waxy skin with stiff joints

In this study two (0.7%) patients had Waxy skin with stiff joints, both are males one patient was 25 and other was 29 years old. Mean duration of DM was three years.

None of the patients had systemic complications

probably because of younger age group and lesser duration of diabetes.

Finger pebbles

Finger pebbles were found in only two (0.7%) patients. Both were males. Both the patients with finger pebbles in the present study were manual labourers. Pebbled appearance of fingers is reported to be common among manual labourers¹¹⁷.

Out of two, one (50%) patient had coexisting hypertension.

Dupuytren's contracture

This was observed in six (2%) patients. In this study all were males, and among six, four were (66%) manual labourers Mean duration of age was 55 years and Mean duration of diabetes was 5 years.

Three patients (50%) had hypertension and one (16.6%) had nephropathy. These complications could be a part of diabetes spectrum.

Xanthelasma palpebrarum

Six (2%) patients had Xanthelasma. All patients were over 50 years of age and the male to female ratio was 1:1. The condition is commonly reported in middle aged women.⁵

All patients had serum cholesterol 200 and above. Elevated serum cholesterol is seen in about 50% of patients with xanthelasma¹³⁵. Three (50%) patients had coronary artery heart disease and hypertension. Xanthelasmas are suggestive of underlying hypercholesterolemia as is observed in this study.

Kyrle's disease

Kyrle's disease was seen in 12 (4%) patients. All patients were more than 55 years of age, as kyrle's disease mainly affects adults.⁶ In all patients, the lesions were mainly in upper and lower limbs as is commonly reported.⁶

It occurs more frequently in patients with co-existing nephropathy.⁵ In the present study also eight out of the 12 (66.66%) patients had co-existing nephropathy and hypertension.

Ear lobe crease

This was present in three (1%) patients. All were males of more than 55 years age, with duration of diabetes more than five years.

All patients (100%) had history of coronary artery disease. Elliot¹⁸⁰ has reported ear lobe crease as a marker of coronary artery heart disease, as is true in this patient. Anderson et al¹⁸¹ has reported the association between ear lobe crease and diabetic retinopathy in this study two (66.66%) patients had retinopathy.

Pruritus

33 (11%) patients had generalized pruritus. All of them had associated dryness of skin with nephropathy or neuropathy.

18 (6%) patients had genital pruritus. 15 were females and three were males. 12(66.66%) of them had associated intertrigo of groin and three (16.66%) had vaginitis which itself can account for their genital pruritus. The remaining three (16.66%) patients had uncontrolled diabetes and glycosuria.

Acanthosis nigricans

Acanthosis nigricans was observed in 39 (13%) patients. In this study acanthosis nigricans was more common in females. The commonest sites affected were neck, axillae and groins as is commonly reported.^{155, 156} 15 patients had associated multiple skin tags also. Among these 30(76%) patients were either obese or over weight. Related to complications 10(25.64%) patients had hypertension and five (12.32%) had nephropathy. This could be a chance occurrence.

Skin tags

Skin tags were present in 54 (18%) patients. In this study most of the patients (95%) were more than 40 years of age. All patients had multiple skin tags and 24 (44.44%) patients had involvement of multiple sites.

In total of 54 eight (14.8%) patients had hypertension, and four (7.4%) had coronary artery disease.

Cherry angiomas

36 (12%) patients had cherry angiomas. All these patients were elderly people more than 55 years of age.

Among 36 only Two (5.5%) patients had hypertension.

Seborrheic keratosis.

Observed in 36(12%) patients, all were more than 40 years of age, and having multiple lesions. Commonest site was face and the upper trunk. 22(66.66%) cases had associated skin tags and 15 (41.66%) patients had acanthosis nigricans. Among 36 eight (22.22%) patients had hypertension and four (11.11%) had coronary artery disease.

Lichen planus

In this study lichen planus was observed in only three (1%) patients and all had oral lesions.

Insulin reactions

Three (3%) patients had insulin reactions. and all three were having uncontrolled diabetic status. Insulin lipoatrophy was observed in one (0.01%) patient. It is reported to occur in 37% of IDDM patients on conventional insulin, more commonly in females.⁹⁹ In our study also lipoatrophy was observed in a female who was on conventional insulin.

Insulin lipohypertrophy was observed in one (0.01%) patient. This is reported in 20% of patients on highly purified insulin, more commonly on males.¹⁰⁰ In this study also lipohypertrophy was observed in a male patient who has used both conventional and highly purified insulin. The lipohypertrophy might have followed the use of purified insulin.

Atrophic scars following insulin injections were found in one (0.01%) patient. Local inflammation and necrosis leading to varioliform scars has been reported following intra cutaneous injections of insulin.¹⁰⁰

All three (100%) had combined retinopathy, neuropathy and nephropathy.

Trophic ulcer

18 (6%) patients had trophic ulcers involving the foot. The commonest site of ulceration was the heel in the present study, but the usual site reported is the ball of big toe.^{6,90}

All (100%) these patients had associated neuropathy and 10 (55.55%) patients had combined retinopathy, nephropathy, and

neuropathy and one (5.55%) patient was having peripheral vascular disease.

Nail changes

Yellow nails were seen in 18(6%) patients. 45(15%) patients had hyper pigmentation and dystrophy of the nail plate without demonstrable fungus, but had associated paronychia. Nail dystrophy can also be attributed to the vascular disturbances and neuropathy associated with diabetes.

Three (1%) patients had white nails with Beau's lines. This patient had associated nephropathy, which can account for the nail change.

Pedal Oedema

Pedal oedema was observed in 13% patients. Among them 61.5% patients had associated nephropathy and or neuropathy which could explain the pedal oedema.

CONCLUSION

In this study about 90% of patients had skin manifestations due to diabetes mellitus and the cutaneous lesions often reflected the underlying systemic involvement. The above-mentioned features were more common in those with uncontrolled DM and in patients with systemic complications.

Both systemic and dermatologic manifestations were the result of a combined effect of hyperglycemia, microvascular angiopathies and impaired host immune mechanisms.

Hence, I conclude that a better glycemic control offers some protection against major organ involvement in DM. Another important highlight of this study is the significance of careful dermatologic examination as a diagnostic and prognostic tool in this common endocrinopathy.

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