Cutaneous manifestations in diabetes mellitus: A study among 500 patients in a tertiary care center in South India

Siddagangaiah Vathsala1, Sambasiviah Chidambara Murthy2*, Jammatige Shashibhusan3

1Assistant Professor, 2Associate Professor, 3Professor, 12Dept. of Dermatology, Venereology and Leprosy, 2Dept. of General Medicine, 1Shridevi Institute of Medical Sciences and Research Hospital, Tumkur, Karnataka, 23Vijayanagar Institute of Medical Sciences, Bellary, Karnataka, India

Corresponding Author: Sambasiviah Chidambara Murthy
Email: chidumurthy@rediffmail.com

Abstract
Introduction and Objectives: Mucocutaneous manifestations are seen at one or the other time in diabetes mellitus. The frequency and type of manifestation may be related to the glycemic control and duration of diabetes. This study was conducted to find the hospital based prevalence of mucocutaneous manifestations in patients with diabetes mellitus, their clinical pattern and relationship with glycemic control and duration of the disease.

Materials and Methods: Five hundred consecutive patients with diabetes mellitus attending medicine and dermatology OPD were included. Detailed history, clinical examination and investigations were done. Those with gestational diabetes, HIV, internal malignancy, other terminal illnesses and steroid-induced hyperglycemia were excluded.

Results: Male to female ratio was 1.63:1. Mucocutaneous manifestations were present in 414(82.6%) patients. Among the various cutaneous manifestations, majority were the dermatoses commonly associated with diabetes, 254(50.8%), followed by cutaneous infections, 219(43.8%). Among the cutaneous infections, fungal infections, 165(33%) were the commonest. There was a statistically significant (p < 0.05) increase in cutaneous manifestations in patients who had poor glycemic control compared to good and moderate control. Cutaneous manifestations were more common in patients with diabetes of more than 5 years duration and was statistically significant.

Conclusion: Mucocutaneous involvement is common among patients with diabetes mellitus, especially in poorly controlled disease. Cutaneous manifestations increase with the duration of the diabetes. Proper skin care and long-term control of blood glucose levels may reduce the risk of development of some of the skin lesions and improve the quality of life in diabetic subjects.

Keywords: Diabetes, Glycemic control, HbA1c levels, Mucocutaneous manifestations.

Introduction
Skin is a window through which internal organs can be visualised. Many a times, skin manifestations may help in the diagnosis of internal diseases. Cutaneous manifestations play a significant role in the early diagnosis and management of the disease. Diabetes mellitus (DM) is one of the commonest endocrine disorders. The prevalence of DM is increasing worldwide, possibly due to the change in lifestyle, dietary habits and many more factors.

Cutaneous manifestations of DM may vary depending on the duration of the disease and glycemic control. Almost all patients with DM eventually manifest skin changes due to the long-term effects of hyperglycemia on microcirculation and skin collagen. Also, anti diabetic drugs can be associated with cutaneous side effects. Furthermore, diabetes-related cutaneous lesions may serve as a portal of entry for microorganisms and eventual secondary infections.

Although cutaneous manifestations appear subsequent to the development of DM, they may be the first/presenting sign or even precede the diagnosis of diabetes by years. Thus, skin manifestations may help in early diagnosis of diabetes.

The measurement of glycated haemoglobin (HbA1c) is the standard method of assessing long term glucose control. Pattern of skin manifestations may vary depending on the glycemic control, measured by levels of HbA1c. Further, the pattern of cutaneous manifestations may also vary with the duration of the disease. Hence we did this study to find the hospital based prevalence of mucocutaneous manifestations in patients with DM, the clinical pattern of mucocutaneous lesions among them and the relation of these mucocutaneous manifestations with the glycemic control and the duration of diabetes.

Materials and Methods
Institutional ethical committee clearance was obtained before starting the study. Five hundred consecutive patients with DM attending medicine and dermatology OPD of our hospital, over a period of 12 months (January 2013 to December 2013) irrespective of duration of diabetes willing to participate in the study were included. Those with gestational diabetes, HIV, internal malignancy, other terminal illnesses and steroid-induced hyperglycemia were excluded from the study.

After obtaining an informed consent, detailed history regarding the duration of diabetes, cutaneous symptoms, other systemic diseases and treatment history was taken. Detailed cutaneous and systemic examinations were done and findings entered in a proforma designed for the study. Fasting and post prandial blood sugar levels, HbA1c, complete hemogram, urine analysis were done for all patients. Relevant microbiological and histopathological investigations were done wherever necessary.
Descriptive statistics like mean, frequency and percentage were calculated. Chi square test was done to analyse data wherever necessary.

**Results**

Among 500 patients with DM, 311(62.2%) were males and 189(37.9%) were females with a male to female ratio 1.63:1. Youngest patient was aged 10 years and the eldest, 88 years, with a mean age of 58.3±11.8 years. DM was more prevalent in the 51-60yrs age group i.e, 172(34.4%), followed by 41 to 50yrs group 143(28.6%).

Four (0.8%) patients had type 1 DM and 496(99.2%) had type 2 DM. The duration of DM varied between 0(newly diagnosed cases) to 35 years, with a mean duration of 9.69 ± 4.85 years. Majority i.e 260(52%) had diabetes for a duration 1-5 years. Four hundred and nineteen (83.8%) patients were taking oral hypoglycemic agents, 18(3.6%) were on insulin, 21(4.2%) were taking both and 42(8.4%) were not on any treatment.

Based on the levels of HbA1c >8% refers to uncontrolled DM, 7.1-8% refers to moderate control and, <7% refers to good control of DM. Majority, 248(49.6%) had uncontrolled diabetes, 117(23.4%) had a moderate control & 135(27%) had good control.

Associated systemic diseases were present in 140(28%) patients. Most common being hypertension in 102(20.4%) patients, followed by dyslipidemia 21(4.2%), ischemic heart disease 4(0.8%), hypothyroidism and pulmonary tuberculosis 3(0.6%) each, cerebrovascular accident and epilepsy 2(0.4%) each.

Based on the cutaneous manifestations of DM, we categorized the patients into 7 groups, i.e, 1) Cutaneous infections, 2) Neuropathic and ischemic diabetic skin disease, 3) Dermatoses associated with microangiopathy 4) Metabolic skin diseases 5) Dermatoses commonly associated with diabetes 6) Cutaneous reactions to therapy of diabetes (Table 1) and 7) Non specific skin diseases. (Table 2)

In our study, 414(82.8%) had cutaneous manifestations. Dermatoses commonly associated with diabetes were the most common category present in 254(50.8%) patients. Cutaneous infections were seen in 219(43.8%), dermatoses associated with microangiopathy in 9(1.8%), neuropathic & ischemic skin disease and metabolic skin disease in 3(0.6%) patients each and non specific dermatoses in 58(11%) patients. Some patients had multiple skin manifestations.

Among cutaneous infections, fungal infections 164(32.8%) were commonest, followed by bacterial 320(64.4%), viral 21(4.2%) and parasitic infections 2(0.4%).

Among fungal infections, candidiasis 85(17%) topped the list, followed by dermatophytes 53(10.6%), pityriasis versicolor 8(1.6%), and mucormycosis 1(0.2%). Candidial balanoposthitis (Fig 1), found in 33(6.6%) patients was the single most common fungal infection.

Among the bacterial infections, furunculosis was the commonest 12(2.4%) followed by folliculitis 11(2.2%), cellulitis and actinomycetoma 2(0.4%) each, impetigo, eczema, carbuncle, necrotising fascitis and acute paronychia in 1(0.2%) each.

Herpes zoster seen in 6(3%) patients was the most common viral infection followed by warts in 8(1.6%) patients.

Dermatoses associated with microangiopathy were observed in 9 patients (1.8%). Among them 6(1.2%) had diabetic dermopathy (Fig 2), 2(0.4%) had granuloma annulare and 1(0.2%) patient had diabetic bullae (Fig 3).

Neuropathic and ischemic diabetic skin disease was present in 11(2.2%) patients, among whom, 7(1.4%) had diabetic foot and 4(0.8%) had peripheral vascular disease.

Xanthelasma palpebrerum, found in 3(0.6%) patients was the only dermatological manifestation due to metabolic condition.

Dermatoses commonly associated with diabetes in our study were, acrochordons (Fig 4) in 71(14.4%), cherry angiomas 44(8.8%), psoriasis 43(8.6%), generalised pruritus 23(4.6%), lichen planus 43(8.6%), vitiligo 14(2.8%), diagonal ear lobe crease 6(1.2%), terry nails 4(0.8%), acquired perforating dermatosis, pigmented purpuriic dermatosis and localised cutaneous amyloidosis 2(0.4%) each.

Of the 458 patients, 458(91.6%), on anti-diabetic treatment, 2(0.4%) patients presented with insulin lipodystrophy. No complications due to oral antidiabetic drugs was noted.

Diabetes was diagnosed based on the presence of cutaneous manifestations in 34(6.8%) patients. Among them, majority, 21(61.76% of newly diagnosed patients) presented with cutaneous infections. Psoriasis, acrocard and generalised pruriitis were present in 2 patients each, lichen planus, vitiligo and foot ulcers in one patient each.

Increased frequency of cutaneous manifestations were seen in patients with uncontrolled diabetes, compared to patients with good and moderately controlled diabetes and was statistically significant (p<0.05) (Table 3). Similarly, cutaneous manifestations were more common with longer duration of the diabetes (>5 years) and was statistically significant (p<0.05) (Table 4). We also found infectious dermatoses to be more common among patients with early diabetes while non infectious dermatoses were more common with increase in the duration of DM.

![Fig. 1: Candidial balanoposthitis](ipindianjournaldermatology/pdfs/2019/52/141-145_Fig1.png)
Table 1: Various dermatoses in patients with diabetes mellitus

| Category of Dermatoses                        | Dermatoses                        | Number (n=500) (%) |
|-----------------------------------------------|-----------------------------------|--------------------|
| Cutaneous infections                          | Fungal infections                 | 164(32.8)          |
|                                               | Bacterial infections              | 32(6.4)            |
|                                               | Viral infections                  | 21(4.2)            |
|                                               | Parasitic infestations            | 2(0.4)             |
| Neuropathic and ischemic diabetic skin disease| Diabetic foot ulcer              | 7(1.4)             |
|                                               | Peripheral vascular disease       | 4(0.8)             |
| Dermatoses associated with microangiopathy    | Diabetic dermopathy               | 6(1.2)             |
|                                               | Granuloma annulare                | 2(0.4)             |
|                                               | Bullous diabeticorum              | 1(0.2)             |
| Metabolic skin disease                        | Xanthelasma palmarbrarum          | 3(0.6)             |
| Dermatoses commonly associated with diabetes mellitus | Acrochordons                  | 71(14.4)           |
|                                               | Cherry angiomas                   | 44(8.8)            |
|                                               | Psoriasis                         | 43                 |
|                                               | Generalized pruritus              | 23(4.6)            |
|                                               | Acanthosis nigricans              | 22(4.4)            |
|                                               | Lichen planus                     | 21(4.2)            |
|                                               | Vitiligo                          | 14(2.8)            |
|                                               | Diagonal ear lobe crease          | 6(1.2)             |
|                                               | Terry’ s nails                    | 04(0.8)            |
|                                               | Pigmented purpuric dermatoses     | 02(0.4)            |
|                                               | Perforating dermatoses            | 02(0.4)            |
|                                               | Localized cutaneous amyloidosis   | 02(0.4)            |
| Dermatoses due to complication of diabetes treatment | Insulin lipodystrophy           | 2(0.4)             |
Table 2: Various nonspecific dermatoses in patients with diabetes mellitus

| S. No | Dermatoses                        | Number (n=500) (%) | S. No | Dermatoses                        | Number (n=500) (%) |
|-------|-----------------------------------|--------------------|-------|-----------------------------------|--------------------|
| 1.    | Seborrheic keratoses              | 58(11.6)           | 18.   | Alopacia areata                   | 02(0.4)            |
| 2.    | Xerosis                           | 30(6.0)            | 19.   | Lentigines                        | 02(0.4)            |
| 3.    | Eczema                            | 24(4.8)            | 20.   | Senile comedones                  | 02(0.4)            |
| 4.    | Idiopathic guttate hypomelanosis  | 23(3.6)            | 21.   | Acne vulgaris                     | 01(0.2)            |
| 5.    | Lichen simplex chronicus          | 09(1.8)            | 22.   | Solar melanosis                   | 01(0.2)            |
| 6.    | Contact dermatitis                | 08(1.6)            | 23.   | Air borne contact dermatitis      | 01(0.2)            |
| 7.    | urticaria                         | 05(1.0)            | 24.   | Miliaria                          | 01(0.2)            |
| 8.    | Cutaneous vasculitis              | 04(0.8)            | 25.   | Keloid                            | 01(0.2)            |
| 9.    | Acquired ichthyosis               | 03(0.6)            | 26.   | Sebaceous cyst                     | 01(0.2)            |
| 10.   | Seborrhoic dermatitis             | 03(0.6)            | 27.   | Disoid lupus erythematosus        | 01(0.2)            |
| 11.   | Polymorphous light eruptions      | 03(0.6)            | 28.   | Squamous cell carcinoma           | 01(0.2)            |
| 12.   | Rosacea                           | 03(0.6)            | 29.   | Syringoma                         | 01(0.2)            |
| 13.   | Chronic actinic dermatitis        | 03(0.6)            | 30.   | Actinic cheilitis                 | 01(0.2)            |
| 14.   | Melasma                           | 03(0.6)            | 31.   | Baboon syndrome                   | 01(0.2)            |
| 15.   | Hirsuitism                        | 03(0.6)            | 32.   | Hidradenitis suppurativa          | 01(0.2)            |
| 16.   | Addisonian pigmentation           | 02(0.4)            | 33.   | Pachydermoperiostoses            | 01(0.2)            |
| 17.   | Erythema multiforme               | 02(0.4)            |       |                                   |                    |

Table 3: Relationship of cutaneous manifestations with glycemic control

| Control status of Diabetes mellitus | Total no. of patients | No. of patients with cutaneous manifestations (%) | No. of patients without cutaneous manifestations (%) |
|------------------------------------|-----------------------|-------------------------------------------------|---------------------------------------------------|
| Controlled diabetes mellitus (HbA1c<8%) | 252                  | 189(75%)                                        | 63(25%)                                           |
| Uncontrolled diabetes mellitus (HbA1c>8%) | 248                  | 225(90.72%)                                     | 23(9.28%)                                         |

Table 4: Relationship of cutaneous manifestations with duration of diabetes

| Duration of diabetes | Total no. of patients | No. of patients with cutaneous manifestations (%) | No. of patients without cutaneous manifestations (%) |
|----------------------|-----------------------|-------------------------------------------------|---------------------------------------------------|
| < 5 years            | 347                   | 269(77.52%)                                     | 78(22.48%)                                        |
| > 5 years            | 153                   | 145(94.77%)                                     | 8(5.23%)                                          |

Discussion

Skin is like a mirror that reflects the internal diseases. DM is a systemic disease that affects every organ system, including skin. In fact, cutaneous findings may be the first indicator of the disease. The prevalence of cutaneous manifestations has varied from 61% to 89.7% in earlier studies. In our study, 86.2% patients had cutaneous manifestations. Majority of the patients belonged to the 5th and 4th decade comprising 34.4% and 28.6% respectively. Cutaneous manifestations were also more common in patients belonging to 5th decade followed by 4th decade. Similar frequencies were seen in earlier studies by Mahajan et al., Nigam and Pande.

In our study, dermatoses having association with diabetes were the most common cutaneous manifestations (50.8%), followed by cutaneous infections (43.8%) Bhait et al reported similar findings, while Mahajan et al, Rao et al., Nigam and Pande, Tamshina et al, Vahora et al reported infections to be the most common cutaneous manifestation.

Among the various dermatoses associated with diabetes, acrochordons were the most common, seen in 14.4% patients. Acrochordons were also single most common dermatoses found in our study. Previous studies have reported an association between multiple acrochordons and diabetes. Acanthosis nigricans, a sign of insulin resistance was observed in 4.4% patients. Increased insulin binds to insulin like growth factor receptors, stimulating growth of keratinocytes and dermal fibroblasts, resulting in development of acanthosis nigricans.

Generalised pruritus is one of the common conditions seen in DM. This could be due to associated xerosis among these patients. Advanced Glycosylation end products of stratum corneum proteins or autonomic neuropathy may be attributed to the pathogenesis of xerosis and pruritus in DM. Generalised pruritus was found in 4.6% of our patients. Pruritus was reported in 4.5% by Nigam and Pande, 10% by Mahajan et al and 15.2% by Timshina et al.

Psoriasis until recently was only thought to be a cutaneous disease. Recently, psoriasis has been increasingly associated with metabolic syndrome, diabetes, hypertension and other diseases. Psoriasis was reported in 3% patients
by Mahajan et al., 5 2.2% and by Timshina et al. 6 We observed psoriasis in 8.6% of patients in our study.

Infections were one of common dermatoses observed in our study, which was present in 43.8% patients. Impaired chemotaxis, leucocyte adherence and phagocytosis and impaired immunity in uncontrolled diabetes and ketoacidosis predisposes them to prolonged and recurrent infections. 14

Fungal infections formed largest group of cutaneous infections found in 32.4% of patients. Fungal infections were common in studies by Mahajan et al. 5 (54.68%) and Bhat et al. 7 (34.34%)

Diabetic microangiopathy is characterised by thickening of capillary basement membrane leading to progressive occlusion of vascular lumen causing impaired perfusion. 15 In our study, 1.8% had dermatoses associated with microangiopathy, wherein 1.2% had diabetic dermopathy, 0.4% had granuloma annulare and 0.2% had diabetic bullae. Diabetic dermopathy has been considered as one of the most common cutaneous manifestations, reported in upto 50% of patients in western literature, in contrast to lower incidence in Indian patients. This may possibly be due to dark complexion in our country, rendering it difficult to detect. 1

Raghunatha et al. 1 reported 0.2% of diabetic dermopathy and 0.4% diabetic bullae. Nigam and Pande 3 reported 3.5% & 1% of diabetic bullae, similar to our study. We did not come across any case of necrobiosis lipoidica diabeticaorum or ruberosis faciei.

In our study, diabetic foot ulcers were seen in 1.4% patients. Bhat et al. 7 in their study, observed 4 cases of diabetic foot ulcers. Mahajan et al. 5 Rao et al. 9 Raghunatha et al. 1 and Nigam and Pande 3 found diabetic foot ulcers in 8.1, 1 and 6 cases respectively.

Only 0.4% of our patients presented with lipodystrophy secondary to insulin therapy, while Raghunatha et al. 1 found 1.8% affected.

Diabetes was diagnosed due to the presence of cutaneous manifestations in 6.8% patients. Rao et al. 9 reported newly detected cases in 19.32% in their study. Cutaneous manifestations can heighten the suspicion of a physician regarding the diagnosis of diabetes. This further helps to prevent both cutaneous and systemic derangements by early institution of appropriate treatment.

Conclusions
Cutaneous manifestations are common in patients with DM. The hospital based prevalence of cutaneous manifestations was 82.8 percent.

The frequency of cutaneous manifestations was significantly associated with both uncontrolled and longer duration of diabetes.

Dermatologists may play an important role in early detection and control of diabetes. This helps in reducing the morbidity and improves the of quality of life in these patients. Proper skin care and long-term control of blood glucose levels may reduce the cutaneous involvement.

Source of Support: None.

Conflict of interest: None.

References
1. Raghunatha S, Anitha B, Inamdar AC, Palit A, Devarmani SS. Cutaneous disorders in 500 diabetic patients attending Diabetic clinic. Indian J Dermatol 2011;56(2):160-4.
2. Pavlovic MD, Milenkovic T, Dinić M, Misovic M, Dakovic D. The prevalence of cutaneous manifestations in young patients with type 1 diabetes. Diabetes Care 2007;30:1964-7.
3. Use of Glycated Haemoglobin (HbA1C) in the diagnosis of Diabetes; January, 2011. Available from https://www.who.int/diabetes/publications/report-hba1c-2011.pdf
4. Nigam PK, Pande S. Pattern of dermatoses in diabetics. Indian J Dermatol Venereol Leprol 2003;69(2):83-5
5. Mahajan S, Koranne RV, Sharma SK. Cutaneous manifestation of diabetes mellitus. Indian J Dermatol Venereol Leprol 2003;69(2):105-8
6. Timshina DK, Thappa DM, Agrawal A. A clinical study of dermatoses in diabetes to establish its markers. Indian J Dermatol 2012;57(1):20-5.
7. Bhat YJ, Gupta V, Kudyar PR. Cutaneous manifestations of diabetes mellitus. Int J Diab Dev Ctries 2006;26(4):152-4.
8. Rao S, Pai G. Cutaneous manifestations of diabetes mellitus. Indian J Dermatol Venereol Leprol 1997;63(4):232-4.
9. Vahora R, Thakka S, Marfatia Y. Skin, a mirror reflecting diabetes mellitus: A longitudinal study in a tertiary care hospital in Gujarat. Indian J Endocrinol Metab 2013;17(4):659-64.
10. Crook MA. Skin tags and athogenic lipid profile. J Clin Pathol 2000;53(11):873-4.
11. Kalus AA, Chien AJ, Olerud JE. Diabetes mellitus and other endocrinial disorders. In: Woiil K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leiffel DJ, editors. Fitzpatrick’s Dermatology in General Medicine. 7th ed. Newyork: The Mc Graw Hill 2008.pp.1461-9
12. Yosipovitch G, Hodak E, Vardi P, Shraga L, Karpi M. The prevalence of Cutaneous Manifestations in IDDM Patients and Their Associations With Diabetes Risk Factors and Microvascular Complications. Diabetes Care 1998;21(4):506-9.
13. Wakee M, Thio HB, Prens EP, Sijbrands EJ, Neumann HA. Unfavourable cardiovascular risk profiles in untreated and treated psoriasis patients. Atherosclerosis 2007;190(1):1-9.
14. Jelinek JF, Cutaneous manifestations of Diabetes. Mellitus. Int J Dermatol 1994;33:605-17
15. Braverman T. Studies in cutaneous aging in dermal microvasculature. J Invest Dermatol 1987;78:444-8.
How to cite this article: Vathsala S, Murthy SC, Shashibhushan J. Cutaneous manifestations in diabetes mellitus: A study among 500 patients in a tertiary care center in South India. Indian J Clin Exp Dermatol 2019;5(2):141-145.