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Original Article

Spectrum of cutaneous manifestations in diabetes mellitus and their association with duration of diabetes mellitus: An observational study in a tertiary care hospital of South India

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Abstract

Objective To study the prevalence and patterns of cutaneous manifestations among diabetic patients and their association with duration of diabetes mellitus (DM).

Methods A cross-sectional study was performed on patients attending the outpatient department of Dermatology, Venereology and Leprosy of a tertiary care hospital in South India. A total of 200 patients with dermatological manifestations having pre-existing diabetes and patients in whom diabetes was diagnosed later were included in the study. Statistical analysis was carried out using analysis of variance (ANOVA) test and SPSS 21 software.

Results Majority of patients (63%) belonged to the age group 40-59 years with female preponderance (58.5%). Cutaneous manifestations as presenting feature of diabetes were observed in 21.5% cases. The diabetic status was uncontrolled in 73% cases. Among the various cutaneous manifestations observed, cutaneous infections (52%) were most commonly observed, especially in early diabetics of upto 5 years duration and dermatoses due to chronic degenerative complications were observed in long-standing diabetics which was statistically significant (P<0.05).

Conclusion Cutaneous manifestations may be the first clue to underlying DM. Through awareness about cutaneous manifestations of DM, dermatologist can not only take credit for detecting DM but also facilitate early diagnosis of systemic complications of DM and thereby play an important role in improvement of quality of life and management strategy of diabetic patients.

Key words
Cutaneous manifestations, diabetes mellitus, infections, South India.

Introduction

Diabetes mellitus (DM) is the most common endocrine disorder which exhibits a variety of multisystem complications involving the blood vessels, eyes, cardiovascular, renal, nervous systems and skin. The number of people with DM in the world increased from 108 million in 1980 to 422 million in 2014.[1] The skin is affected by both the acute metabolic derangements and the chronic degenerative complications of DM.[2] Chronic hyperglycemia resulting in production of advanced glycosylated end products may be responsible for pathogenesis of many diabetic complications.[3] Skin manifestations can be the presenting sign of DM but more often appear in known DM

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patients during the course of the disease, as observed in 30 to 71% of diabetics.[4] This work was an attempt to study the prevalence and patterns of cutaneous manifestations among diabetic patients and their association with duration of DM and help to detect and prevent the related systemic complications of diabetes by early institution of appropriate treatment.

Methods

The present study was a cross-sectional study performed on patients attending the out-patient department of Dermatology, Venereology and Leprosy of a tertiary care hospital in South India after obtaining institutional ethical clearance. A total of 200 patients, including patients with dermatological manifestations having pre-existing diabetes and patients who came with only skin disease in whom diabetes was diagnosed later were included in the study after taking their consent. Drug-induced and pregnancy-induced diabetes mellitus cases were excluded from the study. In the selected patients, a detailed history with particular reference to demographic details, family history of similar complaints and of DM and duration and type of diabetes and treatment taken, duration of various symptoms and evolution of lesions were enquired into. The patients were clinically examined in good light for varied cutaneous manifestations and mucous membrane involvement. Complete systemic examination was done and BMI was calculated and ocular examination was carried out by ophthalmologist. The findings were recorded. Investigations like random blood glucose, fasting and post prandial blood glucose, HbA1c, oral glucose tolerance test, urine glucose, urine ketone bodies, complete hemogram, liver and renal function tests, lipid profile were done. Beside laboratory procedures like Tzanck smear, KOH mount, Wood's lamp examination and Gram staining were carried out when required and skin biopsy was done in few cases.

The ANOVA test was used to assess the association of duration of DM with cutaneous manifestations of DM. $P<0.05$ was considered significant. Statistical analysis was carried out using SPSS software version 21.

Results

In the present study of 200 patients with cutaneous manifestations **(Table 1)**, majority belonged to 5th and 6th decades with 27% and 36%, respectively with mean age of 51.84±11 years. Females constituted 58.5% of cases with male to female ratio being 1:1.4.

Known diabetics constituted 78.5% of the study group, whereas 21.5% patients were unaware of their diabetic status and presented for their dermatological problem only. The diabetic status was uncontrolled in 146 (73%) cases. The mean duration of DM was 5.08±6.68 years. Majority (97.5%) of the patients belonged to type 2 DM and 111 (55.5%) patients had a family history of DM. In this study, 83 (41.5%) patients (51 females and 32 males) were obese.

Infections comprised the commonest group in obese diabetics (24.5%) followed by dermatoses more commonly associated with diabetes (20%) such as acrochordons and acanthosis nigricans (AN). Among the 157 known diabetics, majority

Table 1 Demographic profile (n=200).

Characteristics	*N (%)*
Males	83 (41.5)
Females	117 (58.5)
Uncontrolled diabetes	146 (73)
Freshly detected diabetes	43 (21.5)
Type 1 diabetes	5 (2.5)
Type 2 diabetes	195 (97.5)
With family history	111 (55.5)
Obese diabetics	83 (41.5)

Table 2 Duration of diabetes mellitus and type of skin manifestations (n=200).

Duration	*Infections*	*Microangio-pathy*	*Ischemia and neuropathy*	*Most common dermatoses*	*Co-incidental dermatoses*	*Pruritus*
Incidental	31	2	0	16	3	19
<1 year	17	0	0	9	3	7
1-5 years	24	4	1	33	8	8
6-10 years	21	10	2	11	4	5
11-15 years	7	2	2	7	3	0
16-20 years	3	7	3	2	1	1
21-25 years	1	1	2	1	0	0
>25 years	0	0	1	1	1	0

Table 3 Distribution of cutaneous manifestations of diabetes mellitus (n=200).

Characteristics	*N (%)*
Cutaneous infections	104 (52)
Fungal infections	69 (34.5)
Bacterial infections	29 (14.5)
Viral infections	6 (3)
Dermatoses associated with microangiopathy	
Diabetic dermopathy	20 (10)
Diabetic bullae	5 (2.5)
Disseminated granuloma annulare	1 (0.5)
Dermatoses associated with ischemia and neuropathy	11 (
Pruritus	40 (20)
Generalized pruritus	5 (2.5)
Localized pruritus	35 (17.5)
Dermatoses more commonly associated with DM	80 (40)
Acrochordons	18 (9)
Acanthosis nigricans	15 (7.5)
Cherry angiomas	10 (5)
Lichen simplex chronicus	10 (5)
Xerosis	9 (4.5)
Vitiligo	8 (4)
Psoriasis	7 (3.5)
Lichen planus	5 (2.5)
Amyloidosis	5 (2.5)
Kyrle's disease	2 (1)
Other dermatoses coincidentally associated with DM	
Seborrheic keratosis	5 (2.5)
Drug reactions	4 (2)
Chronic urticaria	4 (2)
Hansen's disease	2 (1)
Vesiculobullous disorders	2 (1)
Scabies	2 (1)
Pyoderma gangrenosum	1 (0.5)
Lichenoid polymorphous light eruption	1 (0.5)
Nevus sebaceous	1 (0.5)
Marginal palmoplantar keratoderma	1 (0.5)

(45.5%) had diabetes of less than 5 years duration. Cutaneous infections (52%) were most commonly observed especially in early diabetics of upto 5 years duration and dermatoses due to chronic degenerative complications were observed in long-standing diabetics **(Table 2)**, (P<0.05). Among the cutaneous infections, fungal infections (34.5%) were most frequently observed, followed by bacterial infections (14.5%) and viral infections (3%), **(Table 3)**. Among the fungal infections, various dermatophytoses (22.5%) were more commonly noted, followed by candidal infections (12%), **(Figure 1)**. Folliculitis and furunculosis (8.5%) were most commonly observed bacterial infections. Generalized pruritus was found only in 2.5% of patients as compared to 17.5% of patients with localized pruritus. Dermatoses due to chronic degenerative complications secondary to microangiopathy and neuropathy were observed in 13% and 5.5% of the cases, respectively. Changes seen in patients due to microangiopathy were diabetic dermopathy (10%), **(Figure 2)**, diabetic bullae (2.5%), **(Figure 3)** and disseminated granuloma annulare (0.5%). Various dermatoses more commonly associated with DM observed were multiple acrochordons (9%), followed by acanthosis nigricans (7.5%), **(Figure 4)** and cherry angiomas (5%), **(Table 3)**.

Initial presentation with more than one dermatological manifestation was seen in 85 patients. Systemic co-morbidity was present in 103 patients which included hypertension in 43 (21.5%) patients, peripheral neuropathy in 14 (7%), coronary artery disease in 12 (6%),

Figure 1 Erythema and fissuring with whitish deposits on the prepuce and the glans penis - candidal balanoposthitis

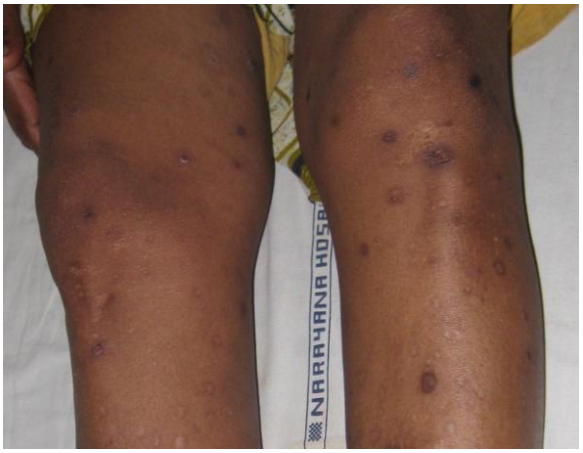

Figure 2 Multiple well-defined hyperpigmented atrophic macules over bilateral shins (shin spots) - diabetic dermopathy

Figure 3 Tense bulla on a non-inflamed base – diabetic bullae

Figure 4 Hyperpigmented velvety plaque topped by acrochordons on the neck – acanthosis nigricans and acrochordons

cataract in 11 (5.5%), retinopathy in 9 (4.5%), chronic renal failure in 7 (3.5%), hypothyroidism in 4 (2%) and one patient each with asthma, HIV and pulmonary tuberculosis, respectively.

Discussion

Diabetes mellitus (DM) is a condition in which there is a chronically raised blood glucose concentration. It is a metabolic disease characterized by relative or absolute insulin deficiency resulting in gross defect in protein, carbohydrate and fat metabolism.[5] DM has taken on the mantle of 'Syphilis' of pre-antibiotic days

of being the clinical imitator with an impressive array of signs and symptoms affecting every organ of the body. Dermatologic disorders associated with DM generally appear after the primary disease or they may signal or appear coincidentally with its onset, or even precede diabetes by many years.[6] The ratio of skin glucose to blood is slightly higher in diabetics (70%) than in normal people (55%).[7] The hyperglycemic state predisposes to wide variety of skin conditions that in part are related to microvascular changes (microangiopathy), macrovascular alterations (atherosclerotic cardiovascular disease), neuropathy, predisposition to infections and a variety of metabolic disturbances.

In the present study of 200 patients with cutaneous manifestations, majority belonged to 6th (36%) and 5th (27%) decades with females (58.5%) out numbering males (41.5%) which is in accordance with studies carried out by Mahajan *et al.*[8] and Nigam *et al.*[9] Studies by Sawhney *et al.*[10] and Rao *et al*.[11] found higher incidence among male diabetics. Type 2 DM (97.5%) was the most commonly observed type which was similar to the studies by Bhat *et al.*[2] (97.7%), Mahajan *et al*.[8] (98%), Nigam *et al.*[9] (82.1%) and Sawhney *et al*.[10] (80%), respectively. Majority of patients 157 (78.5%) had pre-existing DM and 43 (21.5%) presented initially with cutaneous manifestations alone and later were diagnosed as diabetics after appropriate investigations. Similar frequencies were also reported by Rao *et al.*[11] and Al Mutairi *et al*.[12] The diabetic status was uncontrolled in 146 (73%) cases. Uncontrolled DM was seen in 55% of cases by Vahora *et al*.[13] and similar frequencies were observed by Bhat *et al*.[2], Sawhney *et al.*[10] and Yosipovitch *et al*.[14] The poor control itself may be the cause or consequence of concurrent infections.[15] The incidence of cutaneous manifestations was commonest among early diabetics (32.5%) of upto 5 years duration with cutaneous infections being the most common. Similar observations were reported by Bhat *et al.*[2] and Mahajan *et al.*[8] in their studies. The cutaneous dermatoses associated with chronic degenerative complications of diabetes such as microangiopathy were more common in long-standing diabetics (6-10 years) which is in accordance with studies by Sawhney *et al.*[10], Rao *et al.*[11] and Al Mutairi *et al*.[12] The age of onset of diabetes in the patients with family history of DM (55.5%) was earlier. Obese diabetics (41.5%) had higher prevalence of acanthosis nigricans, multiple acrochordons and fungal infections. According to Halher,[16] acanthosis nigricans can be taken as sign of diabetes in obese patients. In the present study, cutaneous infections were the most common dermatoses observed (52%), due to high number of poorly controlled diabetics (73%), which was statistically significant **(Table 4)**.

Table 4 Impact of control of DM on various dermatoses

Dermatoses	*Uncontrolled DM*		*Controlled DM*	
	FBS (mg/dl)	*HbA1c (%)*	*FBS (mg/dl)*	*HbA1c (%)*
Cutaneous infections	198.98±11.09	10.29±0.14	102.05±8.61	6.18±1.12
Dermatoses associated with microangiopathy	187.8±7.34	8.17±0.03	97.36±7.46	5.11±0.12
Dermatoses associated with ischemia and neuropathy	189.14±8.97	9.21±0.12	101.75±12.33	6.08±1.64
Pruritus	189.10±11.51	9.24±0.13	90±7.07	6.14±0.64
Dermatoses more commonly associated with DM	190.01±9.70	9.21±0.05	101.5±8.10	5.13±0.12
Other dermatoses coincidentally associated with DM	189.46±12.76	8.25±0.11	99.2±8.56	4.18±1.14

DM: Diabetes mellitus, FBS: Fasting blood glucose

Table 5 Comparison of specific cutaneous disorders with other studies

Dermatoses	*Present study (%) (n=200)*	*Bhat et al.*[2] *(%) (n=150)*	*Mahajan et al.*[8] *(%) (n=100)*	*Raghunatha et al.*[23] *(%) (n=500)*
Dermatophytoses	19.5	5.3	11	8.1
Candidiasis	12	6.6	10	3.6
Bacterial infections	14.5	9.3	11	6.8
Diabetic dermopathy	10	11.3	6	0.2
Diabetic bullae	2.5	2.6	2	0.4
Granuloma annulare	0.5	0	1	0.2
NLD	0	1.3	0	0.0
Diabetic foot	5.5	0	1	0.2
Eruptive xanthomas	0	0	1	0.6
Diabetic thick skin (finger pebbles and / or scleredema)	0	32.6	2	0.0
Acrochordons	9	11.3	4	26.2
Acanthosis nigricans	7.5	5.3	3	5.0

This increased incidence of cutaneous infections may be attributed to abnormalities of phagocytic function, cell-mediated immunity and microcirculation, peripheral vascular disease, diabetic neuropathy and hypohidrosis.[15,17]

Diabetic dermopathy was found in 6 (3%) patients having peripheral neuropathy in our study. Binkley *et al.*[8] found that diabetics with peripheral neuropathy were more likely to develop diabetic dermopathy. In the present study, diabetic dermopathy was more common in diabetics with duration of more than 5 years, similar to the studies conducted by Sawhney *et al.*[10] and Binkley *et al*.[18] Among the various dermatoses studied, majority had multiple acrochordons (9%). Acrochordon has been regarded as a sign of impaired glucose tolerance, DM and increased cardiovascular risk.[19] Studies by Kahana *et al*.[20] and Thappa *et al.*[21] concluded that acrochordons may serve as markers for DM. Acanthosis nigricans was observed in 7.5% patients of the study group. The first major breakthrough association of AN with insulin resistance came from the study by Kahn.[22] There have been suggestions that insulin at high concentrations may stimulate insulin-like growth factor receptors on keratinocytes, thereby promoting epidermal cell proliferation. So, every patient of AN should be investigated for DM, and every patient of DM should be screened for AN. The absence of diabetic thick skin and necrobiosis lipoidica diabeticorum (NLD) in the present study when compared to other studies,[2,8,23] (**Table 5**) is mainly due to short duration of DM in the majority of the patients. Systemic comorbidities were present in 103 (51.5%) patients, of which hypertension (21.5%) was most commonly observed. According to Bhat *et al.*[2], Mahajan *et al.*[8] and Al Mutairi *et al*.[12] 46.4%, 53.1% and 44% patients were hypertensive, respectively. Nigam *et al.*[9] also reported hypertension as the most common associated systemic disease.

Conclusion

In nearly 30% of patients, the diagnosis of diabetes is preceded by some cutaneous manifestation. As observed in the present study where 21.5% patients were benefitted by early recognition of underlying diabetes and appropriate treatment. Thereby we emphasize the importance of the fact that cutaneous manifestations may be the first clue to underlying diabetic diathesis. A good glycemic control definitely reduces the incidence and severity of cutaneous disorders with or without known pathogenesis. Cutaneous manifestations such as diabetic dermopathy, necrobiosis

lipoidica diabeticorum, syndromes of limited joint mobility are extremely important to the clinician as they are indicators of underlying chronic degenerative complications such as retinopathy, neuropathy and nephropathy and hence an "alarm bell to alert the physician". Thus a dermatologist plays an important role in reducing the dermatologic morbidity, improvement of quality of life and management strategy of diabetic patients.

References

1. Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet.* 2016;**387**:1513-30.
2. Bhat YJ, Gupta V, Kudyar RP. Cutaneous manifestations of diabetes mellitus. *Int J Diab Dev Ctries.* 2006;**26**:152-5.
3. Kalus AA, Chein AJ, Olerud JE. Diabetes mellitus and other endocrinal disorders. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Lefell DJ, editors. *Fitzpatrick's Dermatology in General Medicine. 7th edn*. New York: McGraw-Hill: 2008. p. 1461-84.
4. Al-Mutairi N. Skin diseases seen in diabetes mellitus. *Bull Kuwait Inst Med Special*. 2006;**5**:30-9.
5. Bud JL, Oledur JE. Diabetes Mellitus. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Lefell DJ, editors. *Fitzpatrick's Dermatology in General Medicine. 7th edn. Vol. 2.* New York: McGraw-Hill. p. 1651-61.
6. Jelinek JE. Cutaneous manifestations of diabetes mellitus. *Int J Dermatol.* 1994;**33**:605-17.
7. Peterka ES, Fusaro RM. Cutaneous Carbohydrate Studies IV. The skin glucose content of fasting diabetics with and without infection. *J Invest Dermatol*. 1966;**46**:459-63.
8. Mahajan S, Koranne RV, Sharma SK. Cutaneous manifestation of diabetes mellitus. *Indian J Dermatol Venereol Leprol*. 2003;**69**:105-8.
9. Nigam P K, Pande S. Pattern of dermatoses in diabetics. *Indian J Dermatol Venereol Leprol*. 2003;**69**:83-5.
10. Sawhney M, Talwar OP, Tutakne MA, Rajpathak SD. Diabetic dermoangiopathy: A clinico-pathological correlation. *Indian J Dermatol Venereol Leprol.* 1992;**58**:173-8.
11. Rao S, Pai G. Cutaneous manifestations of diabetes mellitus. *Indian J Dermatol Venereol Leprol*. 1997;**63**:232-34.
12. Al-Mutairi N, Zaki A, Sharma AK, Al-Sheltani M. Cutaneous manifestations of diabetes mellitus. *Med Princ Pract*. 2006;**15**:427-30.
13. Vahora R, Thakkar S, Marfatia Y. Skin, a mirror reflecting diabetes mellitus: A longitudinal study in a tertiary care hospital in Gujarat. *Indian J Endocr Metab*. 2013;**17**:659-64.
14. Yosipovitch G, Hodak E, Vardi P, Shraga I, Karp M, Sprecher E *et al*. The prevalence of cutaneous manifestations in IDDM patients and their association with diabetes risk factors and microvascular complications. *Diabetes Care.* 1998;**21**:506-9.
15. Feringer T, Miller FO. Cutaneous manifestation of diabetes mellitus. *Dermatol Clin.* 2002;**20**:483-92.
16. Hahler B. An overview of dermatological conditions commonly associated with the obese patient. *Ostomy Wound Manage*. 2006;**52**:34-6.
17. Sibbald RG, Schachter RK. The skin and diabetes mellitus. *Int J Dermatol*. 1984;**23**:567-84.
18. Binkley GW. Dermopathy in the diabetic syndrome. *Arch Dermatol*. 1965;**92**:625-34.
19. Crook MA. Skin tags and atherogenic lipid profile. *J Clin Pathol.* 2000;**53**:873-4.
20. Kahana M, Grossman E, Feinstein A, Ronnen M, Cohen M, Millet MS. Skin tags: A cutaneous marker for diabetes mellitus. *Acta Dermatol Venereol*. 1987;**67**:175-7.
21. Thappa DM. Skin tags as markers of diabetes mellitus: An epidemiological study in India. *J Dermatol.* 1995;**22**:729-31.
22. Kahn CR, Flier JS, Bar RS, Archer JA, Gorden P, Martin MM *et al*. The syndromes of insulin resistance and acanthosis nigricans: Insulin-receptor disorders in man. *N Engl J Med.* 1976;**294**:739-45.
23. Ragunatha S, Anitha B, Inamadar AC, Palit A, Devarmani SS. Cutaneous disorders in 500 diabetic patients attending diabetic clinic. *Indian J Dermatol*. 2011;**56**:160-4.