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Original Research Article

Cutaneous manifestations of diabetes mellitus: a clinical study

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ABSTRACT

Background: Diabetes mellitus is a leading cause of morbidity with adverse effects on various systems including skin. Cutaneous manifestations seen in diabetes aid in its diagnosis and some of them may also correlate with diabetic control, duration and other complications. This study was undertaken to estimate burden of skin disorders among diabetics in a tertiary care centre of Uttarakhand.
Methods: The study was conducted at Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India, over a period of one year from January 2016 to December 2016. Three hundred and seventy seven patients irrespective of age and sex were included in the study and those with gestational diabetes were excluded. Patients were examined for mucocutaneous manifestations and evaluated. Structured case reporting form was used to generate data.
Results: Out of 377 patients studies, 114 (30.2%) were in the age group of 51-60 years. Male to female ratio was 1.44:1. Mucocutaneous manifestations were present in 278/377 (73.7%) patients. Common cutaneous manifestations were cutaneous infections [fungal infections (n=106/377; 28.1%), bacterial infections (n=33/377; 8.8%)], pruritus (n=47/377; 12.5%), xerosis (n=39/377; 10.3%), diabetic dermopathy (n=36/377; 9.5%) and diabetic ulcers (n=24/377; 6.4%). Uncommon manifestations were necrobiosis lipoidica diabeticorum, alopecia areata, scleredema diabeticorum and granuloma annulare. Cutaneous reactions due to treatment of diabetes were noted in 4 (1%) patients.
Conclusions: As prevalence of cutaneous manifestations is high in diabetic patients, knowledge of these will help in a timely and comprehensive management of both diabetes and dermatoses.

Keywords: Cutaneous, Diabetes mellitus, Uttarakhand

INTRODUCTION

Abnormal insulin secretion and/or utilization, leads to hyperglycemia which has adverse effects on the heart, blood vessels, kidney, nervous system, eye and skin.[1] The knowledge of the cutaneous signs of diabetes mellitus (DM) can be valuable to the clinicians as their observation can point towards the diagnosis of diabetes. Mostly, these cutaneous findings manifest after the diagnosis of DM, but they may appear coincidentally with its onset, or even precede diabetes by many years.[2] Some manifestations can have direct correlation with diabetic control, duration and other multisystem complications such as neuropathy and nephropathy and maybe of prognostic significance. Etiopathogenesis of cutaneous manifestations is multi-factorial and alteration of metabolic pathways, hyperglycemia, formation of advanced glycation end products, cell apoptosis, decreased vasodilation, induction of proinflammatory cytokines, oxidative stress leading to vascular involvement in the form of atherosclerosis and microangiopathy, neuronal involvement in the form of sensory, motor and autonomic neuropathies, impaired

host mechanisms, etc. have all been variably implicated.[1,3,4]

In India, muco-cutaneous manifestations have been reported in 43-66% of patients with diabetes.[2] The magnitude of cutaneous manifestations maybe grossly under-estimated as the lesions are often neglected, by the patients and their physicians. With India slated to become the diabetes capital of the world in the near future, co-morbidities including cutaneous lesions merit attention. We undertook this study to estimate the burden of skin disorders among diabetic patients presenting to a tertiary care centre of Uttarakhand.

METHODS

The present cross-sectional observational study was conducted at Himalayan Institute of Medical Sciences, Dehradun, India over a period of one year i.e., from January 2016 to December 2016. Three hundred and seventy seven patients of diabetes mellitus were included in the study by systematic sampling method presenting to the outpatient department of medicine and dermatology. Written informed consent was taken from patients and permission from the institutional ethics committee was obtained for conduct of study. Sample size was calculated by estimation of proportion formula z^2 pq/d^2, where z=95% confidence interval, p=43% (estimated prevalence), q=1-p, d=5%. Patients with gestational diabetes were excluded from the study.

Mucocutaneous manifestations were searched for and a provisional clinical diagnosis of dermatoses, if present, was made. Routine investigations like blood sugar levels, glycosylated hemoglobin (HbA1c), serum creatinine & urinanalysis were done and body mass index (BMI) was calculated for all patients. Special investigations like skin biopsy & histopathology, potassium hydroxie (KOH) examination of skin, gram's stain and Woods lamp examination were performed wherever required to establish the diagnosis of cutaneous disease. Data was presented as frequencies and percentage.

RESULTS

Of the 377 diabetic subjects enrolled in the study 59.1% were males. Age of patients ranged from 12 to 85 years with highest number of patients i.e. 114 (30.2%) being in the age group of 51-60 years. Type 1 diabetes mellitus was present in 20 (5.3%) patients of the study group. 47 (12.5%) patients were obese (BMI >29.9 kg/m^2). 134 (35.5%) patients had diabetes for a duration of 1-5 years, followed by 94 (24.9%) for 5-10 years, 84 (22.3%) for more than 10 years and 65 (17.2%) patients had developed diabetes in the previous year. Out of these 65 patients, 41 (10.9%) were new cases of diabetes diagnosed by dermatologist suspected by the presence of cutaneous manifestations. Overall 174 (46.2%) patients had unsatisfactory control (HbA1c >8%), 129 (34.2%) patients had ideal control (HbA1c <7%) and 74 (19.6%) patients had satisfactory control (HbA1c 7-8%) of blood sugar.

Table 1: Spectrum of diabetes associated cutaneous manifestations observed in study subjects.

Pattern of cutaneous manifestations	Number of patients (n=377)	Percentage (%)
Manifestations with known pathogenesis		
Infections (fungal and bacterial)	139	36.9
Acanthosis Nigricans	16	4.2
Xanthelasma	4	1.1
Scleredema diabeticorum	1	0.3
Manifestations with pathogenesis attributable to diabetic neuropathy and vasculopathy		
Diabetic foot ulcers	24	6.4
Shiny atrophic skin with loss of hair	17	4.5
Pigmented purpura	11	2.9
Acral gangrene	6	1.6
Amputation	6	1.6
Cutaneous manifestations of diabetes without clear pathogenesis		
Pruritus	47	12.5
Xerosis	39	10.3
Diabetic dermopathy	36	9.5
Psoriasis	17	4.5
Acrochordons	14	3.7
Diabetic bulla	10	2.7
Acquired perforating dermatoses	6	1.6
Vitiligo	7	1.9
Lichen planus	4	1.1
Necrobiosis lipoidica diabeticorum	2	0.5
Granuloma annulare	1	0.3
Alopecia areata	1	0.3
Cutaneous manifestations due to treatment		
Oral hypoglycemic reactions	2	0.5
Insulin reactions	2	0.5

Cutaneous manifestations were discernible in 278/377 (73.7%) patients. The spectrum of cutaneous manifestations is shown in Table 1. 152/278 (54.7%) patients had a single cutaneous manifestation, two and multiple concurrent lesions were observed in 88/278 (31.6%) and 38/278 (13.7%) patients respectively. Cutaneous manifestations were categorised as cutaneous disorders with known pathogenesis like metabolic and immunologic abnormalities (fungal and/or bacterial infections, acanthosis nigricans, xanthelasma, scleredema diabeticorum), neurovascular abnormalities (diabetic ulcers, shiny skin with loss of hair, pigmented purpura, acral gangrene, amputation); disorders associated with DM but of unclear pathogenesis (pruritus, xerosis,

diabetic dermopathy, psoriasis, acrochordons, diabetic bulla, perforating dermatoses, necrobiosis lipoidica diabeticorum etc.) and cutaneous manifestations due to treatment with oral hypoglycemics or insulin (Table 1).[1]

Cutaneous fungal and bacterial infections (n=139; 36.9%) were the commonest cutaneous manifestation. Other major manifestations were pruritus (n=47; 12.5%), xerosis (n=39; 10.3%), diabetic dermopathy (n=36; 9.5%) and diabetic ulcers (n=24; 6.4%). Uncommon manifestations of diabetes such as necrobiosis lipoidica diabeticorum (n=2, 0.5%), alopecia areata (n=1; 0.3%), scleredema diabeticorum (n=1, 0.3%), and granuloma annulare (n=1, 0.3%) were also observed in small fraction of patients.

Table 2: Pattern of cutaneous infections in study subjects.

Cutaneous Infections	Number of patients (n=377)	Percentage (%)
Fungal infections	106	28.1
Dermatophytosis	74	19.6
Candidiasis	30	8
Pityriasis versicolor	1	0.3
Mucormycosis	1	0.3
Bacterial infections	33	8.8
Folliculitis	3	0.8
Furunculosis	18	4.8
Erysipelas	1	0.3
Cellulitis	6	1.6
Carbuncle	2	0.5
Abscess	1	0.3
NSTI	1	0.3
Scrofuloderma	1	0.3
Parasitic infection (Scabies)	7	1.9
Viral infection	5	1.3

Pattern of cutaneous infections showed fungal and bacterial infections to be present in 106 (28.1%) and 33 (8.8%) patients respectively. Dermatophytosis seen in 74 (19.6%) patients was the most common fungal and furunculosis seen in 18 (4.8%) patients was the most common bacterial infection observed. Notably, one patient with rhinocerebral mucormycosis demonstrated cutaneous spread (Table 2).

The oral hypoglycemic drug, glimiperide, resulted in a lichenoid drug rash in one patient while pioglitazone was implicated for maculopapular rash in another. The conventional premixed insulin caused maculopapular rash in one patient and multiple subcutaneous abscess formation at injections sites in another patient.

Cutaneous manifestations, not known to be associated with diabetes such as eczema and cutaneous amyloidosis were noted in 10 (2.7%) and 9 (2.4%) patients respectively (Table 3).

Table 3: Pattern of other cutaneous manifestations observed in study subjects.

Pattern of cutaneous manifestations	Number of patients (n=377)	Percentage (%)
Eczema	10	2.7
Cutaneous amyloidosis	9	2.4
Tellogeneffulivum	4	1.1
Prurigo nodularis	4	1.1
Urticaria	3	0.8
Seborrhoeic keratosis	3	0.8
Seborrhoeic dermatitis	3	0.8
Acne keloidalisnuchae	2	0.5
Apthous stomatitis	2	0.5
Gouty deposists	1	0.3
Dermatitis herpetiformis	1	0.3
Sarcoidosis	1	0.3

DISCUSSION

Diabetes being the most common endocrine disorder, the vast number of skin manifestations associated with it needs special attention. In the present study a total of 377 diabetic patients were evaluated for presence of cutaneous manifestations.

Maximum number of patients belonged to 51-60 years and 41-50 years of age group and similar observations were reported by Timshina et al and Mahajan et al.[5,6] In our study, males outnumbered females (m:f- 1.44:1) whereas females outnumbered males in a study by Mahajan et al.[6]

Majority of the patients in our study were of type 2 diabetes mellitus which is in accordance with Timshina et al, Mahajan et al, Chatterjee et al, Sanad et al and Vahora et al.[5-9] This reflects the general distribution pattern of type 1 and type 2 diabetes mellitus cases in the world.

In the present study 77.7% patients had diabetes for less than 10 years. This is higher than that reported by Goyal et al and Chatterjee et al, but is lower than that reported by Vahora et al and Ragunatha et al.[7,9-11] 10.9% of our patients were newly diagnosed by dermatologist due to the clinical suspicion of diabetes based on their presenting skin manifestation, emphasising the importance of cutaneous signs of DM that may aid in its early diagnosis and treatment.

Obesity is among the various risk factors for development of diabetes. 47 (12.5%) patients in our study were obese (BMI >29.9 kg/m^2) while Timshina et al reported the mean body mass index to be 25.9±3.9 kg/mtsq among diabetics.[5]

Unsatisfactory glycemic control (HbA1c >8%) was present in 46.2% patients in our study which could be due to ours being a tertiary care centre and patients reporting late for treatment. Vahora et al and Niaz et al observed it in 55% and 68% of their cases respectively.[9,12]

In the present study, cutaneous manifestations were discernible in 73.7% of diabetics which is near similar to Chatterjee et al where 73.9% patients were found to have skin lesions.[7] Higher prevalence were reported by Shahzad et al (91.2%) and Timshina et al (88.3%), while lower prevalence were reported by Mahajan et al (64%), Hoessini et al (64%), Nigam et al (61%), Romano et al (60%) and Ragunatha et al (51.1%).[2,5,6,11,13,14]

Most common manifestations observed in our study were cutaneous infections (fungal and bacterial infections) (36.9%), followed by pruritus (12.5%), xerosis (10.3%), diabetic dermopathy (9.5%) and diabetic ulcers (6.4%).

Fungal infections constituted 28.1% and bacterial infections 8.8% in our study. According to Timshina et al fungal & bacterial infections comprised 30.4% and 15% respectively.[5] One patient in our study had rhinocerebral mucormycosis with cutaneous spread. This is a rare fungal infection with increased propensity to develop in the setting of uncontrolled diabetes. A study by Bala et al found a significant association between occurrence of mucormycosis and diabetes.[16]

Table 4: Pattern of cutaneous manifestations in DM in various studies.

	Studies					
Cutaneous manifestations	**Present study (%)**	**Timshina et al[5] (%)**	**Raghunatha et al[11] (%)**	**Nigam et al[2] (%)**	**Niaz et al[12] (%)**	**Vahora et al[9] (%)**
Cutaneous infections	36.9	46.9	20.6	26.5	48.3	39.6
Pruritus	12.5	15.2	5.2	4.5	8	1
Xerosis	10.3	18.8	4.4	0	0	5.6
Diabetic dermopathy	9.5	6.3	0.2	3.5	9	2.3
Diabetic ulcers	6.4	-	0.2	3	16	1.3
Psoriasis	4.5	2.2	0.6	0.5	0	3.3
Acanthosis nigricans	4.2	28.6	5	0	20	15.3
Acrochordons	3.7	24.6	26.2	5.5	10	13.3
Diabetic bulla	2.7	0	0.4	1	2	0.6

A comparison of the pattern of common dermatoses in diabetes mellitus reported by other authors in their studies is depicted in Table 4.

Among other manifestations, loss of hair over legs (4.5%) and pigmented purpura (2.9) were present in our patients, both of which are reported by Timshina et al.[5] Pigmented purpura over legs is also reported by Sanad et al, Vahora et al, Romano et al, Niaz et al, and Raghu et al.[8,9,12,17,18]

In our study vitiligo was found in 1.9% of patients as compared to 4% by Timshina et al, 3.3% by Vahora et al, 8% by Goyal et al, 1% reported by Niaz et al, and 10% by Raghu et al.[5,9,10,12,17]

Perforating dermatoses was observed in 1.6% of patients in our study which is well in accordance with Timshina et al, Vahora et al and Niaz et al, who reported it in 1%, 4% and 3.3% patients respectively.[5,9,12]

Xanthelesma and lichen planus were seen in 1.1% of patients and comparable figures were described by Vahora et al and Niaz et al.[9,12]

Other complications arising as a result of diabetic neuropathy and vasculopathy were amputation of part of extremity in 1.6% and acral gangrene in 1.6% of our patients. Gangrene has been described by Nigam et al in 2% patients.[2]

Necrobiosis lipoidica was present in 0.5% of our patients as compared to Timshina et al, Sanad et al and Niaz et al, in 0.9%, 2% and 9% patients respectively.[5,8,12]

One patient (0.3%) with uncontrolled diabetes had Scleredema diabeticorum which is also reported by Timshina et al, Vahora et al and Romano et al, in 0.9%, 0.6% and 0.3% patients respectively.[5,9,15]

Granuloma annulare reported in several studies by Ragunatha et al (0.2%), Vahora et al (0.3%), Romano et al (0.3%), Niaz et al (0.5%) and Timshina et al (1.8%) was seen in 0.3% of our patients.[5,9,11,12,15]

Cutaneous reactions to oral hypoglycemics and insulin have been reported by Timshina et al, Vahora et al and Romano et al which is comparable to our study.[5,9,15]

Several other cutaneous manifestations, not associated with diabetes mellitus were also observed in our study. Manifestations like eczema and cuatneous amyloidosis were noted in good number of patients comprising 2.7% and 2.4% respectively. Cutaneous amyloidosis was reported by Timshina et al in 4%, Vahora et al in 2%, Niaz et al and Raghu et al in 6% pateints.[5,9,12,17] Eczema

has been reported by Timshina et al in 1.8% patients, Vahora et al in 15.3% and Ragunatha et al in 7.8% patients.[5,9,11] As these manifestations are noted in many diabetic patients, further studies will help to evaluate their true significance and association with diabetes.

CONCLUSION

The integument is among the various organs affected by diabetes with a much high prevalence. The present study was undertaken to know the spectrum of cutaneous manifestations in diabetes mellitus. The present study revealed the prevalence of cutaneous manifestations in diabetes to be 73.7% with cutaneous fungal and bacterial infections, pruritus, xerosis, diabetic dermopathy and diabetic ulcers to be the commonest manifestations.

As cutaneous manifestations associated with diabetes can manifest prior to the diagnosis of diabetes and may reflect the glycemic control and other neurovascular complications, their knowledge to clinician will help in a more comprehensive management of diabetes and dermatoses and will also help in early diagnosis and prevention of complications of diabetes.

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