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Original Article

Cutaneous manifestations of diabetes mellitus type 2: prevalence and association with glycemic control

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Abstract

Objective To determine the frequency and pattern of skin disorders in patients with type 2 diabetes mellitus and their association with glycemic control in our diabetics.

Methods This descriptive, cross-sectional study was conducted at departments of Medicine and Dermatology, Sir Syed College of Medical Sciences and Hospital, Karachi from 1st January to 30th June 2014. Adult patients belonging to both genders having diabetes mellitus type 2 with cutaneous manifestations were included. After taking the informed consent, demographic details, duration of diabetes, mode of treatment for diabetes, types of footwear, foot care and glycemic profile were documented.

Results In 203 patients (41% male and 59% female), mean age was 50 $\pm$ 11 years and mean duration of diabetes 8.5 $\pm$ 7 years. Mean HbA1c was 8.6 $\pm$ 1.5 with 68% patients having unsatisfactory glycemic control. Most frequently observed skin disease was bacterial infections (26%), followed by fungal infections (22%), acanthosis nigricans (20%), diabetic foot (16%), nail changes (16%), acrochordons (10%), diabetic dermopathy (9%), necrobiosis lipoidica (9%), viral infections (8%) pruritus (8%) and xanthelasma (8%). There was significant association of unsatisfactory glycemic control with bacterial infections (p = 0.037) and fungal infections (p = 0.023). Females especially had a higher frequency of association with acanthosis nigricans (p = 0.030).

Conclusion Patients with type 2 DM have high frequency of infections especially bacterial and fungal. Other manifestations like acanthosis nigricans and diabetic foot are comparatively less common.

Key words
Cutaneous manifestations, diabetes mellitus type 2, glycemic control.

Introduction

Diabetes mellitus (DM) is an endocrinal disorder affecting all ages and socioeconomic groups. It is characterized by hyperglycemia secondary to absolute or relative deficiency of insulin. DM is classified into two types, DM type 1 (insulin-dependent diabetes-IDDM) and DM type 2 (non-insulin dependent diabetes-NIDDM). Global incidence of DM type 2 in the year 2000 was 171 million which is likely to be 366 million in the year 2030.[1] Long standing DM can lead to irreversible functional changes in the body that result in various complications. Disturbed metabolism of glucose, amino acids and lipids leads directly to physical signs in patients with DM. Approximately 30% of patients with DM have skin lesions.

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Cutaneous manifestations of DM can be broadly classified into four groups; skin lesions strongly associated with DM, skin lesions of infectious etiology, lesions secondary to complications of DM and lesions related to treatment of DM.

Various common and rare skin disorders associated with diabetes include diabetic dermopathy, necrobiosis lipoidica, diabetic bullae, diabetic thick skin, yellow skin, acanthosis nigricans, eruptive xanthomas, disseminated granuloma annulare, scleredema, yellow nails, skin tags, diabetic rubeosis, vitiligo and lichen planus.

Commonly seen cutaneous bacterial infections in DM are folliculitis, furunculosis, carbuncle, ecthyma, cellulitis and erysipelas. Cutaneous fungal infections encountered are pityriasis versicolor, oral, as well as, vulvovaginal candidiasis and dermatophytosis. Other associated disorders are calciphylaxis, xerosis, xanthelasma, lipodystrophy, macular amyloidosis and alopecia.[3] Commonly seen viral infections include herpes zoster and viral warts.[4]

A large number of other cutaneous disorders may also be seen in diabetic patients e.g. foot gangrene, pruritus, pallor and cold clammy skin of lower limbs, waxy skin, hemochromatosis and finger pebbles.[3,4]

The current study targeted to determine the frequency and pattern of skin disorders in patients with type 2 DM. The study was further aimed to see the association of skin manifestations with glycemic control in our diabetics.

Methods

Current study was carried out in the Department of Dermatology and Medicine, Sir Syed College of Medical Sciences and Hospital, Karachi, spanning from 1st January 2014 till 30th June 2014 over a period of six months. The study was conducted after a formal approval from the ethical research committee. Adult patients already diagnosed to be suffering from type 2 DM presenting with cutaneous manifestations were included in the study. Patients having skin changes secondary to pregnancy, other systemic illnesses and iatrogenic factors were excluded. An informed consent was obtained from all the enrolled subjects. The demographic details of all the enrolled subjects were also documented.

A detailed history was obtained from the enrolled patients including duration of diabetes and mode of treatment for diabetes (i.e. diet only, oral hypoglycemic, insulin therapy or combination therapy). After a detailed general, systemic and cutaneous examination, the clinical diagnosis of dermatological findings was established. Their fasting blood sugar, random blood sugar and HbA1c were advised to assess the glycemic control. Unsatisfactory glycemic control defined as HbA1c > 7 as per American Diabetic Association (ADA) criteria.

Other relevant laboratory investigations were advised where required including blood complete picture, renal profile, liver function tests, lipid profile, urine examination and pus for culture and sensitivity. Any special tests like Wood's lamp examination, fungal scrapings, skin biopsy, Tzanck smear, nail biopsy and nail clippings were performed in doubtful cases. All the findings were recorded on a specially designed proforma.

Data were compiled, tabulated and analyzed by SPSS (Statistical package for social sciences) version 17. Mean and standard deviation were used to represent quantitative variables like age,

duration of diabetes, fasting blood sugars, random blood sugars and HbA1c. Descriptive variables like presence of various skin changes were presented as frequencies and percentages. Chi-square test was used to determine association of various skin lesions with glycemic control and gender. *P* value < 0.05 is considered as significant.

Results

Total of 203 cases of type 2 DM were included in the study. There were 83 (41%) males and 120 (59%) females. Mean age of presentation was 50 ± 11 years, the age range being 30-80 years. The mean duration of diabetes was 8.5 ± 7 years (range being 1-30 years). The glycemic profile showed mean fasting blood sugar (FBS) 156 ± 50 g/dl (range= 69-360 g/dl), random blood sugar (RBS) 213 ± 79 (range = 98-550 g/dl). Mean HbA1c was 8.6 ± 1.5 % (range = 6 - 13%). On the basis of these, unsatisfactory glycemic control was present in 137 (68%) patients **(Table 1).**

Among the enrolled subjects, the most frequently seen skin disease was bacterial infections in 53 patients (26%), followed by fungal infections 45 (22%), acanthosis nigricans 40 (20%), diabetic foot 32 (16%) and onychomycosis 32 (16%). Other diseases seen with a lesser frequency in the descending order included: acrochordons, diabetic dermopathy, necrobiosis lipoidica, viral infections, pruritus and xanthelasma **(Table 1)**.

With reference to glycemic profile **(Table 2)**, 44 (30%) of patients with bacterial infections had unsatisfactory glycemic control as compared to 12 (18%) with satisfactory glycemic control (p = 0.037). Among patients with fungal infections, 39 (28%) patients had unsatisfactory glycemic control as compared to 6 (9%) with good glycemic control (p = 0.023).

In view of gender (**Table 2**), there were 31 females (25%) with acanthosis nigricans as

Table 1 Demographic variables, glycemic profile, bathing habits, and foot care status (n=203).

Variables	
Age (years)	
Mean	50 ± 11
Range	(30-80)
Gender	
Male	83 (41%)
Female	120(59%)
Duration of diabetes	
Mean ± SD (range)	8.5±7 (1-30)
< 5 years	62 (30%)
5-9 years	67 (33%)
≥10 years	74 (37%)
Mode of treatment for diabetes	
Insulin therapy	47 (23%)
Oral hypoglycemics	111(55%)
Combination therapy	36 (18%)
Diet control only	9 (4%)
Fasting Blood Sugar (mg/dl)	
Mean ± SD (range)	156 ± 50 (69-360)
≤130	72 (36%)
>130	131(64%)
Random blood sugars (mg/dl)	
Mean±SD (range)	213 ± 79 (98-550)
≤180	88 (43%)
>180	115 (57%)
HbA1C (%)	
Mean±SD (range)	8.6 ± 1.5 (6-13)
Glycemic control	
Satisfactory	66 (33%)
Unsatisfactory	137 (68%)
Bathing (per week)	
<5 times	131 (64.5)
≥5 times	72 (35.5%)
Types of shoes preferred	
Open	130 (64%)
Closed	73 (36%)
Footwear design	
Ill-fitting/ inappropriate	77 (38%)
Well-fitting/appropriate	126 (62%)
Foot care	
Good	36 (17%)
Fair	115 (57%)
Poor	52 (26%)
Peripheral neuropathy (sensory)	
Present	75 (37%)

Table 2 Various dermatological manifestations and their association with gender and glycemic control (n=203).

Dermatoses	*Total (n=203)*	*Gender*		*P value*	*Glycemic Control*		*P value*
		Males (n=83)	*Females (n=120)*		*Satisfactory (n=66)*	*Unsatisfactory (n=137)*	
Bacterial infections	53 (26%)	19 (23%)	37 (31%)	0.213	12(18%)	44 (30%)	0.037*
Viral infections	17 (8%)	7 (8%)	10 (8%)	0.748	13(20%)	4 (3%)	0.001*
Fungal infections	45 (22%)	18 (22%)	27 (23%)	0.891	6(9%)	39 (28%)	0.023*
Acanthosis nigricans	40 (20%)	11 (13%)	31 (25%)	0.030*	17(26%)	25 (18%)	0.216
Acrochordons	21 (10%)	9 (11%)	12 (10%)	0.846	7(11%)	14(10%)	0.276
Diabetic dermopathy	18 (9%)	7 (8%)	11 (9%)	0.857	8(12%)	10(7%)	0.258
Necrobiosis lipoidica	18 (9%)	8 (9.6%)	10 (8%)	0.748	8(12%)	10(7%)	0.258
Diabetic thick skin	10 (5%)	4 (4.8%)	6 (5%)	0.953	6(9%)	4(3%)	0.057
Xanthelasma	16 (8%)	8 (9.6%)	8 (6.6%)	0.440	2(3%)	14(10%)	0.075
Eruptive xanthomas	2 (1%)	0 (0%)	2 (1.6%)	0.237	0(0%)	2(1.4%)	0.324
Diabetic foot	32 (16%)	14 (17%)	18 (15%)	0.720	8(12%)	24(18%)	0.323
Pruritus	16 (8%)	4 (5%)	12 (10%)	0.178	8(12%)	8(5.8%)	0.120
Granuloma annulare	1 (0.5%)	0 (0%)	1 (0.8%)	0.404	0(0%)	1(0.7%)	0.487
Yellow skin	4 (2%)	2 (2.4%)	2 (1.6%)	0.708	2(3%)	2(1.5%)	0.451
Nail changes (onychomycosis)	32 (16%)	14 (17%)	18 (15%)	0.860	10(15%)	22(16%)	0.897
Vitiligo	2(1%)	2 (2.4%)	0 (0%)	0.087	1(1.5%)	1(0.7%)	0.596
Lichen planus	1 (0.5%)	1 (1%)	0 (0%)	0.228	1(1.5%)	0(0%)	0.149
Perforating dermatosis	2 (1 %)	0 (0%)	2 (1.6%)	0.237	2(3%)	0(0%)	0.041*
Rubeosis	2 (1%)	2 (2.4%)	0 (0%)	0.087	2(3%)	0(0%)	0.041*
Diabetic bullae	4 (2%)	1 (1.2%)	3 (2.5%)	0.514	2(3%)	2(1.5%)	0.451
Schaumberg dermatitis	2 (1%)	1 (1.2%)	1 (0.8%)	0.597	1(1.5%)	1(0.7%)	0.596
Macular amyloidosis	4 (2%)	1 (1.2%)	3 (2.5%)	0.514	1(1.5%)	3(2%)	0.865

*$P < 0.05$ is significant

compared to 11 males (13%), (p = 0.030). Gender preponderance was not found to be associated with other dermatoses.

Peripheral neuropathy (sensory) was present in 75 patients (37%). Regarding hygiene and bathing habits 131 (64.5%) patients took bath < 5 times a week and 72 (35.5%) took bath $\geq$ 5 times a week. Ill-fitting and inappropriate footwear was observed in 77 (38%) and appropriate footwear in 126 (62%). Overall foot care was fair in 115 (57%), good in 36 (17%) and poor in 52 (26%), (**Table 2**).

Discussion

Skin, being the largest organ of the body, is almost invariably affected by DM. The skin manifestations of DM are numerous and different studies have reported a variable frequency ranging from 30-100% in this regard.[1,3,,] Skin involvement may also be the initial presenting sign in such patients. Therefore, skin changes may even be seen sometime before the development of diabetes. Most of the diabetic patients develop skin manifestations eventually. Patients with longstanding diabetes have more severe skin pathologies.[9] The skin changes are in turn the result of different metabolic abnormalities of diabetes like persistent hyperglycemia leading to glycosylation of various tissue components in the skin. Other factors accounting for dermatologic complications are neuropathy, micro- or macroangiopathy, immunosuppression, and dyslipidemia. There are some cutaneous features specific to insulin resistance and hyperinsulinemia.

The prevalence of cutaneous disorders does not differ between the 2 major types of DM; it is the type of lesions that differs. Patients with type 2 DM develop infections frequently while those with type 1 DM have a frequent association with autoimmune type dermatologic manifestations.

Mean age of presentation in our series of patients was 50 ± 11 years. This seems to be similar to the report from Ahmed *et al.*[1], where the mean age of diabetic patients was 54 years. Likewise, Basit *et al.* also reported a comparable mean age of presentation. Therefore, the mean age of presentation for DM signifies that majority of them had longstanding diabetes affecting their social activities, as well as, productivity.[1]

Majority of patients enrolled in our study were females. Dermatological manifestations were seen more commonly in women in our study as the higher number of females presenting in the OPD indicates greater disease burden and health awareness among females.[1] On the contrary, some regional studies have shown a preponderance of males.

The mean duration of diabetes in our patients was 8.5 years; majority of patients (37%) had diabetes for 10 years or more. Majority of patients (64%) had poorly controlled diabetes with fasting blood sugars more than 130 mg/dl and an HbA1c mean value of 8.6%. Bhat *et al*. have reported similar figures for uncontrolled diabetes and associated dermatological features. Ahmed *et al.*[1] have reported a higher frequency (93%) of uncontrolled diabetes in a similar series of patients. However, the results can vary from one study to another depending upon the study design and setting. This in turn may be correlated with medical facilities, hygiene, literacy level and lack of awareness about the disease.[1,2] Therefore, uncontrolled DM increases the risk of development of complications like dermatological manifestations and progression of the disease.[8,,,]

Infections were the most common group of dermatoses (57%) seen in our study comprising bacterial infections, fungal infections and viral infections. The overall frequency of skin infections in patients with DM varies between in 20-50%.[8] Cutaneous infections are especially seen more frequently in patients with type 2 DM. There was no relationship of skin infections with gender but patients with poor glycemic control were found to be more prone to infections especially bacterial. Basit *et al*.[10] have reported a higher frequency of infections in males in a similar set of patients. This in turn may be due to increased exposure to the infectious organisms and humid climatic conditions.[10] Vahora *et al*.[8] have reported a lesser frequency of bacterial infections in such patients. On the contrary, the frequency of bacterial infections in type 2 DM was reported to be higher by Naheed *et al.*[16] Ahmed *et al*.[1] also reported bacterial infections to be more common in their study. Bacterial infections most commonly seen in diabetics are *Staphylococcus aureus* and *Streptococcus pyogenes* leading to the development of impetigo, folliculitis, furunculosis, carbuncle, ecthyma, cellulitis, and erysipelas. Ahmed *et al.*[1] claimed a lower frequency of fungal and viral infections. The relative high prevalence of these infections in our study could be due to hot and humid weather. Among fungal infections the most common disease was candidiasis which may be an early indicator of undiagnosed diabetes. Dermatophytosis was also seen in our patients, with tinea pedis being the most common can act as a portal of secondary bacterial invasion.

Acanthosis nigricans was the second most common dermatoses associated with type 2 DM in the current study. The frequency was found to be higher in females due to an initially higher

number of enrolled female patients. The associated dermatological feature had a lesser frequency then infections and can be accounted for by the fact that it is not due to uncontrolled diabetes but due to insulin resistance. The high levels of insulin act on the insulin-like growth factor receptors and lead to formation of the acrochordons and acanthosis nigricans. Different domestic and international studies have also confirmed the association in the past.[6,8,9] Acrochordons were seen in 10% of our patients. Similar association of acrochordons with type 2 DM has been reported in another local study.[8]

In our study, 16% of the enrolled patients had diabetic foot. Diabetic foot ulcers are usually related to different mechanisms like impaired immunity, neuropathy, peripheral arterial disease, venous insufficiency and lymphedema. Diabetic patients are more susceptible to infections. Diabetic foot has been reported with a variable frequency in different studies ranging between 10 and 50%.[1,6,8,] Mansour *et al*.[19] have reported foot abnormalities to be more common in male diabetics. Other studies have also confirmed the association.[20] This is in contrast to our study where there was a female preponderance due to an initially higher number of enrolled females. Ali *et al*.[21] have also claimed a higher body mass index for female diabetics with foot ulcers.

Pruritus being a feature of diabetes was also seen in 8% of our patients. Pruritus is well known to have an association with diabetes mellitus as reported in the past literature.[1-4] Al-Mutairi *et al*.[17] have reported the frequency to be 47% in a similar series of patients. This is much higher in frequency as compared to our patients (16%). However, the findings in different studies can be affected by study design and setting.

In our study, the frequency of necrobiosis lipoidica was 9%. The association of diabetes mellitus has been regularly reported in different studies.[20-21] As a marker of diabetes, it can be seen with a frequency as low as 0.3-1.6%. It may precede or follow the development of diabetes in a significant percentage of patients.[18]

Diabetic thick skin was seen in 5% of the enrolled subjects in this study. This is caused by non-enzymatic glycosylation of collagen which makes it less soluble. As the duration of diabetes increases it leads to progressive glycosylation of the subcutaneous components. Similar frequency of thick skin has been reported in other studies.[-22]

Diabetic dermopathy had a frequency of 9% in our patients. However, other workers have reported diabetic dermopathy to be the most common and specific dermatological association of DM.[23-25] Other dermatological features having a frequency less then 5% were: spontaneous blisters, granuloma annulare, lichen planus, vitiligo and eruptive xanthomas. Other workers have also reported low frequency of these disorders in association with DM.[22,26]

Thus, there is a definite association between diabetes mellitus and dermatological diseases. A good glycemic control reduces the incidence and severity of cutaneous disorders with or without known pathogenesis.[26-28] Long-term effects of DM on the microcirculation and dermal collagen eventually results in skin disorders in almost all diabetic patients. Thus, dermatologists play an important role in reducing the dermatological morbidity, improvement of quality of life, and management strategy of diabetic patients.[8]

Conclusion

Patients with type 2 DM have high frequency of infections especially bacterial and fungal.

Different manifestations like acanthosis nigricans and diabetic foot are comparatively less common. Achieving appropriate glycemic control in diabetics can reduce bacterial and fungal infections. Education of patients and health care personnel regarding adaptation of preventive measures and seeking timely dermatological opinion for these skin problems may reduce morbidity, complications, hospital visits and burden on health care facilities.

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