Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2017/566

Original Article

Prevalence of Cutaneous Manifestations in Patients with Diabetes Mellitus of North Kerala

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Abstract

Background: Diabetes mellitus (DM) is the most common endocrinal disease which frequently has skin manifestations. The binding of a glucose molecule to the tissue protein results in an effect on structure and function of that protein and results in clinical manifestations of the disease. It is also suggested that increased cross-linkage of collagen of diabetic patients is responsible for their skin being generally thicker than that of non-diabetics. Advanced glycosylation end products are probably responsible for yellowing of skin and nails. Increased viscosity of blood due to stiff red blood cell membranes results in engorgement of the post-capillary venules in the papillary dermis, detected as erythema of the face, or periungual erythema. It is suggested that these skin changes may eventually be used as a reflection of the patient's current as well as past metabolic status.

Aim of the Study: The aim is to study the prevalence and pattern of cutaneous manifestations in patients with long-standing DM and their association with glycemic control, in this part of Kerala.

Materials and Methods: A prospective, descriptive, cross-sectional study was conducted on adult patients with long-standing DM attending the Department of Dermatology. The demographic data, duration of DM, treatment adopted, skin lesions, foot care, and glycemic details were recorded in a standard pro forma.

Observations and Results: Among 286 patients, 172 (60.13%) were males and 114 (39.86%) females. The male-to-female ratio of the present study was 1.5:1. The mean age was 55.35 ± 4.15 years. Type I DM was observed in 78 (27.27%) and Type II DM in 208 (72.72%). Among the 286 patients included in this study, bacterial infections were observed in 117 (40.09%) patients, fungal infections in 98 (34.26%), pruritus in 103 (36.01%), acanthosis nigricans in 66 (23.07%), nail lesions in 52 (18.18%), diabetic foot 47 (16.43%), viral infections in 42 (14.68%), and acrochordons in 29 910.13%) patients. The cutaneous lesions were more common in patients with unsatisfactory glycemic control.

Conclusions: Cutaneous lesions are common in DM, especially with unsatisfactory glycemic control. Bacterial, fungal, and viral infections are more common than other lesions. Type II DM has a higher frequency of infections and other lesions than Type I. Acanthosis nigricans has a gender predilection to females. Acanthosis nigricans is the next common skin lesions in DM after infections.

Key words: Cutaneous manifestations, Diabetes mellitus, Diabetic foot, Glycemic control, Nail diseases, Pruritus

INTRODUCTION

Skin manifestations in long-standing diabetes mellitus (DM) are common and present clinically in various forms. If metabolic effects of endocrinal disturbance of glucose levels are considered as the cause for its effect on microcirculation and skin collagen, the prevalence of skin manifestations may reach 100%. However, in certain skin manifestations, the pathophysiology is still uncertain. Rahbar[1] in 1968 showed that patients with DM have abnormal hemoglobin (Hb). This was later proven to be due to non-enzymatic condensation of glucose with Hb to form stable covalent adducts. Similar non-enzymatic glycosylation occurs with many tissue proteins including collagen; when the collagen protein is affected it results in skin color change which has been demonstrated by spectrophotometric measurement to correlate with diabetic complications.[2] The amino acid pentosidine and a yellow compound, 2-(2- furoyl)-4(5)-(2-furanyl)-1H-imidazole, have been identified in the skin of DM patients are advanced glycosylation end products which

Access this article online

www.ijss-sn.com

Month of Submission : 10-2017
Month of Peer Review : 11-2017
Month of Acceptance : 11-2017
Month of Publishing : 12-2017

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correlate with a cumulative score of diabetic complications.[3] The process of non-enzymatic glycosylation occurs in a minor extent at normal blood sugar concentrations but at an accelerated rate in persons with elevated blood sugars; glycosylation of the red cell membrane is apparently responsible for the stiffness of diabetic erythrocytes.[4] DM is classified into two types, DM Type I insulin-dependent diabetes (IDDM) and DM Type II non-IDDM- (NIDDM). In the year 2000, the global incidence of DM Type II was 171 million and is likely to be 366 million in the year 2030.[5] Long-standing DM can lead to irreversible functional changes in the body which results in various complications. Disturbed metabolism of glucose, amino acids, and lipids lead directly to physical signs in patients with DM. Approximately 30% of patients with DM have skin lesions. The uncommon lesions are diabetic dermopathy, necrobiosis lipoidica, diabetic bullae, diabetic thick skin, yellow skin, acanthosis nigricans, eruptive xanthomas, disseminated granuloma annulare, scleroderma, yellow nails, skin tags, diabetic rubeosis, and 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.[6] The commonly seen viral infections include herpes zoster and viral warts.[7] 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.[6,7] The present study was conducted to study the prevalence and pattern of cutaneous manifestations in patients with long-standing DM and their association with glycemic control, in this part of Kerala.

Type of Study

This was a prospective, descriptive, cross-sectional study.

Period of Study

The study period was from May 2016 to October 2017.

Institute of Study

The study was conducted at Kannur Medical College Hospital, Anjarakandy, Kannur.

MATERIALS AND METHODS

A prospective, descriptive, cross-sectional study was conducted on adult patients with long-standing DM attending the Department of Dermatology, Kannur Medical College, Anjarakandy, Kannur, Kerala. A total of 286 patients from among the DM patients attending outpatient departments of both the Department of Medicine and Dermatology presenting with skin lesions and complaints were included in the study. The demographic data, duration of DM, treatment adopted, skin lesions, foot care, and glycemic details were recorded in a standard pro forma. An Institutional Ethical Clearance was obtained, and a standard pro forma approved by the Ethical Committee was used in this study.

Inclusion Criteria

The following criteria were included in the study:

1. Patients aged 20 years and above with DM.
2. Patients with DM for more than 5 years duration.
3. Patients with skin lesions or complaints related to the skin.

Exclusion Criteria

The following criteria were excluded from the study:

1. Patients who are pregnant.
2. Patients with critical systemic illnesses.
3. Patients with iatrogenic diseases with skin lesions.

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. Laboratory investigations such as fasting blood sugar (FBS), random blood sugar, and HbA1c were advised to assess the glycemic control. Unsatisfactory glycemic control defined was HbA1c >7 as per the American Diabetic Association 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 such as Wood's lamp examination, fungal scrapings, skin biopsy, Tzanck smear, nail biopsy, and nail clippings were performed in doubtful cases. All the data were analyzed using standard statistical methods.

OBSERVATIONS AND RESULTS

Among the 286 patients included in the study, there were 172 (60.13%) males and 114 (39.86%) females. The male-to-female ratio of the present study was 1.5:1. Patients belonging to the age group of 20–30 were 24 (08.39%), age group of 30–40 were 62 (21.67%), age group of 40–50 were 81 (28.32%), and 50–60 were 73 (25.52%). The mean age was 55.35 ± 4.15 years. Type I DM was observed in 78 (27.27%) and Type II DM in 208 (72.72%). The other personal data are summarized in Table 1.

The mean duration of DM in males was 9.42 ± 1.50 and in females was 7.65 ± 2.05. The glycemic profile showed mean FBS 162 ± 44.70 g/dl (range = 89–260 g/dl) in

males and 164 ± 39.60 g/dl (range 78–230 g/dl) in females. Mean HbA1c was 8.62 ± 1.07 (range: 6–13%) in males and 8.10 ± 1.0 (range; 8–12) in females [Table 2]. Based on this, the unsatisfactory glycemic control was present in 185 (64.68%) patients [Table 1].

Among the 286 patients included in this study, bacterial infections were observed in 117 (40.09%) patients, fungal infections in 98 (34.26%), pruritus in 103 (36.01%), acanthosis nigricans in 66 (23.07%), nail lesions in 52 (18.18%), diabetic foot 47 (16.43%), viral infections in 42 (14.68%), and acrochordons in 29 910.13%) patients. The incidences of other lesions are tabulated in Table 3. The incidence of bacterial, fungal, and viral infections were correlated with the unsatisfactory glycemic profile of patients in the study and were found significant. These infections being more frequent in unsatisfactorily controlled DM. The data were statistically significant as the *P* value was below 0.05 (*P* value taken as significant at <0.05). The *P* value for bacterial infections was 0.038, fungal infections was 0.027, and viral infections was 0.041 [Table 3]. The gender preponderance in acanthosis nigricans was statistically significant as it was found more common in females. The *P* = 0.031 (*P* statistically significant at <0.05). The other values were not statistically significant as the *P* values were >0.05 [Table 3].

In this study, single skin lesion was observed in 178 (62.23%) patients, two lesions were observed in the same patient in 65 (22.72%) patients, three lesions were noted in 11 (03.84%), and four lesions in 06 (02.09%) patients [Table 4].

Table 1: The demographic data and personal data of the study group (*n*=386)

Observation	*n* (%)
Age in years	
20–30	024 (08.39)
30–40	062 (21.67)
40–50	081 (28.32)
50–60	073 (25.52)
60–70	046 (16.08)
Gender	
Male	172 (60.13)
Female	114 (39.86)
Type of DM	
Type I	078 (27.27)
Type II	208 (72.72)
Duration of DM in years	
5–8	085 (29.72)
9–11	139 (48.60)
>11	062 (21.67)
Treatment	
Di*et al*.ne	026 (9.09)
Oral hypoglycemic	095 (33.21)
Insulin	069 (24.12)
Combination	081 (28.32)
Other (Indian)	015 (05.24)
Glycemic control	
Satisfactory	101 (35.31)
Unsatisfactory	185 (64.68)
Personal hygiene bathing	
<5 times/week	021 (07.34)
>5 times/week	267 (93.3)
Pedicure	
Regular	066 (23.07)
Irregular	220 (76.92)
Wound care	
Prompt	242 (84.61)
Delayed	044 (15.38)
Type of footwear	
Open	199 (69.58)
Closed	087 (30.41)
Peripheral neuropathy	
Present	109 (38.11)
Absent	177 (61.88)

DM: Diabetes mellitus

Table 2: The mean values of laboratory data (*n* - 286)

Observation	Male	Female	*P*
Mean duration of DM in years	9.42±1.50	7.65±2.05	0.187
Mean FBS	162±44.70	164±39.60	0.341
Mean HbA1c	8.62±1.07	8.10±1.0	0.278

DM: Diabetes mellitus, FBS: Fasting blood sugar, HbA1c: HemoglobinA1c

DISCUSSION

Skin, being the largest organ of the body, is most likely to be affected by DM. The list of skin manifestations of DM is very big and different studies have reported a variable frequency ranging from 30 to 100%.[5,6] In few patients, the skin manifestation may be a presenting symptom or sign.[6] Therefore, skin changes may even be seen sometime before the development of diabetes. Patients with DM of longer duration have more severe skin pathologies.[8] Apart from the basic molecular level changes in the connective tissue of skin and endothelium of the venules and capillaries causing skin lesion in DM, the factors accounting for dermatologic complications are neuropathy, macro- or micro-angiopathy, immunosuppression, and dyslipidemia.[9] There is no difference in the prevalence of skin lesion according to the type of DM whether Type I or Type II. However, the infections are more common in Type II DM and immune-related dermatoses are more common with Type I DM.[10] The mean age of presentation in this study was 55.35 ± 4.15 years. The study by Ahmed *et al*.[5] observed that the mean age was 54 years. Similarly, Basit *et al*.[11] also reported the mean age of 56.16 years. The male-to-female ratio of the present study was 1.5:1. The mean duration of DM in the present study was 9.42 ± 1.50 in males and was 7.65 ± 2.05 in females. The duration range was 5–13.45 years. The glycemic profile showed mean FBS 162 ± 44.70 g/dl (range = 89–260 g/dl) in males and

Table 3: Various skin diseases encountered in the study (*n*=286)

Skin lesions	*n* (%)	Male - 172 (%)	Female - 114 (%)	*P*	Satisfactory glycemic control	Unsatisfactory glycemic control	*P*
Bacterial infections*	117 (40.90)	87 (50.58)	30 (26.31)	0.321	28	79	0.038
Fungal infections*	98 (34.26)	61 (35.46)	37 (32.45)	0.256	19	79	0.027
Viral infections*	42 (14.68)	30 (17.44)	12 (10.52)	0.411	12	30	0.041
Pruritus	103 (36.01)	56 (32.55)	47 (41.22)	0.125	42	61	0.210
Nail changes	52 (18.18)	28 (16.27)	24 (21.05)	0.401	22	30	0.311
Acanthosis nigricans*	66 (23.07)	17 (09.88)	49 (42.98)	0.021	19	47	0.031
Acrochordons	29 (10.13)	17 (09.88)	12 (10.52)	0.153	11	18	0.351
Diabetic thick skin	22 (07.69)	14 (08.13)	08 (07.01)	0.190	07	15	0.283
Necrobiosis lipoidica	21 (07.34)	16 (09.30)	15 (13.15)	0.311	08	13	0.311
Eruptive xanthomas	06 (02.09)	04 (02.32)	02 (01.75)	0.432	02	04	0.412
Diabetic foot	47 (16.43)	28 (16.27)	19 (16.66)	0.610	20	27	0.378
Granuloma annulare	05 (01.74)	03 (01.74)	02 (01.75)	0.311	01	04	0.291
Lichen planus	06 (02.09)	03 (01.74)	03 (02.63)	0.279	02	04	0.510
Perforating dermatosis	08 (02.79)	05 (02.90)	03 (02.63)	0.241	03	05	0.601
Diabetic bullae	07 (02.44)	04 (02.32)	03 (02.3)	0.186	02	05	0.438
Schamberg's dermatitis	05 (01.74)	03 (01.74)	02 (01.75)	0.153	0	04	0.361
Macular amyloidosis	07 (01.74)	04 (02.32)	03 (02.63)	0.205	03	04	0.251
Xanthelasma	30 (10.48)	18 (10.46)	12 (10.52)	0.561	12	18	0.214
Macular amyloidosis	09 (03.14)	05 (02.90)	04 (03.50)	0.701	03	06	0.184
Rubeosis	04 (01.39)	02 (01.16)	02 (01.75)	0619	02	02	0.231

**P* value is significant at <0.05

Table 4: Number of patients showing more than one lesion (*n*=286)

Skin Lesions (%)	Male- 172	Female- 114
1 lesion - 178 (62.23)	100	78
2 lesions - 065 (22.72)	42	23
3 lesions - 011 (03.84)	06	05
4 lesions - 006 (02.09)	04	02

164 ± 39.60 g/dl (range 78–230 g/dl) in females. Mean HbA1c was 8.62 ± 1.07 (range: 6–13%) in males and 8.10 ± 1.0 (range; 8–12) in females in this study. The study by Bhat *et al.*[12] has reported similar figures for uncontrolled diabetes and associated dermatological features. however, Ahmed *et al.*[5] reported a higher frequency in uncontrolled diabetes. The wide variation in reporting may be due to various factors such as study design and setting which in turn may be dependent on the availability of medical facilities, hygiene, literacy level, and lack of awareness about the disease.[3,4] In this study, bacterial infections were observed in 117 (40.09%) patients, fungal infections in 98 (34.26%), pruritus in 103 (36.01%), acanthosis nigricans in 66 (23.07%), nail lesions in 52 (18.18%), diabetic foot 47 (16.43%), viral infections in 42 (14.68%), and acrochordons in 29 (910.13%) patients. 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. However, in the study by Basit *et al.*,[11] there was a preponderance of bacterial infections in males. The higher incidence of infections in this part of Kerala may be due to high humidity during rainy seasons and dry heat in summer.

Vahora *et al.*[10] reported a lesser frequency of bacterial infections in their patients. Naheed *et al.*[13] reported a higher frequency of bacterial infections in Type 2 DM. Bacterial infective lesions commonly seen in DM are impetigo, folliculitis, furunculosis, carbuncle, ecthyma, cellulitis, and erysipelas caused by *Staphylococcus aureus* and *Streptococcus pyogenes*. Candidiasis was the most common fungal infection in this study. This fungal infection may be taken as an indicator for undiagnosed DM. Tinea pedis was the most common dermatophytosis observed in this study. The second most common dermatosis was acanthosis nigricans, especially in DM Type II patients. This was less frequent than the infections in this study. Al-Mutairi[14] gave an explanation for this associated dermatological feature with lesser frequency due to 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 the formation of the acrochordons and acanthosis nigricans. National and international studies have shown the association of acrochordons with Type II DM. In this study, the incidence was 10.13% similar to the study by Vahora *et al.*[10] The incidence of diabetic foot in this study was 16.43%. Diabetic foot is usually related to different mechanisms playing their role in its development and resistance for treatment in DM. They are usually related to different mechanisms such as impaired immunity, neuropathy, peripheral arterial disease, venous insufficiency, and lymphedema. Mansour and Imran[15] observed the diabetic foots being more common in males. Other studies have also confirmed the association.[16] Pruritus was the fourth common complaint with 36.01% of the patients presented in this study group. Al-Mutairi[14]

has reported the frequency in a study similar to this as 47%. This was much higher in frequency as compared to our study with 36.01% presenting with pruritus. In the present study, the frequency of necrobiosis lipoidica was 07.34%. The association between DM and this skin lesion was reported by many authors[17,18] of DM has been regularly reported in different studies. Diabetic thick skin was seen in 7.69% of the study group patients. This is caused by non-enzymatic glycosylation of collagen making it less soluble. As the duration of diabetes increases, it leads to progressive glycosylation of the subcutaneous components. Korkmaz *et al.*[19] reported a similar frequency of thick skin in their study. Other dermatological features having a frequency <5% were as follows: Spontaneous blisters, granuloma annulare, lichen planus, vitiligo, and eruptive xanthomas. Other workers have also reported a low frequency of these disorders in association with DM.[12,20] The present study showed that there is a definite association between unsatisfactory glycemic control and prevalence of dermatological diseases in patients with DM irrespective of their type. A good glycemic control reduces the incidence and severity of cutaneous disorders with or without known pathogenesis.[21,22] Longer the duration of DM in patients, long-term effects of DM on the microcirculation and dermal collagen eventually result in skin disorders in almost all diabetic patients. The role of a dermatologist is to identify the skin lesions and in undiagnosed DM patients to investigate for confirmation of the pre-existing disease. This would help in reducing the dermatological morbidity, improvement of the quality of life, and management strategy of diabetic patients.

CONCLUSION

Cutaneous lesions are common in DM, especially with unsatisfactory glycemic control. Bacterial, fungal, and viral infections are more common than other lesions. Type II DM has a higher frequency of infections and other lesions than Type I. Acanthosis nigricans has a gender predilection to females. Acanthosis nigricans is the next common skin lesions in DM after infections. Other dermatological features having a frequency <5% were as follows: Spontaneous blisters, granuloma annulare, lichen planus, vitiligo, and eruptive xanthomas. Achieving good glycemic control can reduce bacterial and fungal infections.

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How to cite this article: Kambil S. Prevalence of Cutaneous Manifestations in Patients with Diabetes Mellitus of North Kerala. Int J Sci Stud 2017;5(9):110-114.

Source of Support: Nil, **Conflict of Interest:** None declared.