

# Skin Lesions in Type 2 Diabetic Patients

Mahboobeh-Sadat Hosseini, MD<sup>1</sup>  
 Amir Hooshang Ehsani, MD<sup>2</sup>  
 Farhad Hosseinpanah, MD<sup>3</sup>  
 Fereydoon Azizi, MD<sup>3</sup>  
 Maryam Salami, MD<sup>4</sup>  
 Hossein Khedmat, MD<sup>5</sup>

1. Department of Endocrinology;  
 Baqiyatallah University of Medical  
 Sciences

2. Department of Dermatology; Tehran  
 University of Medical Sciences, Tehran,  
 Iran

3. Obesity Research Center, Research  
 Institute for Endocrine Sciences, Shaheed  
 Beheshti University of Medical Sciences,  
 Tehran, Iran

4. Taleghani Hospital, Shaheed Beheshti  
 University of Medical Sciences, Tehran,  
 Iran

5. Research Center for Gastrointestinal  
 and Liver Disease, Baqiyatallah  
 University of Medical Sciences, Tehran,  
 Iran

Corresponding author:  
 Amir Hooshang Ehsani, MD  
 Razi Hospital, Vahdat\_e\_eslami Square,  
 Tehran, Iran  
 ehsanah@sina.tums.ac.ir

Received: June 22, 2008

Accepted: August 10, 2008

## Abstract

**Background:** Skin lesions are common in type 2 diabetic patients and its association with microvascular complications been reported.

**Methods:** In this study, 1135 type-2 diabetic patients were included and examined by a dermatologist for diabetes mellitus related skin lesions, skin infections and cutaneous complications of the treatment. Smear, culture and biopsy of the lesions were done for definite diagnosis. Weight, height, blood pressure were also done. FBS and HbA1C were measured for all patients

**Results:** The mean age of the study population was  $54 \pm 11$  years; 619 were (55%) female and 516 were (45%) male. Mean duration of the disease was  $9 \pm 7$  years and HbA1c was  $7.8 \pm 1.6$ . The prevalence of skin lesions was 64% (95%CI: 61.2-66.8). The most common solitary skin lesion was diabetic dermopathy (32.3%) while the most common condition observed overall was skin infections (41.5%). Acanthosis nigricans with a prevalence of 26.4% was the third most common lesion. Other skin conditions had a prevalence of less than 12%. Skin disorders were apparently more prevalent in male than in female patients.

**Conclusion:** More than sixty percent of patients with type-2 diabetes mellitus have skin lesions (*Iran J Dermatol 2008;11: 113-117*)

**Keywords:** diabetes, type 2, skin

## Introduction

Diabetes mellitus (DM) is characterized by hyperglycemia resulting from impaired secretion or function of insulin.<sup>1</sup> This disease can affect any organ such as the skin.<sup>2</sup> Skin lesions of DM can be classified in four categories: skin manifestations with weak or strong association with diabetes including necrobiosis lipoidica, diabetic dermopathy, diabetic bulla, cutaneous manifestations due to diabetic complications such as microangiopathy, macroangiopathy and neuropathy, skin lesions due to treatment of DM and finally, infections (bacterial, fungal).<sup>3</sup>

In most studies, skin lesions have been observed in both types of DM. However, there is little

information about the prevalence of skin lesions in patients with type 2 DM<sup>4-6</sup>. Skin manifestations are common in DM and could be expressed in various forms; if we considered metabolic effects on microcirculation and changes in skin collagen, the prevalence of such manifestations would be 100 percent<sup>7</sup>. The aim of this assay was to determine the prevalence of skin lesions in patients with type 2 DM.

## Patients and Methods

This cross-sectional study was done in 2005 in Tehran, Iran. According to the prevalence of diabetic bulla (5.6%), which is one of the less common lesions in DM, the calculated sample size

was 1135 cases ( $\alpha=10\%$ ,  $\beta=0.2p$ ). We included all patients with type 2 diabetes mellitus (according to AAD criteria: FBS  $\geq 126$  for 2 times) who were over 40 years of age, did not show any obvious signs and symptoms of insulin deficiency and had a positive family history of type 2 diabetes.

All outpatients were recruited through the Iran Diabetic Association and the dermatology and endocrine clinics affiliated to our medical universities. From July 2005 to March 2006, over a period of 8 month, they were examined by a dermatologist to determine the presence of diabetes mellitus-related skin lesions, skin infections and skin lesions caused by treatment. Other skin lesions were attended to and taken care of, just on the basis of patients' complaints. Definite diagnosis of necrobiosis lipoidica, scleroedema, perforating dermatoses, granuloma annulare, xanthoma and diabetic bullae were made through skin biopsies by a qualified dermatopathologist. Skin smears and cultures were taken to confirm the presence of cutaneous infections. All patients were assessed for blood pressure, height and weight. Neurological assessments were done using Michigan neuropathy screening instrument.<sup>8</sup>

At the same time, FBS and HbA1c were measured. Only the skin lesions with a duration of less than 3 months were studied to find their association with HbA1c. All tests were done in a single laboratory.

This study was approved by ethical committee of our institute research board and an informed written consent was obtained from all subjects. All data was analyzed by SPSS-11 (SPSS inc. Chicago, IL, USA, version 11) using chi-square or t-test. P values  $<0.05$  were considered statistically significant. A multivariate logistic regression model

was used to estimate the adjusted odds ratio (OR) for having diabetes related skin lesions.

## Results

The mean age of 1135 patients was  $54\pm 11$  years, 619 (55%) were female and 516 (45%) were male. The mean duration of the disease was  $9\pm 7$  years and mean HbA1c level was  $7.8\pm 1.6$  g/dl. Oral hypoglycemic agents were used by 913 (82%) patients, while insulin injection was used by 162 (14%) and both were used by 34 (3%) ones. The prevalence of cutaneous lesions was 64%. Most of them appeared after the diagnosis of DM (91%) was made. 8% of the patients had skin lesions before the diagnosis of DM. The total number of cutaneous lesions was 1833 and 70% had more than one lesion (table 1). Only about 8% of lesions appeared within one year of diabetes diagnosis. In 49% of patients with acantosis nigricans, the lesions appeared during the first year of DM diagnosis in contrast to diabetic dermopathy with an incidence of 6% appearing in the first year of DM diagnosis.

The most common individual lesion was diabetic dermopathy (32.3%), but different types of skin infections were seen in 41.5% of patients and thus forming the most common lesions. The third most common manifestation was acantosis nigricans (26.4%). The prevalence of other skin lesions was less than 12%. (table 2)

The mean age of patients with cutaneous lesions was significantly higher than others ( $P<0.05$ ). The mean age of patients was lower in patients with granuloma annular ( $48\pm 14$  years old in contrast to  $54\pm 11$ ) ( $p<0.05$ ). The level of HbA1c was higher in those suffering from diabetic foot ulcer and candidial intertrigo ( $9.3\pm 1.4$ ,  $8.5\pm 1.4$  in contrast to  $7.7\pm 1.6$  and  $7.7\pm 1.6$ , respectively) ( $p<0.05$ ).

**Table 1: Demographics of diabetic patients with or without skin lesions**

Variable	All patients	With skin lesion	Without skin lesion
Age (years)	$54\pm 11$	$55\pm 11$ †	$51\pm 6$
Sex (Female)	619 (55)	353 (48) †	266 (64)
*Duration of disease (years)	$9\pm 7$	$10\pm 7$ †	$7\pm 7$
+Family history of DM (%)	827 (73)	535 (74)	292 (73)
BMI ( Kg/m <sup>2</sup> )	$27\pm 4$	$28\pm 3$	$27\pm 3$
±Type of treatment			
Oral drugs (%)	913 (82)	576 (81)	337 (84)
Insulin (%)	162 (14)	111 (15)	51 (12)
Both (%)	34 (3)	23 (3)	12 (3)
HbA1c (%)	$7.8\pm 1.6$	$7.8\pm 1.6$	$7.7\pm 1.7$
Total	1135	723 (64%)**	412 (36%)

\* duration of disease : time from diagnosis

+family history : parent, siblings, offspring

± 21 patient did not use any medication

† P<0.05 in comparison with patients without skin lesions except for gender that has been compared between females and males with skin lesions

\*\* 95% confidence interval: 61.2-66.8

**Table 2:** Frequency of cutaneous manifestations in patients with type 2 diabetes mellitus

DM related skin lesions	Frequency (percent)	CI (95%)
Diabetic dermopathy	367(32.3)	29.6-35.0
Acanthosis nigricans	300(26.04)	23.8-29.0
Diabetic foot ulcer	77(6.8)	5.3-8.3
Generalized granuloma annulare	35(3.1)	2.1-4.1
Facial erythema	18(1.6)	0.9-2.3
Diabetic bulla	10(0.8)	0.3-1.3
Perforating dermatoses	6(0.5)	0.1-0.9
Scleroedema	6(0.5)	0.1-0.9
Necrobiosis lipoidica	5(0.4)	0.0-0.8
*Xanthoma	3(0.3)	0.0-0.6
Sclerodermic changes in hands	1(0.8)	0.3-1.3
Total	828(73)	70.4-75.6
<b>Skin infections</b>		
Tinea pedis	137(12)	10.1-13.9
Erythrasma	135(11.8)	9.9-13.7
Tinea versicolor	131(11)	9.2-12.8
Candidial paronychia	101(8.8)	7.2-10.4
+ Onychomycosis	90(7.9)	6.3-9.5
± Pyoderma	76(6.7)	5.2-8.2
Candidial intertrigo	61(5.4)	4.1-6.7
Total	731(64)	61.2-66.8
<b>Skin lesion due to treatment</b>		
Lipohypertrophy	4(0.3)	0.0-0.6
Lipohypotrophy	2(0.1)	-0.1-0.3
Total	6(0.5)	0.1-0.9
<b>Miscellaneous</b>		
Pruritus	97(8.5)	6.9-10.1
Pigmented purpuric dermatosis	50(4.4)	3.2-5.6
Contact dermatitis	47(4.1)	2.9-5.3
Lichen planus	23(2)	1.2-2.8
Vitiligo	23(2)	1.2-2.8
Psoriasis	20(1.7)	0.9-2.5
Keloid	2(0.1)	0-0.3
Atopic dermatitis	6(0.5)	0.1-0.9
Total	268(24)	21.5-26.5

\* All 3 patients with xanthoma had TG more than 1000mg/dl and they were eruptive.

+ 137 patients (12%) had nail dystrophy. Ninety patients had dermatophyte and 10 had candida. In 30 patients, smear and culture were negative and in 7 of them, smear and culture were not taken.

± Pyoderma includes folliculitis, furunculosis and carbuncle.

## Discussion

This study demonstrated that the prevalence of type 2 diabetes skin lesions is about 64%. The prevalence of DM related skin lesions, skin infections and skin lesions due to treatment were 73% (70.4-75.6), 64% (61.2-66.8) and 0.5% (0.1-0.9), respectively. The frequency of skin lesions in type 2 diabetic patients has been reported to be in a range of 49-84% which is compatible with the results of the present study.<sup>4-6</sup>

The most frequent single skin manifestation was diabetic dermopathy [32.3%], which is compatible with the results of other studies<sup>12,13</sup>, but obviously higher in comparison with the studies by Romano (12.5%) and Foss (1.2%)<sup>15,4</sup> who evaluated the skin manifestations in both types of DM; however, only patients with type 2 DM have been included in our study. The prevalence of diabetic dermopathy in this study was higher than Sasmaz's findings in type

2 diabetic patients.<sup>5</sup> It can be the result of differences in the types of evaluated lesions or differences in the mean age, duration and complications of DM, not evaluated in Sasmaz's study. The prevalence of infectious lesions was 41.5% and tinea pedis was the most common; however, this prevalence was reported to be 61%, 62.2% and 31% by Romano, Talat and Sasmaz, respectively<sup>4,14,15</sup>. The difference can be explained by differences in blood sugar level, hygiene, socioeconomic and health status in the studied population. Acanthosis nigricans was the third most prevalent skin lesion (26.4%). In three articles mentioned above, this prevalence was reported to be 5.9%, 16.7%, and 7%, respectively<sup>15,16,17</sup>. These findings can be related to the high prevalence of insulin resistance in our study; because in those studies, patients with both type 1 and 2 DM were included and as we know insulin resistance and

consequently the possibility of acantosis nigricans is more common in patients with type 2 DM.

Lipohypertrophy and Lipohypotrophy were found in 0.3% and 0.1% of patients respectively. These lesions have not been reported in any other studies, except in a study by Tariq in which its prevalence was reported to be about 2.4%<sup>7</sup>. In our study, about 40% of the patients were visited in a dermatology clinic which can be the reason for the high prevalence of these complications. Cold injuries, alcohol contamination and inappropriate angle of needle at the time insulin injection are responsible for inducing lipohypotrophy; therefore, a possible cause for the occurrence of this complication may be inadequate education on the method of insulin injections.

Mean age, HbA1c and the duration of the disease were significantly higher in patients with dermopathy; also men were more affected by these complications. These findings are compatible with previous studies<sup>13,17</sup>.

Neuropathy induces skin xerosis, trauma, and fissures and increases the risk of infections. Bouguerra et al reported that patients' age and duration of DM are the major risk factors for cutaneous mycosis<sup>18</sup>. In a group of patients affected by candidal intertrigo during the previous 3 months, level of HbA1C was significantly higher than the others without intertrigo. It has been mentioned in a study by Rayfield.<sup>20</sup> Therefore, strict control of blood glucose and precise education on feet hygiene is necessary in patients with these infections.

Miller has reported that the prevalence of accompanying neuropathy and peripheral vessel disease combination in diabetic foot ulcer is about 15-20%<sup>21</sup>, indicating that all diabetic patients with foot ulcer should be evaluated for microvascular complications and blood glucose control and should receive education on diabetic foot ulcer prevention and treatment.

However, our study design was cross sectional and obviously with this design we can only prove the association between variables and this association does not mean causality. In conclusion, about two third of type 2 diabetic patients have skin lesions and the most common is cutaneous infections. Proper skin care and long-term control of blood glucose levels may reduce the risk of some of the skin lesions in diabetic subjects. Thus, it is important that all general practitioners and related specialist identify these disorders, recommend therapy and refer the patients to dermatologists for further evaluation. Some interventional researches

are needed to evaluate the possible role of glycemic control in reducing skin lesions.

## Acknowledgement

The authors wish to thank Dr. Rajab and other members of Iranian Diabetes Association and also our colleagues at the Endocrinology Research Center of the Shaeed beheshti University of Medical Sciences for their contributions to this research.

## References

1. American Diabetes Association, Screening for type 2 diabetes. *Diabetes Care* 2004; (supp 1): S11-S13.
2. Gupta AK, Konnikov N, MacDonald P, et al. Prevalence and epidemiology of toenail onychomycosis in diabetic subjects: a multicentre survey. *Br J Dermatol* 1998; 139: 665-71.
3. Perez MI, Kohn SR. Cutaneous manifestations of diabetes mellitus. *J Am Acad Dermatol* 1994; 30: 519-31.
4. Romano G, Moretti G, Di Benedetto A, et al. Skin lesions in diabetes mellitus: prevalence and clinical correlations. *Diabetes Res Clin Pract* 1998; 39: 101-6.
5. Sasmaz S, Buy Ukbese MA, Cetin Kaya A. The prevalence of skin disorders in type -2 diabetic patients. *J Dermatol* 2005; 3: 3-8.
6. Wahid Z, Kanjee A. Cutaneous manifestations of diabetes mellitus. *J Pak Med Assoc* 1998; 48:304-5.
7. Tariq M, Arfan B, Humayun A. Cutaneous manifestations of diabetes mellitus. *J Pak Assoc Dermatol* 2005; 15: 227-32.
8. Mogtaderi A, Bakhshipour A, Rashidi H. Validation of Michigan neuropathy screening instrument for diabetic peripheral neuropathy. *Clin Neurol Neurosurg* 2006; 108: 477-81.
9. Halprin KM, Ohkawara A. Glucose entry into the human epidermis: the concentration of glucose in the human epidermis. *J Invest Dermatol* 1967;49: 559 – 60.
10. Chiheb S, Khadir K, Jarmouni R. Cutaneous manifestations of diabetes mellitus. *Nouvelles Dermatologiques* 2002;21: 64-7.
11. Boulton AJ, Vileikyte L. The diabetic foot: The scope of the problem. *J Fam Pract* 2000; 49(supp): S3-S8.
12. Borssen B, Bergenheim T, Lithner F, et al. The epidemiology of foot lesions in diabetic patients aged 15-50 years. *Diabet Med* 1990; 7: 438-44.
13. Shemer A, Bergman R, Linn S, et al. Diabetic dermopathy and internal complications in diabetes mellitus. *Int J Dermatol* 1998; 37: 113-5.
14. Talat N, Nabeel A, Naveen A, et al. Skin manifestations among diabetic patients admitted in a general medical ward for various other medical problems. *Pak J Sciences* 2002; 18: 291-6.
15. Foss NT, Polon DP, Takada MH, et al. Skin lesions in diabetic patients. *Rev Saude Publica* 2005; 39:1-5.

16. Beisswenger PJ, Moore LL, Curphey TJ, et al. Relationship between glycemia control and collagen-linked advanced glycosylation end products in type I diabetes. *Diabetes Care* 1993; 16 : 689-94.
17. Diris N, Colomb M, Leymarie F, et al. [Non infectious skin conditions associated with diabetes mellitus: a prospective study of 308 cases] . *Ann Dermatol Venereol* 2003;130 :1009-14.
18. Danowski TS, Sabeh Co, Sarver ME, et al. Shin spots and diabetes mellitus. *Am J Med Sci* 1966; 251: 570-5.
19. Bouguerra R, Essais O, Sebai N, Ben Salem L. Prevalence and clinical aspects of superficial mycosis in hospitalized diabetic patients in Tunisia. *Med Mal Infect* 2004; 34:201-5.
20. Rayfield EJ, Ault MJ, Keusch GT, et al. Infection and diabetes: the case for glucose control. *Am J Med* 1982; 72:439.