Skin lesions in diabetic patients

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Keywords
Skin diseases. Dermatomycoses. Diabetes mellitus. Metabolic control.

Abstract

Objective
It is yet unknown the relationship between diabetes and determinants or triggering factors of skin lesions in diabetic patients. The purpose of the present study was to investigate the presence of unreported skin lesions in diabetic patients and their relationship with metabolic control of diabetes.

Methods
A total of 403 diabetic patients, 31% type 1 and 69% type 2, underwent dermatological examination in an outpatient clinic of a university hospital. The endocrine-metabolic evaluation was carried out by an endocrinologist followed by the dermatological evaluation by a dermatologist. The metabolic control of 136 patients was evaluated using glycated hemoglobin.

Results
High number of dermophytosis (82.6%) followed by different types of skin lesions such as acne and actinic degeneration (66.7%), pyoderma (5%), cutaneous tumors (3%) and necrobiosis lipoidic (1%) were found. Among the most common skin lesions in diabetic patients, confirmed by histopathology, there were seen necrobiosis lipoidic (2 cases, 0.4%), diabetic dermopathy (5 cases, 1.2%) and foot ulcerations (3 cases, 0.7%). Glycated hemoglobin was 7.2% in both type 1 and 2 patients with adequate metabolic control and 11.9% and 12.7% in type 1 and 2 diabetic patients, respectively, with inadequate metabolic controls. A higher prevalence of dermatophytoses was seen in the both groups with inadequate metabolic control.

Conclusions
The results showed a high prevalence of skin lesions in diabetic patients, especially dermatophytoses. Thus, poor metabolic control of diabetes increases patient's susceptibility to skin infections.

INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome of chronic and degenerative course caused by a disorder in insulin secretion and/or action which results in metabolic changes, especially high blood glucose.[12] Based on its etiopatogenic and pathophysiological mechanisms, this condition is classified into type 1 DM and type 2 DM.

Type 1 DM is usually an autoimmune disorder characterized by the production of autoantibody against ß-cells of Langerhans islets, which in turn leads to reduced insulin production. DM develops in genetically susceptible individuals and could be associated to several environment factors.[8] Conversely, type 2 DM has a different pathogenic mechanism and chronic high blood glucose predominantly results from resistant target cells (muscle, fat and liver cells)

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Received on 21/10/2004. Approved on 11/3/2005.

to the action of circulating insulin. Type 2 DM is often associated to quantitative and qualitative deficiency of insulin secretion for maintaining normal blood glucose.[4]

It is described high incidence of infections in both DM types. Infections in DM patients have a more severe clinical course and are one of the most commonly seen chronic complications of DM.[15] The causes of increased infection susceptibility in these patients are not yet clear. Previous studies have suggested a possible immune response abnormality specific to DM patients[5] but have also pointed out to the role of macro and microangiopathy and/or diabetic neuropathy.[13]

Understanding the pathophysiological mechanisms involved in chronic DM complications is key as they constitute compromising factors to patients' quality of life resulting in significant increased disease burden and mortality. Multicentric studies as the Diabetes Control and Complication Trial (DCCT)[6] and the United Kingdom Prospective Diabetes Study (UKPDS)[19,20] have shown metabolic control as an important factor for preventing chronic complications.

It is known that chronic high blood glucose contributes for the development of chronic complications by inducing non-enzymatic glycation of proteins.[2] The end-products are first reversible but, due to chronic high blood glucose, some proteins of vessel walls undergo significant changes compromising the local tissue.[7] This process can involve, for instance, endothelial and collagen proteins, leading to increased infection susceptibility. The higher blood glucose, the greater the deposit of glycated metabolites.

Besides the metabolic change, other factors favoring increased infections in DM patients should be mentioned. Among them, chronic vascular and neurological complications, and impaired immune response mostly characterized by reduced neutrophil chemotaxis and phagocytosis in DM compared to non-DM individuals. Epithelial and mucosa cells of DM patients have also been described as having increased adhesion of pathogens such as *Candida albicans* in oral and vaginal mucosa cells and *Escherichia coli* in urinary epithelial cells.[17]

Given DM patients' susceptibility to infections, the present study aimed at investigating the occurrence of skin lesions in these patients, even if they did not specifically report any lesions.

METHODS

A total of 403 patients seen at the outpatient clinic of a university hospital in the city of Ribeirão Preto, Brazil, in 2000, were studied. Of them, 31% were type 1 and 69% were type 2 DM patients, most were white (70.3%) females (65.3%) and had a mean age of 19.9±2.3 and 63.1±3.4 years old respectively. The study patients were examined by an endocrinologist for a metabolic evaluation and then were seen by a dermatologist who conducted a dermatological evaluation. DM metabolic control was documented in 136 patients by measuring their levels of glycated hemoglobin using ion-exchange chromatography.[18] Glycated hemoglobin below 8% was considered as an adequate control and values above 8% as an inadequate control.

Statistical analyses were carried out using the parametric Student's t-test at 5% significance level.[16]

RESULTS

The dermatological evaluations showed skin lesions in most patients, though they hadn't been reported before in the visits. There were identified 1,198 skin lesions, about three to four (mean=3.7) lesions per patient. The prevailing skin lesions were dermatophytoses (82.6%), followed by a group of skin conditions such as acne (4.7%), actinic degeneration, which comprised actinic, solar and seborrheic keratoses, solar melanosis and poikiloderma (62.0%), pyodermites (5%), malign skin tumors (3%) and necrobiosis

Table 1 - Occurrence of skin lesions in diabetes mellitus patients seen at a university hospital. Ribeirão Preto, Brazil, 2000.

Skin lesions	Cases (N=403)	%
Acne	19	4.7
Acanthosis nigricans	24	5.9
Alopecia	11	2.7
Candidiasis	52	12.9
Follicular keratosis	12	2.9
Scar	51	12.6
Epidermal cyst	7	1.7
Actinic degeneration	250	62.0
Atopic dermatitis	27	6.6
Dermatophytosis	333	82.6
Diabetic dermopathy	5	1.2
Eczema	24	5.9
Scabies	5	1.2
Hyperkeratosis	35	8.6
Guttate leukoderma	5	1.2
Vascular lesions	17	4.2
Lesions secondary to metabolic conditions	11	2.7
Foot ulceration	3	0.7
Hanseniasis	5	1.2
Necrobiosis lipoidica	2	0.4
Skin xerosis	84	20.8
Prurigos	25	6.2
Pyodermitis	19	4.7
Pityriasis versicolor	21	5.2
Benign skin tumors	95	23.5
Malign skin tumors	11	2.7
Verruga vulgar	20	4.9
Others	25	6.2
Total	1,198	

Table 2 - Clinical characteristics of diabetes mellitus (DM) patients according to metabolic control. Ribeirão Preto, Brazil, 2000.

Metabolic control	Type 1 DM patients		Type 2 DM patients	
	A	IN	A	IN
No. patients (%)	4 (14%)	24 (86%)	20 (17.6%)	88 (82.4%)
Age (years)	23.7	20.3	58.5	58.3
Gender	3 F/1 M	14 F/10 M	16 F/4 M	60 F/28 M
Disease course (years)	12.7	9.6	11.9	13
Glycated hemoglobin (%)	7.2	11.9	7.2	12.7

F: Female; M: Male; A: Adequate; IN: Inadequate

lipoidica (0.4%). Only 19% of the patients studied did not show any skin lesions, as shown in Table 1.

Of all dermatophytoses, 42.6% were onychomycoses (n=172) and 29.2% were tinea pedis (n=118). The association of different tineas (*tinea pedis* and *cruris* or *tinea pedis*, *corporis* and *cruris*) was seen in 30 patients, 9% of all cases of dermatophytoses. Interdigital candidiasis was found in 13% (n=52) and pityriasis versicolor in 5.2% (n=21). There were 19 cases (5%) of pyodermites with no previous reporting, among them folliculites, furuncles, ecthyma and even two cases of erysipela, one of them in an early phase without treatment.

Both type 1 and type 2 DM patients had skin infections such as pyodermites and superficial mycoses. Acne cases were exclusively found among type 1 DM patients. Skin tumors, such as basocellular epithelioma, were identified only in type 2 DM patients, whether or not associated with elastosis.

Acanthosis nigricans was identified in 6% (n=24) of cases. This is an interesting finding, since these lesions had been unnoticed before. However, conditions more commonly seen in DM patients, such as diabetic dermopathy and necrobiosis lipoidica *diabeticorum*, were rare. Only two cases of necrobiosis (0.4%), five cases of diabetic dermopathy (1.2%) and three cases of foot ulcerations (0.7%) were confirmed in the histopathology exam. Another significant finding was that most DM patients had skin xerosis. Skin xerosis and dermatophytosis; seborrheic keratosis, onychomycosis and xerosis; and juvenile acne and *tinea pedis* were the most common concomitant lesions.

Of 136 DM patients metabolically evaluated using glycated hemoglobin, 28 (20.6%) were type 1 and 108 (79.4%) type 2. Among type 1 DM patients, 14% had adequate metabolic control, while 17% of type 2 DM patients had glycated hemoglobin below 8% (Table 2).

Among type 1 DM patients, mean age was 23.7 years in those with adequate metabolic control and 20.3 years in those with inadequate metabolic control. Among type 2 DM patients, mean age was about 58 years in the whole group regardless of their metabolic control. Glycated hemoglobin was on average 7.2% in those with adequate metabolic control in both type 1 and 2 DM patients and 11.9% in type 1 and 12.7% in type 2 DM patients with inadequate metabolic control (Table 2). No statistical significant differences were found for age and DM course in both adequate and inadequate metabolic control groups for type 1 as well as type 2 DM patients.

However, when patients were grouped according to their metabolic control, those with adequate control had mostly xerosis (25%), followed by seborrheic keratosis (20.8%), solar elastosis (20.8%), dermatophytosis (12.5%), seborrheic dermatitis (12.5%) and acanthosis nigricans (4.2%), while those with inadequate metabolic control had mostly dermatophytosis (55.3%), followed by candidiasis (12.5%), acne (7.2%), seborrheic keratosis (6.2%), acanthosis nigricans (5.4%), solar elastosis (5.4 %), seborrheic dermatitis (4.4%) and xerosis (3.6%) (Table 3).

DISCUSSION

The study findings showed high occurrence (81%) of several different skin lesions in DM patients. Some of them were chronic well-defined lesions which had not been reported before and were only detected in the dermatological examination. The occurrence of more than one lesion per patient corroborates Bub & Olerud[3] findings when they verified that almost all DM patients had skin lesions. Hence, DM patients should undergo careful skin examination.

Among skin lesions identified, it has also been noted 82.6% of dermatophytoses and 42.6% fungal ony-

Table 3 - Distribution of skin lesions among diabetes mellitus patients with adequate and inadequate metabolic control. Ribeirão Preto, Brazil, 2000.

Skin lesions	Metabolic control	
	Adequate %	Inadequate %
Dermatophytosis	12.5	55.3
Candidiasis	4.2	12.5
Skin xerosis	25	3.6
Solar elastosis	20.8	5.4
Seborrheic keratosis	20.8	6.2
Seborrheic dermatitis	12.5	4.4
Acanthosis nigricans	4.2	5.4
Juvenile acne	ND	7.2
Total	100.0 (n=24)	100.0 (n=112)

ND: Not detected

chomycoses. About 10% of all fungal lesions were asymptomatic cases of *tinea corporis* and *cruris*, which corroborates Lugo-Somolinos & Sanches[11] findings. Superficial mycoses (*tineas*) are known to cause pruritus[17] and its absence could suggest a compromised response in DM patients. It might be due to impaired superficial innervations caused by diabetic neuropathy, a condition that predisposes infections and traumas.[1]

Another contributing factor to skin lesions is the presence of macro and microangiopathy seen in DM patients. They cause vascular alterations with increased permeability and reduced vascular response to sympathetic nerve stimuli leading to a reduced ability to respond to thermal stress and/or local hypoxy.[3]

Besides, to colonize a keratin-covered skin, fungal agents need to cross a natural barrier created by corneal layer, which requires, among others, overcoming the fungistatic action of fatty acids produced by keratin cells.[14] Thus, epidermis invasion by spores occurs when this natural barrier is compromised and deeper epidermal layers are not able to activate the immune response against infections, as both mechanisms are impaired in the skin of DM patients.[3]

In addition to the significant number of dermatophytoses, exfoliating, thickened dry skin – a condition known as cutaneous xerosis – was the most frequent condition seen in the patients studied. Skin xerosis was either an isolated condition (21%) or associated to other skin lesions (64%). This condition is probably derived from an increased production and accumulation of free radicals or advanced glycosylation end-products (AGE), in excess in the skin of DM patients.[3] In fact, high blood glucose or high levels of other hexoses, pentoses and their phosphorilated derivatives seen in DM result in increased production of Amadori products which act as precursors in AGE production.[2] The occurrence of skin xerosis can be associated to metabolic changes that lead to AGE production, and even to the metabolic control. High blood glucose leads to non-enzymatic glycosylation of these glycated products, which are directly associated to the level of DM metabolic control.

These findings were seen in type 1 DM patients with adequate metabolic control, of which 41% did not have any skin lesions. However, among those of same age and disease course but with inadequate metabolic control, skin infections and acanthosis nigricans were more prevalent. In this group, only 6% of patients with inadequate metabolic control did not have any skin lesions.

It is also worth highlighting that, in type 1 DM patients, seborrheic keratosis (13%) was the skin lesion most commonly seen among patients aged over 50. This suggests that disease progress associated to the production of glycation products would facilitate the occurrence of these lesions.[7]

Among type 2 DM patients, skin infections, such as dermatophytosis and candidiasis, were more common compared to seborrheic and actinic keratosis. Similarly, those with inadequate metabolic control had considerably more dermatophytoses and skin candidiasis than those with adequate metabolic control. This is in agreement to Gupta et al[9] findings, showing a 26% frequency of onychomycoses in both type 1 and 2 DM patients, about one-third of all patients.

While no association between lesion frequency and DM course was found, a higher frequency of lesions, such as solar elastosis, were found to be associated to aging processes and skin deterioration in older age groups. Lesions such as acne were more common in younger age groups.

The study findings suggest that DM potentially enhances skin aging processes, as shown in Table 3. High solar elastosis and seborrheic keratosis were seen in type 2 DM patients and a significant frequency of seborrheic keratosis was found in type 1 DM patients, a group comprising mostly young patients (mean age: 20 years old), regardless of their metabolic control. Also, increased skin infections, both fungal and bacterial, were detected among type 1 and type 2 DM patients with inadequate metabolic control. This finding indicates that inadequate metabolic control renders DM patients more susceptible to skin infections. Furthermore, it could become more severe, aggravating these patients' metabolic imbalance and compromising their general condition.[10]

In conclusion, careful dermatological examination and outpatient follow-up of DM patients is required to provide them adequate treatment of their skin conditions and thus eliminate factors which could render it more difficult to manage their disease.

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