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PREVALENCE AND RISK OF APPEARENCE OF SKIN LESIONS CONSIDERED TO BE CUTANEOUS MARKERS OF DIABETES IN A POPULATION GROUP IN BIHOR COUNTY

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Abstract

Objectives: *The aim of the study was to calculate the prevalence rates and risk of appearance of cutaneous lesions in diabetic patients with both type-1 and type-2 diabetes.* ***Material and Method:*** *384 patients were analysed, of which 47 had type-1 diabetes (T1DM), 140 had type-2 diabetes (T2DM) and 197 were non-diabetic controls.* ***Results:*** *The prevalence of the skin lesions considered markers of diabetes was 57.75% in diabetics, in comparison to 8.12% in non-diabetics ($p<0.01$). The risk of skin lesion appearance is over 7 times higher in diabetic patients than in non-diabetics. In type-1 diabetes the prevalence of skin lesions was significantly higher than in type-2 diabetes, and the risk of skin lesion appearance is almost 1.5 times higher in type-1 diabetes than type-2 diabetes compared to non-diabetic controls.* ***Conclusions:*** *The diabetic patients are more susceptible than non-diabetics to develop specific skin diseases. Patients with type-1 diabetes are more affected.*

key words: *cutaneous markers, diabetes, prevalence*

Introduction

Diabetes is an extremely important pathological state, particularly regarding it's prevalence, it's negative impact on the patient's lifespan and quality of life, and of course, the very high costs involved in patient care. Recent data point out an extremely important diabetes prevalence increase at a worldwide level [1].

It is not surprising that diabetes, which affects the entire organism, has very important manifestations in the largest organ of the human body, the skin. As a matter of fact, in 1935 (pre-antibiotic era), Joslin noted that 31% of diabetics presented with skin disease symptoms in relation with diabetes [2].

Almost all the articles that deal with this subject state that 28-30% of patients with diabetes present with skin disorders throughout it's evolution period.

There are many skin conditions to note in diabetes mellitus, some of which can actually appear before the diagnosis of diabetes itself, can signal the disease's presence or can appear at a later date together with metabolic

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abnormalities induced by diabetes (mostly non-enzymatic and enzymatic glycosylation, essential and irreversible processes that affect many structural proteins) [3].

According to current data, necrobiosis lipoidica – the best known cutaneous marker of diabetes, and first described by Oppenheim – is a relatively rare cutaneous condition even in diabetes, with a prevalence of 0.3-0.7% in diabetic patients with optimal glycemic control. At the same time it is a pretty rare skin manifestation in non-diabetic patients [4].

Granuloma annulare, described by Fox in 1895, due to the fact that it's difficult to distinguish from necrobiosis lipoidica, has a reported prevalence (that we consider to be relative) of 0.2-0.5% in patients with optimal glycemic balance [5, 6]. A report by J.E. Jelinek and collaborators points out to the visceral extension (kidney, retina) of granuloma annulare in diabetes associated with polyendocrine diseases [7]. The authors rise the hypothesis of a common autoimmune pathogenic background that involves the conjunctive structures, both vascular and visceral.

Diabetes thick skin (including diabetic hand syndrome) is a condition described from 1970 by Rosenbloom, appearing in 60% of diabetic males younger than 50 years and 29% of diabetic women of the same age [7]. This tegumentary condition is also described in non-diabetic patients.

Diabetic thick skin syndrome includes fibroproliferative complications of the diabetic hand (Dupuytren's contractures), tenosynovitis, Garrod's plantar syndrome and carpal tunnel syndrome [8].

Recent studies communicate the presence of thick skin manifestation in 22-40% of type 1 diabetes (T1DM) adults and 51% of T1DM children. Prevalence in non-insulin-dependent diabetic patients is placed between 4% and 70% [9].

Scleroderma diabeticorum is viewed as a pretty rare disease, with a prevalence not higher than 2.5% [10].

In 1976, Kalan and collaborators indicated the association between acanthosis nigricans and insulin-resistance syndrome, even if the prevalence of this association is not significant, around 0.6%-0.9% [11].

The association of diabetes with vitiligo was also reported, with recent studies estimating a 2% prevalence in T1DM patients and 5% in T2DM patients.

All these facts warrant questions regarding aspects that are so far insufficiently known in Romania and were at the base of elaborating this study.

The aim of the study was to calculate the prevalence rates and risk of appearance of cutaneous lesions in diabetic patients with both T1DM and T2DM.

Material and Method

384 patients were analysed, of which 47 had type-1 diabetes, 140 had type-2 diabetes and 197 were non-diabetic controls. Patients were followed at the Clinical Center for Diabetes, Nutrition and Metabolic Disease of the Emergency Clinical County Hospital and Department of Dermatology in Oradea, Romania, all of them having a diabetes duration of at least 5 years, while the non-diabetic patients were followed in the Internal Medicine Department of the same hospital.

The statistical analysis was undertaken using the application EpiInfo version 6.0, program belonging to the Center of Disease

Control and Prevention in Atlanta, adapted for medical statistics. Significance was tested by χ^2 method. A p value < 0.05 was considered significant.

We also calculate the relative risk (RR) - the ratio of the chance of a disease developing among members of a group exposed (diabetics, respectively T1DM) to a factor compared with a similar group not exposed (nondiabetics, respectively T2DM) to the factor.

Demographic characteristics of the study group are given in Table 1.

Table 1. Study group characteristics.

Parameters	**Diabetics**	**T1DM**	**T2DM**	**Nondiabetics**
Females	50.27	48.94	50.71	50.76
Average Age (years)	52.46±13.56	45.96±15.60	54.64±12.62	51.19±16.21
Average duration of DM (years)	14.56±3.14	11.61±3.85	15.14±4.22	_

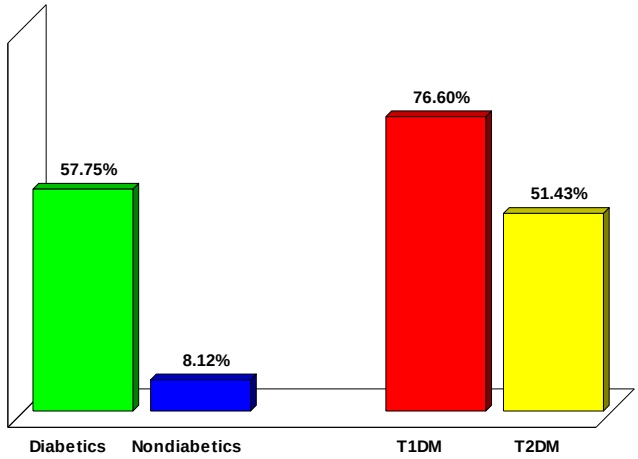

Figure 1. Prevalence of cutaneous lesions in diabetics compared to non-diabetics and type-1 diabetes compared to type-2 diabetes.

Results

The prevalence of skin lesions (Table 2 and Figure 1) was 57.75% in diabetics, in comparison to 8.12% in non-diabetics (p<0.01).

The risk of skin lesion appearance is over 7 times higher in diabetic patients than non-diabetics (RR=7.1). If we eliminate cutaneous lesions specific to diabetes (scleroderma diebeticorum and diabetes thick skin), the risk of skin lesion appearance is 3 times higher in diabetics than in non-diabetics (RR=3.4).

In T1DM, the prevalence of skin lesions was 76.60%, significantly higher (p<0.01). than in T2DM (51.43%).

The risk of skin lesion appearance is almost 1.5 times higher in T1DM than T2DM (RR=1.5).

The skin lesions which are specific to diabetes, scleroderma diabeticorum and diabetes thick skin had a prevalence of 18.18% and 12.30% respectively (Table 2 and Figure 2).

Table 2. Skin lesion prevalence.

	Diabetics (n=187)		T1DM (n=47)		T2DM (n=140)		Nondiabetics (n=197)	
	No.	%	No.	%	No.	%	No.	%
Dupuytren's disease	29	15.51	8	17.02	21	15.00	11	5.58
Necrobiosis lipoidica	3	1.60	1	2.13	2	1.43	2	1.02
Granuloma annulare	5	2.67	3	6.38	2	1.43	–	–
Scleroderma diabeticorum	34	18.18	12	25.53	22	15.71	–	–
Diabetes thick skin	23	12.30	6	12.77	17	12.14	–	–
Acanthosis nigricans	1	0.53	1	2.13	0	0.00	–	–
Vitiligo	13	6.95	5	10.64	8	5.71	3	1.52
Total	108	57.75	36	76.60	72	51.43	16	8.12

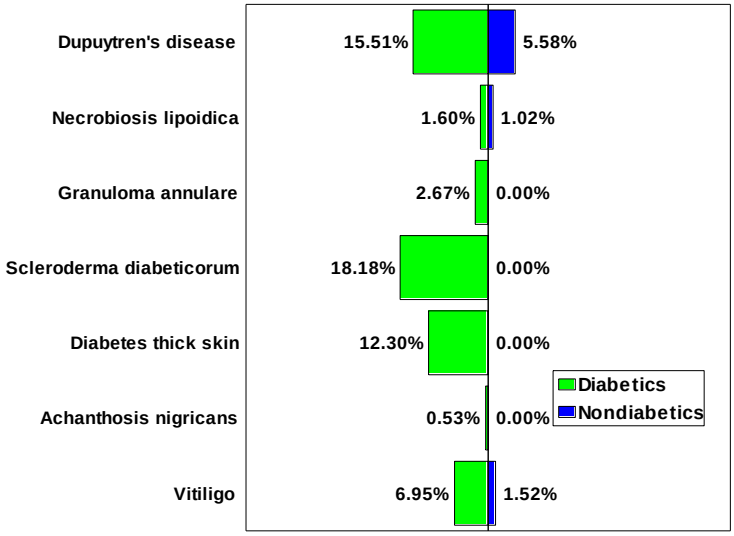

Figure 2. Prevalence of specific cutaneous lesions in diabetics compared to non-diabetics.

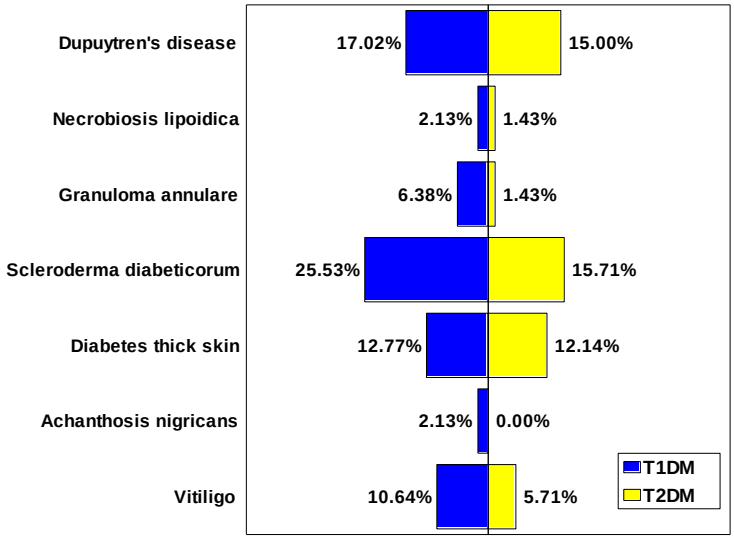

Figure 3. Prevalence of cutaneous lesions in type-1 diabetes compared to type-2 diabetes.

Dupuytren's disease had a prevalence of 15.51% in diabetics and 5.58% in non-diabetics ($p<0.01$), with a risk over 2.5 times higher in diabetics than in non-diabetics (RR=2.8).

Necrobiosis lipoidica had a prevalence of 1.60% in diabetics in comparison to 1.02% in non-diabetics, with a risk over 1.5 times higher in diabetics than in non-diabetics (RR=1.6, $p<0.01$).

Granuloma annulare and acanthosis nigricans were encountered only in diabetic patients, having a prevalence of 2.67% and 0.53% respectively.

Vitiligo had a prevalence of 6.95% in diabetics and 1.52% in non-diabetics, with a risk over 4.5 times higher in diabetics than in non-diabetics (RR=4.7, $p<0.01$).

The prevalence of specific skin conditions in T1DM compared to T2DM patients is given in Figure 3.

Dupuytren's disease had a prevalence of 17.02% in T1DM patients and a prevalence of 15.00% in T2DM patients, with a relative risk of 1.1, indicating a non-significant risk difference ($p=0.59$).

Necrobiosis lipoidica had a prevalence of 2.13% in T1DM patients and a prevalence of 1.43% in T2DM patients, resulting in a risk 1.5 times higher in T1DM patients than T2DM (RR=1.480 ; $p=0.052$).

Granuloma annulare had a prevalence rate of 6.38% in T1DM patients and a prevalence of 1.43% in T2DM patients, resulting in a risk 4.5 times higher in T1DM patients than T2DM patients (RR=4.5, $p<0.01$).

A similar prevalence of diabetes thick skin was found in T1DM and T2DM: 12.77% and 12.14% respectively ($p=0.847$).

Surprisingly, acanthosis nigricans was found in only one T1DM patient (2.13%).

Vitiligo had a prevalence of 10.64% in T1DM patients and 5.71% in T2DM patients, resulting in a risk almost 2 times higher in T1DM patients than T2DM patients (RR=1.9, $p=0.034$).

Discussions and Conclusions

The studies on skin lesions considered to be cutaneous markers of diabetes are quite few, and some diseases are underreported.

In our study, the patients with diabetes present with a risk of cutaneous lesions appearance over 7 times higher than non-diabetic patients (RR=7.1). Skin lesions considered to be cutaneous markers of diabetes like Dupuytren's disease, necrobiosis lipoidica, granuloma annulare, scleroderma diabeticorum, acanthosis nigricans and vitiligo had a prevalence significantly higher in diabetic patients than in non-diabetics. In all cases, in T1DM patients the prevalence of skin lesions was significantly higher than in T2DM patients and the risk of skin lesion appearance was almost 1.5 times higher in T1DM than T2DM.

For every investigated skin condition the prevalence in our study was higher than the prevalence reported by other studies, probably due to a poor metabolic control.

In conclusion, although our study was performed on a rather small number of cases, we want to add an additional argument to the theory according to which these skin lesions can represent cutaneous markers of the presence and of the evolutivity of both T1DM and T2DM.

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