Original Article

Cutaneous manifestations of diabetes mellitus

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Abstract

Background Diabetes is a common disease with a variety of skin manifestations encountered by dermatologists, Skin and diabetes may be linked by association (e.g. necrobiosis lipoidica); infections (bacterial, viral or fungal); diabetic complications (e.g. neuropathic ulcers or treatment reactions). The skin manifestations of diabetes affect up to two thirds of patients both type I and II diabetes mellitus. Cutaneous manifestations of diabetes occur because of the microvascular complications of diabetes, impaired wound healing, and other yet undetermined mechanisms.

Objective The aim of the present study was to look for major skin findings in patients with diabetes mellitus and to see their clinical correlation.

Patients and methods All patients attending the diabetic clinic during a period of one year from July, 2002 to June, 2003 were examined in detail for cutaneous manifestations of the disease.

Results 162 patients, 92 females and 70 males, were enrolled. The overall prevalence of cutaneous manifestations was 81.5% (80% in type I and 83.4% in type II diabetics). These manifestations were microvascular (n=73), neurological (n=61), infections (n=46), iatrogenic (n=7) and miscellaneous (n=184).

Conclusion Cutaneous manifestations are quite frequent in both types of diabetics. A number of new findings were observed.

Key words Diabetes mellitus, cutaneous manifestations.

Introduction

The term 'diabetes mellitus (DM)' describes several syndromes of abnormal carbohydrate metabolism that are characterized by hyperglycemia. It is associated with a relative or absolute impairment in insulin secretion along with varying degrees of peripheral resistance to the action of insulin.[1] Presently, diabetes mellitus is classified into type I and type II. The majority of patients with type I diabetes have autoimmune destruction of pancreatic beta cells as the underlying cause, have an absolute requirement for insulin therapy and will develop ketoacidosis without treatment. In type II, there is relative insulin deficiency and resistance to insulin. A causal association between glycemic control and the development and progression of the microvascular complications i.e. (retinopathy, nephropathy and neuropathy) of is well-established. By virtue of

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microvascular involvement any system or organ can be affected in DM, thus skin is no exception.

Skin manifestations in diabetes mellitus are common and expressed in numerous forms. If one considers metabolic effects on microcirculation and changes in skin collagen, prevalence approaches 100 percent. Findings range from the presenting manifestations of the disease to signs of long term involvement, from a mild discomfort to indications of serious, even life-threatening problems. For all of these, recognition is the key to treatment and/or prevention. According to various studies, 30%-82% of persons with diabetes mellitus have some types of cutaneous involvement during the course of their chronic disease.[1,2] Although the overall prevalence of cutaneous disorders does not seem to differ between type I and type II DM, type II patients do develop more frequent cutaneous infections, whereas type I patients develop more auto-immune-type cutaneous lesions.[3,4] Cutaneous manifestations generally appear subsequent to the development of the diabetes, but may be the first presenting sign or even precede the diagnosis by many years.[5] The attachment of glucose to protein may result in a profound effect on structure and function of that protein, and account for the clinical manifestations of the disease. It has been suggested that increased cross-slinking of collagen in diabetic patients is responsible for thicker skin.[6,7] Advanced glycosylation end products are probably responsible for the 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.[8] It is obvious that cutaneous lesions are quite common manifestations in diabetic patients, especially in those with long standing disease and dermatologist may be the first physician to detect hidden diabetes in a patient.

Cutaneous findings in DM may be classified into four major groups: (1) skin diseases with strong to weak association with DM, such as necrobiosis lipoidica (NL), diabetic dermopathy and diabetic bullae; (2) cutaneous infections; (3) cutaneous manifestations of diabetic complications; such as neuropathic foot ulcers; and (4) skin reactions to diabetic treatment.[1]

The present study was aimed to see the prevalence of cutaneous manifestations in diabetic patients reporting to medical outdoor of Pakistan Air Force Hospital, Sargodha and to look for their clinical correlation with diabetes mellitus.

Patients and methods

A total of 162 patients of any age, both sexes and having either type of diabetes reporting in diabetic clinic of P AF Hospital Sargodha, from July 2002 to June 2003, were included in the study. Majority of them were serving or retired persons of Pakistan Air Force and their families. Civilians belonging to adjacent urban as well as rural area were also included. A thorough medical history was taken and detailed clinical examination was carried out in each case, especially taking into account the duration of illness, dietary control, height and weight of the patient, associated illnesses, and treatment record of the patients. Blood pressure and random blood sugar readings

were recorded on three visits and average of these was noted. According to the duration of disease, the patients were categorized into three groups; group 1: patients having DM for less than 5 years; group 2: with 5-10 years duration; and group 3: those having DM for more than 10 years e. After proper documentation, all of these patients were referred to consultant dermatologist in the same hospital who carried out a detailed dermatological survey and recorded cutaneous findings present in the patients at that time. These findings were later categorized into different groups based on possible etiopathogenesis, like infections, microvascular, neurological, drug reactions and miscellaneous. Important cutaneous lesions were also photographed.

Data were analyzed in computer software programme SPSS-8 and frequencies of occurrence of various cutaneous manifestations were obtained.

Results

Patients included in the study belonged to heterogeneous group of population. There were 92 females and 70 males. Age ranged from 2-75 years (mean=50.6 years). Duration of illness was 2 months to 29 years (60 patients had disease of 5 years duration, 48 for 5-10 years and 54 for more than 10 years). 36 patients had type I DM, while 126 had type II disease. Out of 162 patients, 30 (22 females and 8 males) did not have any dermatological findings. Rest of them revealed a wide spectrum of cutaneous signs. A total of 58 skin manifestations were classified into various categories, e.g. microvascular, neurological/neurovascular, infections, treatment related and miscellaneous. Each category was further evaluated to see the frequency of occurrence of individual finding (**Tables 1-5**). The prevalence was 80% in group 1, 81.5% in group 2, and 83.4% in group 3. Cutaneous lesions were seen in 80% of type I and 83.4% of type II diabetics. The overall prevalence was 81.5%.

Table 1 Microvascular manifestations seen in patients of diabetes mellitus

Dermatologic findings	*n (%)*
Shin spots	26 (15.3)
Sclerosis fingers	18 (10.6)
Rubeosis faciei	12 (7.1)
Palmar erythema	7 (4.1)
Diabetic hands	4 (2.4)
Ecchymoses	2 (1.2)
Pigmented purpuric dermatosis	2 (1.2)
Granuloma annulare	1 (0.6)
Necrobiosis lipoidica diabeticorum	1 (0.6)

Table 2 Neurological manifestations seen in patients of diabetes mellitus.

Dermatological findings	*n (%)*
Paresthesia	34 (20)
Hyperhidrosis face	10 (5.9)
Generalized hyperhidrosis	6 (3.5)
Diabetic bullae	6 (3.5)
Diabetic feet	5 (2.9)

Table 3 Cutaneous infections seen in patients of diabetes mellitus

Dermatological Findings	*n (%)*
Onychomycosis	21 (12.4)
Tinea pedis	10 (5.9)
Cellulitis	5 (2.9)
Furunculosis	4 (2.4)
Herpes zoster	3 (1.8)
Folliculitis	2 (1.2)
Mucormycosis	1 (0.6)

Table 4 Cutaneous complications of treatment seen in patients of diabetes mellitus

Dermatological Findings	*n (%)*
Lipodystrophy	4 (2.4)
Chronic urticaria	3 (1.8)

Discussion

A broad spectrum of cutaneous disorders

Table 5 List of miscellaneous cutaneous manifestations seen in patients of diabetes mellitus

Dermatological findings	*n (%)*
Acquired ichthyosis	37 (22.4)
Generalized pruritus	16 (9.4)
Alopecia legs	12 (7.1)
Intertrigo	11 (6.5)
Pruritus vulvae	11 (6.5)
Post inflammatory hyperpigmentation	10 (5.9)
Calossities	9 (5.3)
Chronic eczema	8 (4.7)
Hyperkeratosis feet	8 (8.1)
Xerosis	6 (3.5)
Acrokeratoelastoidalis	6 (3.5)
Dupuytren's contracture	6 (3.5)
Dry palms	6 (3.5)
Skin tags	5 (2.9)
Melasma	3 (1.8)
Miliaria rubra	2 (1.2)
Seborrheic keratosis	2 (1.2)
Dyschromia	2 (1.2)
Addisonian pigmentation hands & face	2 (1.2)
Geographic tongue	2 (1.2)
Yellow palms	2 (1.2)
Koilonychia	2 (1.2)
Campel de Morgan Spots	2 (1.2)
Papular urticaria	2 (1.2)
Glossitis	2 (1.2)
Keratosis pilaris	1 (0.6)
Postinflammatory hypopigmentation	1 (0.6)
Acrodermatitis enteropathica	1 (0.6)
Hirsutism	1 (0.6)
Atopic dermatitis	1 (0.6)
Gingival hypertrophy	1 (0.6)
Scarring over face (small pox)	1 (0.6)
Androgenic alopecia	1 (0.6)
Longitudinal melanonychia	1 (0.6)
Cicatricial alopecia	1 (0.6)

may be encountered in patients with both type I and type II DM. At times, these dermatologic findings may even precede any clinical or biochemical evidence for diabetes. Some of these dermatoses are so called marker lesions and can predate the manifestation of the diabetes by years. The exact pathogenesis of most of these dermatoses is unknown. It is assumed that vessel and connective tissue alterations as well as the impairment of the immune system and other associated metabolic changes caused by diabetes play an important role in cutaneous manifestations. The main mechanism behind all these changes is thought to be non-enzymatic glycosylation product formation.[6,9] This process occurs to a minor extent at normal blood sugar concentrations and is apparently accelerated in persons with elevated blood sugar levels. This reaction results in changes in the physical and chemical properties of connective tissue and other body proteins. These modified proteins and glycosylation products are responsible for change in colour and texture of skin and various complications seen in DM.[7,10,11] Glycosylation of the red cell membrane is apparently responsible for the stiffness of diabetic erythrocytes.[12] Glycosylation of collagen results in increased stiffness and resistance to enzymatic degradation, mechanical changes of collagen which are also characteristic for aging. At least 30 % of the persons with DM have some type of cutaneous involvement during the course of their chronic disease.1 In various other studies 30% to more than 80% of diabetics were found to have skin signs.[2] The findings of 81.5% overall prevalence (81.5% in type I and 83.4% in type II diabetes), the proportion of two types of diabetics (78.9% type I and 21.1 % type II) in our study are in agreement with various other international and local studies.[2] We tried to find out the

difference in prevalence among patients with disease of variable duration but surprisingly, skin manifestations were found to occur with almost same frequency in all three groups (≤5, 5-10 and >10 years duration groups). Cutaneous findings were apparently more frequent in males (89.5%) as compared to females (76%), but this difference was not significant.

The most frequent manifestations seen were; acquired ichthyosis (22.4%), paresthesia of feet (20%), shin spots (15.3 %), onychomycosis (12.4%), sclerosis of fingers (10.6%) and generalized pruritus (9.4%). Relatively common findings were; alopecia over legs, rubeosis faciei, pruritus vulvae, intertrigo, hyperhidrosis of face, tinea pedis, callosities and diffuse hyperkeratosis of feet. Diabetic foot occurred in about 3% and diabetic hand in 2.4%. Most of the cutaneous markers of diabetes mellitus e.g. necrobiosis lipoidica, diabetic bullae, granuloma annulare, shin spots (diabetic dermopathy) and acanthosis nigricans, were encountered in our study but we did not observe any patient with lichen planus, acquired perforating disorder, vitiligo and xanthomas as seen in other studies.

Cutaneous infections have been reported in 20%-50% of diabetics in earlier studies but we encountered skin infections, especially bacterial, less frequently in our study. The likely cause of this reduction may be the better awareness, good hygiene and prompt management on the part of our patients. One of our patients was diagnosed with mucormycosis of nose and nasal sinuses, which is an extremely rare form of deep fungal infection, but has an established association with diabetes mellitus.

Skin manifestations due to diabetic complications were frequently observed. Paresthesia due to peripheral neuropathy and hyperhidrosis due to autonomic neuropathy were most common. Diabetic foot secondary to neuropathy, vasculopathy and poor wound healing was also seen. We also encountered skin reactions like lipodystrophy and chronic urticaria arising from diabetic treatment (insulin and oral hypoglycemics, respectively).

Some of the uncommon findings seen in our study like Duputyren's contracture, dry palms, yellow palms, palmar erythema, pigmented purpuric dermatosis, xerosis and skin tags have also been described previously. Other rare findings like atopic dermatitis, chronic eczema, ecchymosis, glossitis, seborrheic keratosis, melanonychia, koilonychia, androgenic alopecia, cicatricial alopecia, hirs1tism, melasma, herpes zoster, addisonian pigmentation, keratosis pilaris, miliaria rubra and papular urticaria seen in this study are probably a chance occurrence, as these are not clearly associated with DM. A two-year-old female child was having acrodermatitis enteropathica and type I diabetes for the last six months. This could probably a new association.

Conclusion

In the diabetic patient, it is important to be familiar with and to look for the possible cutaneous alterations, which have to be diagnosed on mainly clinical grounds. Some of these can be a consequence or an accompanying symptom of poorly controlled diabetes and therefore these can potentially help the attending physician to prevent more serious complications. A large

number of new cutaneous findings are being observed in patients of diabetes mellitus and further large scale multicentre studies are needed to establish these new associations.

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